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Abstracts

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Keynote Speaker Abstracts

Introduction à la Conférence Internationale “Nice WALT 2018” (12ème Congrès de la “World Association for Laser Therapy and Photobiomodulation”)

Prof. Rene-Jean Bensadoun
WALT 2018 Congress Chairman

La thérapie par laser de faible energie (LLLT) [aujourd’hui appelée Photobiomodulation (ou PBM)] est devenue ces dernières années l’un des domaines de la médecine à la croissance la plus rapide.

A l’origine considérée comme « sequestrée » dans l’arène de la «médecine alternative et complémentaire», la PBM a vécu une sorte de rupture.

Les raisons de ce changement remarquable dans la perception par la profession médicale et le grand public sont intéressantes à considérer.

Premièrement, nous avons bénéficié de progrès substantiels dans la compréhension des mécanismes d’action sous-jacents. Nous n’en sommes plus à des commentaires vagues sur les « cellules qui se nourrissent de lumière», d’une manière analogue à la photosynthèse dans le règne végétal. Maintenant nous comprenons les mécanismes moléculaires de l’absorption des photons, nous connaissons les organelles subcellulaires qui réagissent à la lumière, et apprécions certaines des voies de signalisation et les facteurs de transcription activés, ainsi que les réponses tissulaires incluant l’activation et la mobilisation des cellules souches.

Le deuxième grand changement a été la prise de conscience que nous n’avons pas nécessairement besoin de “lasers” pour réaliser la PBM, les LEDs sont aussi efficaces si leur qualité se rapproche de celle des lasers. Autrefois, une grande partie de la thérapie « laser de basse énergie » était pratiquée par des thérapeutes de diverses spécialités, et était considérée comme une technique pour laquelle une formation importante était requise. Cela était raisonnable compte tenu des préoccupations réelles concernant la sécurité des yeux au laser et la protection contre d’autres dangers possibles.

Aujourd’hui, l’utilisation de diodes électroluminescentes (LED) a changé la donne, ces appareils sont même facilement disponibles sur les sites Web d’achat en ligne… Mais certaines connaissances soient encore nécessaires pour comprendre les meilleurs paramètres à utiliser pour chaque indication et le danger d’une utilisation large et sans contrôle est réel…

Troisièmement, nous sommes de plus en plus conscients que la PBM a un large éventail d’effets systémiques et régionaux, en plus des effets locaux qui étaient au départ l’objet principal de l’attention de tous. Comme les matrices de LED ont par définition une large zone d’illumination, des quantités significatives de tissus sont exposées à la lumière, la lumière est aussi absorbée par le sang circulant, dans la peau et les autres tissus exposés à la lumière. La lumière peut ainsi être appliquée aux nerfs et aux ganglions lymphatiques pour donner des effets régionaux.

Quatrièmement, nous avons vu une augmentation impressionnante du nombre d’applications de la PBM dans différents domaines comme la prise en charge des effets secondaires des traitements anti-cancéreux, et dans différents pathologies du système nerveux central. Autour de la triade de ses effets antalgiques, anti-inflammatoires et de cicatrisation des tissus, la PBM est utilisée avec succès dans les mucites et épithélites après radiothérapie ou chimiothérapie, ainsi que dans les nécroses et plaies aiguës ou chroniques, et dans de nombreux secteurs en physiothérapie, gynécologie et rhumatologie. En neurologie, la PBM a été testée à l’origine comme un traitement de l’AVC ischémique aigu. Aujourd’hui sa sphère d’utilisation s’est élargie et elle est utilisée par exemple dans les traumatismes cérébraux aigus ou chroniques. Un certain nombre de maladies neurodégénératives chroniques, y compris la maladie d’Alzheimer et la maladie de Parkinson, se sont révélées répondeuses à la PBM. Un large éventail de troubles psychiatriques, y compris la dépression, l’anxiété, le stress post-traumatique et les troubles autistiques ont été jugés susceptibles d’être traités par PBM.

Cinquièmement, nous commençons à voir des progrès significatifs dans l'utilisation de la PBM pour l'amélioration de la performance chez les personnes non malades. Le domaine le plus développé de cette application est l'amélioration de la performance musculaire chez les athlètes et les compétiteurs dans un large éventail de sports.

Non seulement la PBM peut augmenter la quantité de travail et de puissance qui peut être produite par les muscles, mais elle peut également augmenter la vitesse de récupération après l'exercice et peut être une aide précieuse dans les programmes d'entraînement. Un domaine moins développé est celui de l'amélioration de la performance cognitive, et l'amélioration de la mémoire et de l'humeur.

Enfin, ceci mérite aussi d'être mentionné, l'utilisation de la PBM pour des améliorations cosmétiques et esthétiques: la stimulation de la repousse des cheveux est une indication maintenant bien établie, et l'amélioration des ridules et des rides du visage est également de plus en plus populaire. L'utilisation de la PBM pour lutter contre l'obésité et l'excès de graisse commence également à décoller. Ces applications traitent de nouveaux problèmes qui déterminent le marché de l'utilisation à domicile des appareils PBM, car les consommateurs sont généralement prêts à consacrer leur revenu disponible à des améliorations esthétiques...

Tous ces progrès sont fortement associés à un énorme développement de la physique de la PBM. Le choix des paramètres PBM corrects est crucial pour l'efficacité de cette méthode de traitement. La dosimétrie de PBM est déterminée par plusieurs paramètres, qui peuvent être subdivisés en deux groupes, les paramètres d'irradiation, "le médicament" (y compris la longueur d'onde, densité de puissance, densité d'énergie, structure d'impulsion) et les paramètres de traitement, "la dose" et sa distribution). En ce qui concerne la longueur d'onde, la PBM utilise principalement des longueurs d'onde au sein d'une fenêtre de lumière, rouge, IR ou NIR entre 600 et 1000 nm. La pénétration tissulaire est maximisée dans la plage IR. Les longueurs d'onde comprises entre 600 et 700 nm (lumière rouge) sont choisies pour le traitement des tissus superficiels, et les longueurs d'onde entre 780 et 1000 nm (lumière NIR) sont choisies pour les tissus plus profonds en raison de leur pénétration plus profonde dans les tissus.

En cancérologie par exemple, la sécurité de ce type de rayonnements (quant au risque hypothétique de développement des cellules cancéreuses) est intimement dépendante de la dosimétrie, de la fiabilité optimale des machines utilisées et de la qualité des paramètres de traitement.

Ce congrès "Nice WALT2018", en présence de la plupart des experts reconnus dans ce domaine, et avec un public international, principalement composé d'étudiants, de cliniciens et de jeunes chercheurs, représente l'approche la plus complète dans le domaine de la PBM qui ait jamais été faite.

Il offre une large couverture des nombreux sujets qui composent cette thérapie médicale: principes de base, mécanismes d'action, dosimétrie, dispositifs médicaux, études in vitro, modèles animaux, applications cliniques en dentisterie, médecine humaine et vétérinaire, et large couverture d'études en cours et d'utilisations cliniques humaines. De plus, nous visons à terminer ce Congrès mondial avec un grand nombre de recommandations internationales et de directives techniques, ainsi que d'un certain nombre de normes cliniques établies dans ce domaine...

When is there enough scientific evidence to implement PBM in clinical settings?

Prof. Jan M. Bjordal
PT, MSc, PhD, University of Bergen

Empirically-based therapies (EBT) have been used in the treatment of musculoskeletal pain for centuries. Photobiomodulation (PBM) is one of the EBTs that has largely been dropped from recommendation in most clinical treatment guidelines.

We have over two decades reviewed the evidence for PBM in several musculoskeletal injuries and disorders. Our conclusions have mostly been split, because PBM can be delivered both with inefficient or efficient doses. A few decades ago, this was a problem because nobody knew what the ranges for effective and ineffective doses were. In the PBM subcategory commonly labeled Low Level Laser Therapy (LLLT), the scientific evidence is particularly strong for effectiveness. There are more than 12,000 published studies registered under the term" low laser therapy" in Pubmed. This includes a vast number of basic science trials that are mapping anti-inflammatory and other beneficial therapeutical mechanisms, comparisons with non-steroidal anti-inflammatory and biophysical penetration studies.

They show that laser light in the red and near-infrared wavelengths, can penetrate the skin barrier and make a difference in tissue metabolism.

In the 250 randomized clinical LLLT studies registered in the PEDro database with moderate to high quality scores, clinical effectiveness can be predicted with a 90% precision by using the WALT LLLT dosage recommendations. Nine years ago, we published a meta-analysis which showed that LLLT was highly effective in neck pain. But implementation has been sparse. It took the FDA the same time before they finally this year admitted that moderate evidence showed short-term effectiveness of LLLT in neck pain (Skelly et al. 2018).

If we take all this back to our initial question, "When is there enough scientific evidence to implement PBM in clinical practice?" then the answer is simple: Right now!

LIGHTSITE I: A Double-Masked, Randomized, Sham-Controlled Study with Photobiomodulation in Dry Age-Related Macular Degeneration Subjects

Dr. Clark E. Tedford

PhD, President and CEO, LumiThera, Inc.

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Introduction:

Dry age-related macular degeneration (AMD) is a prevalent ocular condition that underlies significant visual dysfunction and blindness. Recent evidence suggests that photobiomodulation (PBM) using wavelengths of light in the 500 nm to 1000 nm range improves visual and anatomical impairments observed in ocular disease states. The LIGHTSITE I study evaluated PBM as a new treatment option in dry AMD.

Methods:

Thirty subjects with dry AMD were enrolled into the study and randomized (1:1) into PBM or sham treatment groups. Subjects received PBM or sham treatment with the LumiThera Valeda™ light delivery system (LumiThera, Poulsbo, WA, Valeda™). Device specifications are as follows: wavelengths were 590 nm (average power, 28 mW; power density, 4 mW/cm^2), 660 nm (power, 459 mW; power density, 65 mW/cm^2) and 850 nm (average power, 4 mW; power density, 0.6 mW/cm^2); fluence was 11.9 J/cm^2 and total energy per eye was 84.2 J; area of irradiation was 7.07 cm^2 using a 30 mm (nominal) beam diameter at treatment plane. The 590 and 850 nm wavelengths were pulsed a 3 Hz (71%:29% duty cycle), 660 nm was continuous wave. Device and treatment parameters have been measured and/or calculated from pre-determined specifications. Subjects were treated with the Valeda™ during 9 treatment sessions over 3-4 weeks with a second series initiated 6 months from baseline (BL). Each treatment session was applied locally to the subject's eyes for a total of 250 sec (70 seconds for the 850 nm and 590 nm combined then 180s for the 660 nm) per treatment per eye. This double-masked, randomized, sham-controlled study evaluated changes in clinical (best-corrected visual acuity (BCVA) and contrast sensitivity (CS)) and anatomical (central drusen thickness (CDT) and volume (CDV)) endpoints. Quality of Life (QoL) was also assessed using the Visual Function Questionnaire-25 (VFQ-25).

Conclusion:

Significant improvements in clinical (BCVA and CS) and anatomical (drusen volume and thickness) outcomes were observed following PBM. Beneficial improvements in clinical outcomes following PBM were more robustly seen in subjects with earlier stages of AMD. Repeated treatment of PBM is necessary to maintain benefits. No safety concerns were noted related to the device. These findings support previous reports and demonstrate the utility of PBM in subjects with early dry AMD.

Statements: This study was IRB-approved and conducted in compliance with the protocol, Good Clinical Practice guidelines, Health Canada regulatory requirements and all other applicable regulatory requirements. Patient informed consent was obtained prior to any study-related procedures. Drs. M. Munk, R. Rückert, and M. Walker are LumiThera, Inc. consultants. Drs. S. Markowitz and R. Devenyi are PIs and were partially supported by SBIR NIH/NEI grant # 3R43EY025508-01S1. Drs. C. Tedford, S. Tedford, C. Croissant are employees of LumiThera, Inc.

A Photoceutical approach to Molecular Mechanisms and Clinical Dosimetry for Photobiomodulation Therapy Can 'light' be a drug?

Prof. Praveen R Arany
BDS, MDS, MMSc, PhD, University at Buffalo, NY

To satisfy the definition of an active pharmaceutical agent, a substance must be capable of being absorbed and changing body functions. Our understanding of human vision, vitamin D metabolism and circadian rhythms clearly indicate light is capable of both phenomenon. Photobiomodulation therapy is defined as the use of non-thermal, non-ionizing forms of photonic devices including lasers, LEDs and broad-band light to alleviate pain, inflammation, modulate immune responses and promote wound healing and tissue regeneration. There is tremendous excitement on the breadth and scope of this treatment to significantly impact human health from oral mucositis, dry age-related macular degeneration, wound healing, improving skeletomuscular performance to neurorehabilitation in Alzheimer's, Parkinson's, Multiple Sclerosis and concussions. The ability of PBM therapy to modulate pain and inflammation presents a non-pharmacological, non-invasive clinical modality that can significantly address the ongoing opioid epidemic. There are exciting new studies on the ability of PBM therapy to harness the regenerative potential of endogenous, resident stem cells that are enabling real world delivery of the promise of regenerative medicine. However, a major limitation in the PBM field has been a lack of efficacy and reproducibility. Given the complexity of the light tissue interactions, the low doses utilized for PBM therapy appear to defy conventional linear photobiological processes and demonstrate dynamic, non-linear phenomenon within the quantum realm. Advances in technologies from several parallel fields especially optogenetics, optical imaging, spectroscopy and photodynamic therapy are improving our understanding of these complex light-tissue interactions. It is hence suggested that we pursue a Photoceutical approach where we examine the ability of light to affect biological systems (pharmacodynamics) and how interactions with biological systems affects light (pharmacokinetics). This plenary talk will provide an overview of current understanding of PBM molecular mechanisms and approaches to optimized clinical dosimetry. A roadmap for clinical translation of PBM therapy highlighting the critical missing gaps will be presented. The ultimate goal of this talk is to emphasize that a photoceutical, precision-medicine mechanistic approach will enable development of more robust, safe and efficacious PBM clinical treatment regimens.

Photobiomodulation therapy of cells in the bone marrow: from bench to bedside

Prof. Uri Oron
School of Zoology, The George S. Wise Faculty of Life Sciences, Tel-Avi University

The mammalian heart has a very limited capacity to regenerate following damage or an acute ischemic event like myocardial infarction (MI), due to the very low level of cardiomyocyte proliferation and the limited number of cells expressing stem-cell marker proteins. Stem-cell-based therapy has been suggested as a potential solution to the above situation. In recent years cell-based therapy for cardiac repair has undergone a rapid transition from basic science research to clinical reality. The general outcome of the clinical trials has been that the procedures and long-term outcome post-stem-cell implantation to the heart via the coronary arteries are safe. However, improvement in long-term functional performance of the heart was either not achieved or was marginal.

Remote photobiostimulation therapy (rPBMT) involves application of PBMT to the bone marrow (BM) in order to stimulate stem cells and other cells in the BM for the benefit of an ischemic/injured organ. rPBMT caused a marked and significant reduction (79%) in infarct size 3 weeks post-MI in rat model of the infarcted heart.

This extent of infarct size reduction was even more effective in reducing scarring than that of laser application directly to the infarcted heart, as also found in our previous studies with infarcted rat and dog hearts. A significantly higher density of c-kit+ (marker of MSCs) cells was found in the myocardium of the laser treated rats relative to non-treated rats post-MI. In preclinical study the effect of rPMBT was tested in the porcine model of infarcted heart. The c-kit+ cells (stem cells) in the circulating blood of the laser treated (LT) pigs was 2.62 and 2.4-fold significantly higher than in the non- laser treated (NLT) pigs 24 and 48 hrs post-MI, respectively. The infarct size (% of scar tissue out of the LV volume as measured from histology) in the LT pigs was 3.2±0.82, significantly lower, 68% ($p<0.05$), than that (16.6±3.7%) in the NLT pigs.

A follow-up clinical study was designed to determine the long-term safety and possible feasibility of rPBM application to the BM in patients with acute myocardial infarction (AMI). The study comprised patients suffering acute ST segment elevation myocardial infarction (STEMI) as well as candidates for primary percutaneous coronary intervention (PPCI) In the active group (rPBMT, LT group),r PBMT was applied to the tibia bone non-invasively prior to PPCI, 24 and 72 hours post-PPCI. In the placebo group (NLT group) laser source was powered-off. Blood samples were taken on admission and during the first week post-STEMI as well as echocardiography flow up. Twenty-four patients in total (12 in treated and 12 in placebo group) were enrolled.

No adverse effects of the treatment were detected. as indicated by blood markers and kinetics of echocardiograpy. Levels of creatine phosphokinase accumulation in the blood (indicator of cardiac muscle leakage) in the NLT patients group was 49 ±12, while in the LT patients group a lower ($P=0.08$) level of 22+10 was detected. Peak Troponine-I was 5.2±1.8 ng/ml in the NLT group, which was significantly higher ($P<0.05$) than the value in the LT group (2.7±1.4 ng/ml), indicating possible cardio-protection of the ischemic heart by rPBMT to the BM. Application of rPBM to the BM in order to photobiostimulate stem-cells for the benefit of the infarcted heart seems to be a safe procedure for application in humans, and offers a novel approach in cell therapy adjunctive to the PPCI in patients post-AMI.

Can photobiomodulation treat obesity and metabolic syndrome?

Prof. Nivaldo A. Parizotto
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Department of Physical Therapy, Federal University of São Carlos, Brazil.
Biomedical Engineering, University of Brasil, São Paulo, Brazil.

New applications of photobiomodulation (PBM) are increasing over time. We can mention the use of PBM in muscle performance, improve of neuropathic pain and stem cell stimulation for tissue repair, among others. For metabolic syndrome and obesity, as well as the spectrum of its comorbidities, the PBM has some evidence of its actions at experimental level in animal models, and already has a spectrum of randomized clinical trials studies proving its action in the fat metabolism and modifying the metabolic profile of these patients. Among the most prominent aspects of the results are the modification of body shape, but mainly changes is in the lipid profile, glucose metabolism, changes of insulin and glucose sensitivity, as well as better use of muscle energy by influence of light, leading to a reduction of the body mass of the treated patients. In addition, references should be made regarding diabetes and its comorbidities and the influence that PBM has on such conditions.

There are already studies showing changes in glycemia and signs that the pancreatic beta cells can be regenerated in an animal model, with alterations that led to an improvement in insulin secretory function. The underlying mechanisms that explain these actions should be approached using the signaling genes and proteins to explain and to offer some evidence to be explored in the future by other researchers around the world, whose ultimate goal is the global health of individuals.

Photobiomodulation for the Brain: Has the Light Dawned?

Prof. Michael R. Hamblin
PhD, Wellman Center for Photomedicine, Assc. Professor at Harvard Medical School

Photobiomodulation (PBM) describes the use of red or near-infrared light to stimulate, heal, regenerate, and protect tissue that has either been injured, is degenerating, or else is at risk of dying. One of the organ systems of the human body that is most necessary to life, and whose optimum functioning is of most concern to humans in general, is the brain. The brain suffers from many different disorders that can be classified into three broad groupings: sudden events (stroke, traumatic brain injury, and global ischemia), degenerative diseases (dementia, Alzheimer's and Parkinson's), and psychiatric disorders (depression, anxiety, post-traumatic stress disorder, autism). There is some evidence that all these seemingly diverse conditions can be beneficially affected by applying light to the head. There is even the possibility that PBM could be used for cognitive enhancement in normal healthy people. In this transcranial PBM (tPBM) application, near-infrared (NIR) light is often applied to the forehead because of the better penetration (no hair, longer wavelength).

Some workers have used lasers, but recently the introduction of inexpensive light emitting diode (LED) arrays has allowed the development of light emitting helmets or "brain caps". Transcranial LED light sources are ideally suited to be home use devices. This lecture will summarize the mechanisms of action of PBM and our studies on TBI in mice. The key clinical trials in TBI, dementia (Alzheimer's) and psychiatric disorders and the MGH ELECTRA trial for cognitive enhancement will be discussed.

General Abstracts

Acupuncture

Laser Acupuncture – Traditional Aspects and Innovative Trends

Gerhard Litscher
Chairman of the Laser Acupuncture WALT Consensus Committee and Head of the TCM Research Center Graz, Medical University of Graz, Austria, Europe

One of the aims of this session is to provide the prerequisites for a consensus of worldwide leading authorities on the optimal use of laser acupuncture in different clinical applications, and particularly, on the way to make the treatments clinically useful for the management of individual patients.

Since the early days of laser acupuncture and laser medicine in general, there are still many open questions concerning technical parameters of this innovative technique. In this consensus session we will discuss about the most important technical parameters (e.g. wavelength, output power, power density, energy density, dose range, and continuous or pulsed laser) for laser acupuncture and present quantitative results for optimal laser stimulation, which allow eliciting reproducible effects in the periphery and in the brain. There are several position statements on laser acupuncture and also several review articles in scientific literature concerning clinical effectiveness of laser acupuncture. However, results of previous research studies and of current innovative research clearly show that dose must be adjusted according to the individual responses.

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The scientific investigations are supported by the Austrian Federal Ministry of Education, Science and Research ("Sino-Austrian TCM Research on Lifestyle-Related Diseases: Innovative Acupuncture Research" (2016–2019); project leader G. Litscher).

Laser Watch – A New Option for Simultaneous Laser Acupuncture and Laser Blood Irradiation

Daniela Litscher and Gerhard Litscher
TCM Research Center Graz, Medical University of Graz, Austria, Europe

The new laser watch applies laser acupuncture and laser blood irradiation in the area of the wrist in parallel.

Heart rate variability during laser watch stimulation shows an increase in the frequency band 0.05–0.15 Hz in which effects on the blood pressure control system manifest themselves during the optical stimulation. There was also an improved microcirculation (15% increases) during a 20-min laser stimulation applied through the laser watch. Simultaneously, a temperature increase in the area of the fingertip of the index finger can be observed.

Laser acupuncture and laser medicine in general have experienced enormous progress over the last years. The latest innovation is a so-called laser watch. The watch is applied to the wrist, where simultaneous and continuous acupuncture point and blood irradiation using different laser light can be performed. This results in new and promising therapeutic approaches for different diseases. The laser watch is practicable; however, further scientific research is necessary.

Reference: G. Litscher, D. Litscher. A Laser Watch for Simultaneous Laser Blood Irradiation and Laser Acupuncture at the Wrist. Integr Med Int 2016; 3:75–81, DOI: 10.1159/000448099

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The scientific investigations were supported by the Austrian Federal Ministry of Education, Science and Research ("Sino-Austrian TCM Research on Lifestyle-Related Diseases: Innovative Acupuncture Research" (2016–2019); project leader G. Litscher).

Laser Acupuncture and Auricular Medicine

Gerhard Litscher
Head of the TCM Research Center Graz, Medical University of Graz, Austria, Europe

LASER (Light Amplification by Stimulated Emission of Radiation) and Traditional Chinese Medicine (TCM) do not seem to have much to do with each other. However, if one thinks of laser acupuncture, for example, it is indeed a wonderful example of the combination of innovation (laser) and tradition (acupuncture). The list of Nobel Prize winners is very long; however, very few Nobel Prizes were awarded on laser and/or TCM so far. This presentation will deal with previous research that led to the respective Nobel Prizes. For the first time, the Nobel Prize in Medicine or Physiology was awarded to a Chinese researcher who is specialized in Traditional Chinese Medicine in 2015. Prof. Tu Youyou received this highest award for her excellent work in malaria research.
The second part of the presentation deals with transcontinental laser acupuncture studies within the field of high-tech acupuncture research and with auricular medicine. The treatment by auricular therapy has a long history. Ear acupoint research has been advancing step by step worldwide. The introduction of lasers into medicine brought besides the already existing stimulation with needles, electricity, pressure and liquids an additional technique to auricular acupuncture. The RAC (Reflex Auriculo-Cardiac) represents an important scientific method in the field of auricular medicine. At the TCM Research Center of the Medical University of Graz, new methodological strategies for recording and objectifying the dynamic pulse changes were scientifically investigated and described. With high-resolution imaging of pulsatile surface changes, the RAC can be reproducibly quantified for the first time.
In this presentation the latest basic and clinical research on laser acupuncture will be demonstrated.

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The scientific investigations were supported by the Austrian Federal Ministry of Education, Science and Research (“Sino-Austrian TCM Research on Lifestyle-Related Diseases: Innovative Acupuncture Research” (2016–2019); project leader G. Litscher) and by Eurasia-Pacific Uninet.

A Systematic Review of Photobiomodulation for Oral Mucositis with a Dose Analysis

Mr. J.D. Carroll
THOR Photomedicine Ltd, Photobiomodulation, Amersham, GB

Co-Authors: R.M. Vasconcelos, J.D. Carroll, A. Barash, R.-J. Bensadoun, I. Das, L. Ramalho, A. Kerr, P. Corby, K. Hu

1. Introduction and Hypothesis

Photobiomodulation Therapy (PBM) formerly known as Low Level Laser Therapy (LLLT) is an effective treatment or reducing the incidence and severity of oral mucositis (OM) after high dose chemotherapy and/or radiotherapy. However, reported PBM irradiation parameters, dose per point, number of treatment points or treatment intervals vary widely. The objective of this study is to systematically review randomized controlled clinical trials (RCTs) and summarize the PBM parameters and determine the range of effective treatment parameters.

2. Methods

Online databases were searched for articles published between 1995-2018 describing RCTs that compared the efficacy of PBM versus a control for the prevention or treatment of cancer therapy-induced OM. Publications were reviewed for inclusion of PBM irradiation parameters and dose. If these parameters were specified, their scientific justification was assessed.

3. Results

44 controlled clinical trials were identified, 21 were excluded for lack of randomization, duplicate data, no placebo or insufficient treatment parameter data leaving 23 papers for review. The median scores: wavelength 660 nm (range 637-660), laser power 0.040 W (range 0.025-0.060), beam area 0.040 cm^2 (range 0.030-0.496), treatment time per point 28 secs (range 10-57), irradiance 1.0 W/cm^2 (range 0.2-2.1), energy dose 1.4 Joules (range 0.3-3.0), fluence dose 6.1 J/cm^2 (range 4.0-80.0).

4. Conclusion

No precise dose recommendation can be drawn due to a large variation on the reported data, but there is evidence of a dose window in the results. Dose and dose rate studies must be performed to identify optimal combination of treatment parameters.

Photobiomodulation Therapy for Burning Mouth Syndrome and Oral Iatrogenic Nerve Injuries, a Case Series

Mr. J.D. Carroll

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Co-Authors: R. Hanna, J.D. Carroll, P.M. Burton

1. Introduction and Hypothesis

Background: Burning mouth syndrome (BMS) and oral iatrogenic nerve injuries can be painful and debilitating. Symptoms interfere with eating, social interaction, self-image and quality of life (QoL). Photobiomodulation (PBM Therapy), previously known as Low-Level Laser Therapy (LLLT), has been shown in multiple studies to reduce pain and improve the sensory function of injured nerves.

Objective: To investigate the effect of PBM Therapy on neuropathic pain, sensory function and perception of health in patients with BMS and inferior alveolar and lingual nerve injuries.

2. Methods

18 patients received a course of ten treatments (twice a week for five weeks). PBM Therapy was administered to the site of injury (if known) and 9 points along the inferior alveolar and lingual nerve with a 810 nm, 200 mW laser, 2 W/cm^2, 30 sec, 60 J/cm^2, 6 J. Treatment was also applied to the stellate ganglion with a 5 x laser cluster probe, each laser 810 nm, 5 x 200 mW, each 5 W/cm^2, 30 sec, 150 J/cm^2 per beam, 6 J / beam (THOR Photomedicine Ltd).

Outcome Measures: Patient-reported health status using the EQ-5D-5L comprising measures of mobility, self-care, usual activities, pain/discomfort and anxiety/depression, together with VAS for overall self-rated health reported before, mid-way through and at the end of 5-week treatment period with further follow-up at 1, 3, 6 and 9 months.

3. Results

Preliminary analysis; A trend in improved QoL from 61 (40,80) to 79 (60,90) mean (min, max) %, and a trend in increased EQ-5D- index values, from 0.60 (0.08,0.80) to 0.77 (0.52,1.0). Index Values represent quantified formats/conversions of all EQ-5D-5L scores. Both trends were reported from the first PBM treatment through to the 9-month follow-up.

4. Conclusion

Preliminary analysis shows a trend of improved self-reported health status in patients with Burning Mouth Syndrome and Oral Iatrogenic Nerve Injuries. Importantly, this is maintained for 9 months following initiation of a 5-week treatment schedule.

Clinical Entrepreneurship

PBMT in the Clinical Setting – a Model for Success

Dr. Shikha Parmar
Laser Pain Therapy Australia, Tok H Centre, Level 1, 459 Toorak Rd, 3142, Toorak, AU

Co-Authors: S. Parmar; Toorak

1. Introduction and Hypothesis

(Please note - this is not a Research-based abstract, but a qualitative discussion on real world application of PBMT).

I am a General Practitioner in Melbourne, Australia. When I started out in the field of photomedicine 7 years ago I was surprised to encounter low uptake and much resistance to the utilisation pf PBMT. Research is king in advancing innovative medical therapies and the WALT 2018 conference showcases excellence in leading edge research to its audience. Curiously and unfortunately photobiomodulation therapy (PBMT) still suffers from lack of mainstream medical acceptability in wider practice, despite 50 years of knowledge and scientific research and decades of evidence-based trials published in leading journals, particularly in the realm of musculoskeletal medicine.

2. Methods

PBMT practitioners are disrupters of traditional paradigms of pain management and there is a lot of skepticism, even hostility, from ignorant quarters. Combatting this in the patients we seek to help is half the battle.

I head a dedicated medical clinic focussed on delivering PBMT at the centre of a comprehensive and holistic approach to assist recovery from chronic pain and restoration of function and strength. I conduct about 120 patient consultations a week.

I see patients who self-refer and who are referred by other clinicians and I am an approved treatment provider for medical insurance policies covering work-place injuries and road trauma. It has been quite a journey reaching this point, navigating numerous obstacles and barriers, to promote this treatment to achieve acceptance from patients, colleagues, health-care providers and the wider public.

Thousands of patient encounters later, I share my depth of clinical experience of delivering our unique and valuable treatment successfully. I discuss what the challenges have been and how I have negotiated them.

3. Results

I present a clinical model that has maintained a track record of success and acceptability by patients and health providers, including health insurers, in delivering positive outcomes that persist. This in an environment of competing yet failing drug, surgical and manual therapies which do not address the essence of what underlies chronic musculoskeletal pain – an unresolved, “dystopian” inflammatory response.

4. Conclusion

I demonstrate how I have overcome barriers to help patients in chronic pain on their road to recovery, well beyond just pain management, to achieve successful treatment outcomes, where patients enjoy freedom from drugs and poor health, and return to meaningful service, leisure and normal life.

ABSTRACT

Oral Mucositis: How a UK recommendation guideline from the National Institute of Health and Care Excellence (NICE) was achieved

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Background:

Oral Mucositis (OM) is a painful side effect of Radiotherapy, high dose chemotherapy and Hematopoietic Stem Cell Transplantation (HSCT). Photobiomodulation (PBM Therapy) previously known as Low-Level Laser Therapy (LLLT) has been shown to be effective in reducing and even preventing side effects.

Acceptance:

Since 2013 the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC) have recommend low-level laser for the prevention of oral mucositis in transplant patients, and there is a suggestion for H&N patients.

2014 Bezinelli et al. showed a 30% reduction of the costs of hospitalisation in PBM OM patients. Since 2016, the American insurance providers Blue Cross Blue Shield declare "medically necessary for prevention of oral mucositis in select patients."

2017 Antunes et al. published a paper showing that LLLT may improve survival of head and neck cancer patients treated with chemoradiotherapy. A median follow-up of 41.3months (range 0.7-101.9), patients receiving LLLT had a statistically significant better complete response to treatment than those in the placebo group (LG=89.1%; PG=67.4%; p=0.013). Patients subjected to LLLT also displayed increase in progression-free survival than those in the placebo group (61.7% vs. 40.4%; p=0.030; HR:1:93; CI 95%: 1.07-3.5) and had a tendency for better overall survival (57.4% vs. 40.4%; p=0.90; HR:1.64; CI 95%: 0.92-2.91).

2017 the UK NIHR funded an RCT called www.liteform.org.uk investigating the Clinical and Cost-Effectiveness of Low-Level Laser in the Management of Oral Mucositis in Head and Neck Cancer Irradiation, 10 NHS hospitals, 380 patients in progress

2018 The National Institute of Health and Care Excellence (NICE) recommends Low-level laser therapy for preventing or treating oral mucositis caused by radiotherapy or chemotherapy. Current evidence on the safety of low-level laser therapy for oral mucositis shows no major safety concerns. Evidence on efficacy is adequate in quality and quantity. Therefore, this procedure can be used provided that standard arrangements are in place for clinical governance, consent and audit.

2018 Vasconcelos et al from NYU conduct a Systematic Review of Photobiomodulation for Oral Mucositis with a Dose Analysis, Wavelength 660 nm (IQR 637-660), laser power 0.040 W (IQR 0.025-0.060), beam area 0.040 cm^2 (IQR 0.030-0.496), treatment time per point 28 secs (IQR 10-57), irradiance 1.0 (W/cm^2 0.2-2.1), energy dose 1.4 Joules (IQR 0.3-3.0), fluence dose 6.1 (J/cm^2 4.0-80.0).

Conclusion:

PBM is safe, effective and reduces the cost of care and may even improve survival. The optimal treatment regime is not clear but there is evidence of a dose window in the results. More dose and dose rate studies must be performed to identify the optimal combination of treatment parameters

Dentistry

Antimicrobial photodynamic therapy (aPDT) for medication-related osteonecrosis of the jaws (MRONJ): a cohort study and a treatment protocol proposal

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1. Introduction and Hypothesis

Medication-Related Osteonecrosis of the Jaws (MRONJ) treatment is complex and varied with no effective therapeutic protocol. The aim was to propose an aPDT-based protocol for treatment and prevention of MRONJ lesions.

2. Methods

Thirty-two patients in use or with history of antiresorptive drugs usage were followed-up between 2015-2018. MRONJ treatment included four preoperative aPDT sessions, as follows: 0.01% methylene blue solution was applied inside the lesion and after 5 minutes the lesion was irradiated with a continuous-wave AsGaAl diode laser.The laser irradiation parameters were: 660 nm (red laser), 0.028cm^2, 0.1W, 3.57W/cm^2 90s per point, 9J per point, 321J/cm^2, 3 points and total energy of 27J per session. The aPDT was applied inside surgical wound just after necrotic bone removal and was re-applied until healing. For MRONJ prevention, immediately after tooth extraction the aPDT was applied inside dental socket using the same aPDT protocol and irradiation was repeated weekly until tissue repair. In both situations, laser probe was placed at the centre of lesion and in two equidistant points. Antibiotics were administered pre or postoperatively for no longer than 7 days.

3. Results

Twenty-seven patients were female and 5 were male. The mean age was 69.5±8.77. Eighty per cent used alendronate for osteoporosis and 20% used zoledronate for cancer treatment. Twelve patients underwent preventive protocol and none of them presented signs of MRONJ. Twenty patients presented MRONJ at stages 1 and 2 after oral surgery. They underwent aPDT protocol and necrotic bone removal when necessary. Seventeen showed total regression of lesions after a mean of two postoperative aPDT sessions. Three remained with stage 1 and periodical aPDT was maintained with occasional sequestration removal.

4. Conclusion

The aPDT protocol applied is a valuable choice for preventing MRONJ lesions. Moreover, aPDT is an effective therapeutic approach for controlling MRONJ lesions at early stages.

Cell-free scaffold and Photobiomodulation therapy for enhance dental pulp tissue engineering: In Vitro and In Vivo Analyses

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1. Introduction and Hypothesis

Cell-homing approaches for dental pulp engineering are based on the recruitment of endogenous stem cells, bioactive molecules, and scaffolds, aiming cell migration, proliferation and differentiation. The recruitment of endogenous stem cells into root canals to regenerate pulp tissues may offer opportunity for the near-term clinical translation of biology-based therapies for dental pulp regeneration. Photobiomodulation therapy (PBMT) can improve survival, proliferation, migration and differentiation of stem cells. The hypothesis is that PBMT would facilitate the three-dimensional spatial organization of endogenous stem cells in dental pulp regeneration using an injectable functionalized scaffold inside the root canal

2. Methods

The injectable hydrogel was developed with thermosensitive chitosan/β-glycerol phosphate disodium salt. Stem cells from apical papilla (SCAPSs) were isolated and characterized by flow cytometry and used to analyze the chemotactic of the hydrogel and the effect of PBMT in its migration (Transwell) and differentiation (Alizarin Red) in scaffold. The in vivo wistar rodents received regenerative endodontic procedure inside the root canal of molars based on homing of stem cells in chitosan or hybrid scaffold (chitosan+ blood clot) and PBMT. PBM therapy was carried out with a continuous wave InGAlP diode laser (660 nm; DMC, São Carlos, SP, Brazil). Irradiation parameters were as follows: power output of 20 mW, beam area of 0.028 cm^2, and energy density of 5 J/cm^2 7 s. Irradiation was at a single point and in contact with the crown of each tooth on top of the scaffolds. After 28 days the tissue was processed for histological analysis. Samples with tissue inside the root canal were analyzed by immunohistochemistry for tissue characterization (HSP-25). Chitosan scaffold (CS) was loaded with Vascular Endothelial

Growth Factor (VEGF). ELISA assay confirmed the kinetic release of VEGF in hydrogel for 7 days. We also assessed the effect of PBMT in SCAPs proliferation (Alamar Blue) on CS-VEGF 3D system.

3. Results

The Injectable chitosan scaffold presented low initially viscosity (7,6cP) and shows porous structures of gel, similar to a honey comb, which have a suitable pore size. Also promoted chemotactic recruitment/ migration of SCAPs. PBMT group presented higher migration (p=0.0214) and proliferation rate of SCAPs (p= 0.0195) in comparison with control group. The injectable scaffold did not interfere in stem cell differentiation.The new pulp-like tissue was observed in hybrid scaffoldand PBMT group with blood vessels and the presence of odontoblastic like cells (HSP-25). A peak release of VEGF was observed in 24 h (1,4 ng/ml), and a controlled release was observed until 7d. PBMT group presented higher proliferation rate of SCAPs (p= 0.0195).

4. Conclusion

The hybrid scaffold and PBMT promoted orthotopic new tissue formation in the root canal. CS-VEGF can be a promising biomimetic scaffold for dental pulp tissue engineering.

Photobiomodulation therapy after lower third molar surgery: a randomized crossover clinical trial comparing intra versus extraoral single-session

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1. Introduction and Hypothesis

Photobiomodulation therapy (PBMT) has shown benefits in multiple or everyday protocols for postoperative inflammatory distress after third molars extraction. However, there is no established single-session protocol. We aimed to compare the effects of intraoral and extraoral single-session PBMT approaches after lower impacted third molar surgery.

2. Methods

Sixteen patients underwent bilateral lower third molar removal. Each side was randomly allocated to intraoral (IL) and EL-placebo or extraoral (EL) and IL placebo groups. Immediately after surgery patients received PBMT in a single session. For the intraoral group (IL), the irradiation parameters were: visible red wavelength of 660 nm, power of 100 mW, beam spot area of 0.028 cm^2, power density of 3.57 W. cm^2, duration of 30 seconds, energy density of 107 J.cm^2 per point and energy of 3 J per point and total energy of 12 J. Four points around the dental socket were irradiated: center, middle third of the lingual surface, middle third of the labial surface and at the retromolar region. For the extraoral group (EL), the irradiation parameters were the same used for the IL, except for the wavelength, that was infrared (808 nm). Irradiations were done in contact with the skin on the Masseter region insertion in four points: mandibular, lower middle region, upper middle region and zygomatic arch. For IL and El placebo, the same procedures were applied however the equipment was kept off. Mouth aperture was assessed by interincisal distance. Anatomical facial points distances evaluated edema. A visual analogical scale assessed pain at five moments after surgery.

3. Results

Pain levels and edema were similar between the groups. Mouth opening was significantly higher in the EL group 7 days after surgery.

4. Conclusion

A single session of extraoral PBMT is more efficient in improving postoperative mouth opening.

Laser speckle image analysis as a diagnosis tool for tooth lesions

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1. Introduction and Hypothesis

The carious lesion is a prevalent disease. Nevertheless, the majority of the diagnostics are based on visual inspection, therefore are subjective. However, prevention programs and awareness of the population are mitigating the impact of the disease, besides modern minimally-invasive techniques are reducing its impact. On the other hand, the pace of modern life replaces fresh foods with industrialized, containing several acidic ingredients, increasing the prevalence of tooth erosion, which still lacks an objective diagnostic technique.

Such diseases are different in origin and treatment, but both produce microstructural changes in the enamel that results in changes in the optical parameters of the tooth

Laser speckle imaging analysis is a diagnostic technique based on the study of features of scattered coherent light. The images of speckle patterns contain information on the microstructure of the surface, which, by applying a suitable computer vision and/or statistical approach, can be explored to diagnose lesions in the tooth enamel, regardless its origin.

2. Methods

Schematic diagram of the experiment: a) laser source, b) expanding telescope, c) sample, d) camera.

A HeNe laser (Uniphase, USA), λ=633nm, 40mW (CW) was used. The bean expander (f =100 mm K&F concept, China) resulted in a circular spot size of 6 mm in diameter (target area = 0,28cm^2, irradiance 142mW/cm^2). The image acquisition system was a Canon camera and lens (Rebel T1i; lens: macro 100mm). The parameters were 1/200s; f/29; ISO100. The energy is irrelevant to this experiment

3. Results

The LSI presents statistically significant different patterns in the sound and in the lesioned region; therefore it is possible to detect the presence of the decay or of the erosion. Besides, the fig1.jpg

LSI is proportional to the lesion's severity, allowing for quantitative assessment.

4. Conclusion

This approach allows for an objective low-cost non-destructive real-time diagnostic method for tooth lesions.

Efeitos hemodinâmicos e autonômicos da terapia de fototerapia associada ao treinamento aeróbio na osteoartrite de joelhos em ratas ooforectomizadas

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1. Introduction and Hypothesis

The physiological aging of women is accompanied by hormonal deprivation and complications resulting from these, in particular, deleterious alterations to the cardiovascular system and impairment of the locomotor system. By 2030, there will be an exponential increase in women with menopause around the world. This context is accompanied by several women's health commitments, including osteoarthritis (OA). To evaluate the action of low intensity laser (LLLT) combined with aerobic training (AT) in knee OA in oophorectomized rats

2. Methods

Foram utilizados ratos Wistar (n = 38) (200 a 280 g). A menopausa foi realizada com surgery ooforectomia bilateral sem dia 1^{r} e OA foi induzida POR Três doses de 20 ul (10 ml de 4% de papaína e 0,03 M de cisteína), NOS Dias 1^{r} , 4^{r} e 7^{r} , com inclusão via injeção na junção intra-articular do joelho direito. Ratos randomizados em 5 grupos: Sham (SH) (n = 6) com cirurgia de pseudo-ooforectomia e procedimento de indução da OA com solução salina; (OO) (n = 8) ooforectomia bilateral (OF) e indução de OA; (OL) (n = 8) DE + OA + LLLT; (OT) (n = 8) DE + OA + AT e (OLT) (n = 8)OF + OA + TA + LLLT Os grupos OT e OLT foram com um protocolo de 8 semanas (5 dias / semana) de AT moderada em esteira rolante. OL e OLT foram submetidos a terapia LLLT (685mm, 10mW de potência, 2,5J / cm^2 de energia energética, 26s de irradiação e 0,1cm^2 de área) duas vezes por semana, ratos levados à tricotomia e 16 sessões de terapia LLLT foram instruções sobre o tema patelar, o grupo SH e OO realizaram os mesmos procedimentos com o equipamento desligado. Os ratos foram pesados no início e no final do protocolo. O teste de esforço máximo (MST) foi realizado no início, meio e fim do protocolo. Após 48 horas da última sessão de tratamento, dados hemodinâmicos e autonômicos foram vistos. Comitê de Ética n ° AN 012/2016.

3. Results

These that ratos with mystas having minor gain de peso, em which when MST (OT = 14,43 ± 1,7 e OLT = 14,68 ± 1,9 min) em matching ao MST (OT = 9, 61 ± 0,6 e OLT = 9,5 ± 0,78 min) p <0,05. A frequência cardíaca também foi diminuída nos grupos OT e OLT em comparação com OO. Não houve diferença na pressão arterial média entre os grupos. Melhora do sistema autonômico no índice ALFA dos grupos (OT = 0,55 ± 0,26 e OTL = 0,55 ± 0,40 ms / mmHg) comparado com (OO = 1,33 ± 0,73 ms / mmHg) p <0,05. O mesmo acontece com a frequência da banda (OT = 8,33 ± 3,48 e OTL = 12,69 ± 3,54%), p <0,05, representando menor atividade simpática entre os grupos.

4. Conclusion

It was shown that LLL therapy combined or with AT induces benefits in reducing body weight, functional capacity, hemodynamic and autonomic indices in oophorectomized rats with knee OA, reducing local and systemic disease involvement.

Effects of Photobiomodulation associated with Mesenchymal Stem Cell Implant Adipose derived MMPs and Decrease Type II Collagen Degradation in an Experimental Osteoarthritis Model

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1. Introduction and Hypothesis

This study aims to determine if photobiomodulation therapy (PBMT) can improve the bioavailability and chondroprotective benefits of mesenchymal stem cells injected into the knees of rats used as an experimental model of osteoarthritis (OA), as well as reduce the expression of matrix metalloproteinases (MMPs) and the degradation of type II collagen (COL2-1) in the cartilage.

2. Methods

Adipose-derived stem/stromal cells (ADSCs) were collected from three male Fisher 344 rats and then characterized by flow cytometry. Fifty female Fisher 344 rats were distributed into five groups of 10 animals each. These groups were control group, OA group, OA PBMT, OA ADSC group, and OA ADSC PBMT group. OA was induced in the animals using a 4% papain solution. Animals from the OA ADSC and OA ADSC PBMT groups received an intra-articular injection of 10 × 106ADSCs and were treated with PBMT by irradiation (wavelength: 808 nm, power: 50 mW, energy: 42 J, energy density: 71.2 J / cm^2, spot size: 0.028, power density: 1,78 W/cm^2, Continous Mode). Euthanasia was performed 7 days after the first treatment, and articular cartilages.

3. Results

The use of PBMT alone and the injection of ADSCs resulted in the downregulation of pro-inflammatory cytokines and metalloproteinases in articular cartilage tissue, when compared to the OA group. They also caused the upregulation of tissue inhibitors of metalloproteinases 1 and 2 (TIMP-1 and TIMP-2), mRNA and protein expression of COL2-1 in articular cartilage tissue, when compared to the OA group.

4. Conclusion

The intra-articular injection of ADSCs combined with PBMT prevented joint degeneration resulting from COL2-1 degradation and modulated inflammation by downregulating cytokines and MMPs in the OA group.

Photomodulation In The Treatment Of Chronic Pain In Patients With Temporomandibular Disorder: Protocol For Cost-Effectiveness Analysis

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1. Introduction and Hypothesis

Epidemiological data show that the signs and symptoms of Temporomandibular disorder (TMD) start to become apparent from six years of age, and in adolescence these signs and symptoms are similar to those of adults. The present study aims: to estimate the direct costs in the treatment of chronic muscle full in patients with TMD with photobiomodulation therapy and with occlusal splint and a placebo group; to evaluate the effectiveness of the treatments with photobiomodulation therapy and occlusal splint for muscle pain in patients with TMD; to analyze the cost-effectiveness of the two proposed treatments for pain; and to describe and compare the results of analyses of treatments for pain in patients with TMD. Trial registration: NCT03096301

2. Methods

It will include 135 patients aged between 15 and 25 years with TMD, randomly assigned to a treatment group: G1 (photobiomodulation), G2 (occlusal splint) and G3 (placebo). The outcome for the analysis of the effectiveness will be the pain, measured periodically by means of the clinical examination of the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD). Laser: Twin Flex Evolution ®, from MM Optics, twelve laser applications will be applied, with 2 sessions per week, a wave length of 780 nm, with an energy density of 25 J/cm^2, a power of 50 mW and power density of 1.25 W/cm^2, will be used for a duration of 20 seconds per point, resulting in a total energy of 1J per point. The laser will be applied at each point, using a conventional tip in contact with the skin, thus considering an area of 0.04 cm^2.The laser will be applied to 3 points of the masseter muscle (upper, middle, and lower bundles) and 1 point in the anterior temporalis on each side of the face.

Evaluation of periodontal treatment associated with photodynamic therapy (PDT) in experimental model of chronic obstructive pulmonary disease (COPD)

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1. Introduction and Hypothesis

The correlation between periodontitis and COPD has been studied. Conventional methods of periodontal treatment (PT) have been associated with adjuvants. PDT emerges as a promising treatment with no side effects, unlike antibiotics, that are associated with bacterial resistance. The main objective was to evaluate if PT associated with PDT may influence in the modulation of pulmonary inflammation.

2. Methods

64 C57Bl/6J mice were randomly divided into 8 groups (Basal, Periodontitis (P), P+PT, P+PT+PDT, COPD, COPD+P, COPD+P+TP and COPD+P+TP+PDT. COPD was induced by orotracheal instillation of cigarette extract. Periodontitis was induced by the ligation technique, performed at the 3rd week after induction of COPD, and remained for 15 days. PT was performed with a curette. PDT was performed with methylene blue (0.005%) with 3 minutes' pre-irradiation with diode laser (Therapy XT® DMC, São Carlos, Brazil, ANVISA 80030810157) Device and treatment specifications: λ: 660nm duty cycle, power 100mW, irradiance 3,5W/cm^2, spot size 0,02827cm^2, irration mode: continuous wave, energy density 318J/cm^2, dose 9J per point (2 points application in-contact probe), 90s per point, total energy 18J and treatment is realized once. Euthanasia was performed 51 days after the first induction of COPD. It was realized histomorphometrical analysis of lung and mandible to characterize the experimental model, total and differential bronchoalveolar lavage (BAL) and serum count, femoral lavage. Inflammatory cells were assessed by flow cytometry. Statistical test was ANOVA one-way followed by the Student-Newman-Keuls.

3. Results

The P+PT+PDT group showed an increase in the total number of leukocytes in the BAL when compared to the P group ($p<0.05$). This increase was represented by lymphocytes CD3 ($p<0.05$) and neutrophils ($p<0.05$) followed by macrophages ($p>0.05$). The total count of femoral lavage was increased in P +PT and P +PT+PDTgroups. Also, in COPD+ P +PT and COPD+ P +PT+PDT groups total cells count decrease in serum, ($p>0.05$).

4. Conclusion

Conventional PT associated or not with PDT, was able to influence systemic response. Further studies are needed to understand the link with a regulatory process.

The parameters were measured. Approved by Ethics Committee of UNINOVE, CEUA #021/2017. We have no conflicts of interest. Financial support: CAPES #1690040 and FAPESP 2015/20535-1.

Influence Of Bioactive Particles On Remineralization Of Early Enamel Caries Lesions By Speckle Analysis

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1. Introduction and Hypothesis

It has been known that the acid-producing bacteria in the biofilm diffuse into the tooth and dissolve the carbonated hydroxyapatite mineral, forming a caries lesion. Clinically, the early enamel lesion appears as a white spot with an intact surface zone of enamel, and prior to cavitation, the aforementioned subsurface lesion with partial demineralization still can be remineralized. This study aimed at evaluating the potential remineralizing of different bioactive glass fillerson the early enamel caries lesions (EECL). There is very good clinical evidence that such lesions can be remineralized if the surface remains intact, provided they are kept free of plaque, salivary flow is adequate or is regularly stimulated by use of sugar-free gum and topical fluoride treatments are given. It has been known that fluoride acts to remineralize damaged tooth tissue following demineralization. even small amounts of fluoride provide some degree of cariostatic efficacy, and in this way, a great number of restorative materials and oral care products contain fluoride: mounth rinses, dentifrices, glass ionomer cements, resin-modified glass ionomer cements, composites, adhesives and varnishes. Caries lesions result from loss of calcium ions, and it would be advantageous if a single additive to some formulation could act as a source of both fluoride and calcium ions. Bioactive glass (BAG) is such an additive; study on BAG containing glass ionomer cements showed that BAG is a good source of both fluoride and calcium ions.

2. Methods

Forty sound bovine teeth were selected after consent and donation by freezer. Blocks of 6 x 6 mm^2 were carried out from the crowns, vestibular surface of bovine incisors were polished and teeth were isolated with two layers of acid resistant nail varnish. Vestibular surface were divided in sound and treated areas. The sound area was isolated with duct tape (3 x 3 mm^2), and the treated area was firstly immersed into demineralization/remineralization solution (1 week) to create the EECL. The areas were treated with a slurry of different bioactive particles with deionized water for 1 week. Samples were analyzed by laser speckle after formation of EECL and compared to the sound area, and then the treated area was analyzed again by laser speckle. In laser speckle imaging system the surfaces of each sample were imaged under a coherent light illumination at normal incidence. A HeNe laser (Uniphase, USA) emitting at 633 nm with 10 mW of continuous wave power was used. The laser was positioned approximately 76 cm from de sample and a lens (f=100 mm lens-K&F Concept, China) was placed in the optical path to expand its beam and illuminate a larger area of the sample. The image irradiated was captured by a colored CCD chamber, capturing the images in RGB (Canon 500D).

3. Results

After analysis with laser speckle, EECL showed a lower average intensity of the backscattered light. After remineralization, a higher average intensity of the backscattered light was observed, which was similar to the sound areas.

4. Conclusion

It could be concluded that the different bioactive fillers were able to remineralize the demineralized surface of the teeth.

Reparative Action Of The Red Laser On Photoaged Skin Of Hairless Mice

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1. Introduction and Hypothesis

Environmental and chronological factors have a great influence on the skin aging, with photodamage being one of the most important in this process. Different strategies are used in the treatment and prophylaxis of photoaging. Photobiomodulation (PBM) is known as a non-invasive therapy with almost complete absence of side effects that can both reduce and repair damage caused by ultraviolet radiation. Due to this potential, it is necessary to investigate different protocols and experimental models for a better elucidation of the biological mechanisms involved in the photoaging, for the construction of effective aesthetic procedures in their prevention and treatment.

2. Methods

The project was approved in UFSCar's ethics committee on animal experimentation (040/2014). Female hairless mice (HRS/J), approximately 8 weeks old (n=9), were randomly divided in 3 experimental groups: HC (animals that were not photoaged); PC (photoaged animals) and PLASER (photoaged animals, treated with red laser). The photoaging was induced through chronic exposure to an incandescent light bulb (Ultravitalux 300W-OSRAM), during 6 weeks according to the adapted protocol1. The following parameters were used for the treatment of the dorsal region of the animals with red laser: Photon Lase III device (DMC, Brazil) with wavelength-continuous InGaAlP laser (660nm), power of 40mW, power density of 1.42W/cm^2, spot size of 0.028cm^2, energy density of 40J/cm^2, with application in direct contact for 28 seconds and 1.12J/cm^2 energy per point (6 points). The treatments were performed with the aid of an mold (4x2cm) drilled with standard distance (0.5cm) between the points, in a total of 12 sessions divided into 3 sessions/week (Monday, Wednesday and Friday) during 4 weeks after the photoaging process. After the treatment, the dorsal skin of each animal was collected. The samples were submitted to immunofluorescence for quantification of metalloproteinases 1 and 2 (MMP1 and 2).

1.HWANG, E. et al. Enzyme-processed Korean Red Ginseng extracts protects against skin damage induced by UVB irradiation in hairless mice. J Ginseng Res, v. 37, n. 4, p. 425-34, Oct 2013. ISSN 1226-8453.

3. Results

Findings revealed a significant reduction of the MMP1 ($p=0.0134$) and 2 ($p=0.0023$) after photoaged animal treatment with red laser when compared to the PC group by statistical analysis two-way ANOVA and Tukey post hoc test with $p<0.05$ as significant level, suggesting a consequent reduction of the collagen breakage and degradation, repairing the photoaged skin of treated animals.

4. Conclusion

The red laser demonstrated efficacy in the recovery of the skin integrity of photoexposed mice to ultraviolet radiation.

Financial support: FAPESP

Efficacy Of Photobiomodulation On Oral Lichen Planus: A Pilot Study.

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1. Introduction and Hypothesis

Oral lichen planus (OLP) is an idiopathic chronic mucocutaneous disease with distinct clinical manifestations, including white reticular patches, erosive/ulcerative and atrophic lesions, both associated with intense symptomatology. Topical corticosteroids are used as standard therapy. However, OLP frequently present relapses and patients develop resistance to corticosteroid therapy. Photobiomodulation (PBM) has been shown to be a potential therapeutic tool to treat inflammatory disorders, including OLP. The aim of this study was to compare the efficacy of PBM (660nm) to corticosteroid therapy with clobetasol propionate 0.05% for the treatment of OLP.

2. Methods

Six patients with symptomatic and biopsy-proven OLP were randomized into 2 experimental groups in a double-blind manner: Control group (n=3)- clobetasol propionate 0.05% + placebo PBM and PBM group (n=3)- PBM + placebo gel. In Control group, patients were treated with topical clobetasol propionate gel 0.05% (three times a day) for 30 consecutive days and with placebo laser (switched off) twice a week for four weeks, totaling 8 sessions. To prevent oral candidiasis, patients used anti-mycotic solution (Nystatin oral suspension 100,000 USP/ml) once a day for 30 consecutive days. In PBM group, patients were treated with low-level laser therapy with a continuous wave diode laser (Laser Therapy XT, DMC Equipment, São Carlos, SP, Brazil), single probe, $\lambda = 660 \pm 10$ nm; power 100mW; power density 35.38 W/cm^2, spot size of 0,003 cm^2, energy density 177J/cm^2; 0.5J of total energy per point, 5-s exposure time per point, applied directly to the surrounding oral mucosa and to the center of OLP, always by the same operator, twice a week for 4 weeks, totaling 8 sessions. OLP lesions located at buccal mucosa, tongue and gingiva were treated and the total number of point were variable according to lesion size. The placebo gel was applied three times a day for 30 consecutive days. The OLP pain was accessed by the Visual Analog Scale (VAS) and clinical sign scores as well as functional scores (chewing function, swallowing, fluid intake and altered sense of taste) were evaluated at baseline and once a week during treatment.

3. Results

A total of 10 OLP lesions were treated in each group and no statistical difference was observed at baseline between the two groups regarding gender, OLP localization, VAS, clinical and functional score. Only treatment with propionate clobetasol 0.05% showed a significant difference in VAS ($p<0.0001$) and in clinical sign score ($p=0.0004$) before and after treatment. Most of OLP lesions in Control group showed complete remission or atrophic aspect < 1cm^2 after treatment. No significant difference was observed in relation to functional scores in both groups before and after treatment.

4. Conclusion

This pilot study indicates that corticosteroid therapy is more effective in the treatment of symptomatic OLP than PBM. However, further clinical trials are needed to support this result. Statements: This study was approved by Nove de Julho University's Research Ethics Committee (#2.375.410) and was registered at www.clinicaltrial.gov (NCT03320460). All patients signed the informed consent.

Slep Bruxism: A Complement Diagnostic And Alternative Treatment By Photobiomodulation In Children

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1. Introduction and Hypothesis

Sleep bruxism(SB)is a muscle disorder characterized by claenching and grinding teeth. The SB diagnosis in children is difficult because there is no polyssomnograpy protocal for them. So clinical exam must be more complete as it can, Treatments are also difficult for them, because the gold standart, occlusal splints therapy, has some limitations, like cooperation to use it full time. Literature shows positives results in photobiomodulation treaments in muscles disordes,

so the present study aimed to investigate the occurrence of bite marks on the buccal mucosa in children with sleep bruxism(SB), as a complement sign to diagnosis, and the effectiveness of photobiomodulation, as an alternative treatment for SB.

2. Methods

SB diagnosis was obteined according to ICDS-4 guideline: guardian's report and presence of wear facets in permanent teeth. Seventy six children, aged 6-12 years old were divided into 4 groups: G1-With SB, Laser therapy treated in acupuncture points (λ=94 nm,5J/cm^2, 1.675 mW/cm^2, 0,070W, 20 s/point); G2–With SB, Occlusal Splint treated, G3–With SB, Placebo treated; and G4–Without SB, Control group. All were evaluated according to muscle strength, assessed by a digital gnatodynomometer. Statistical analysis was performed with the aid of the SPSS20.0 program with a 5% significance level ($p \leq 0.05$),using Kolmogorov-Smirnov,Shapiro-Wilk and Anova tests.

3. Results

There was no significant differences in age or gender in intra or inter-groups($p=0.34$).There was a statistically significant association between bite marks on buccal mucosa and SB($p<0,001$). When inter-groups were compared before and after treatments, there was a decrease statistically significant difference ($p=0.021$) in bite force in G1 (means=29.49,SD=9.92).

4. Conclusion

Therefore, complete diagnostic may be done analyzing bite marks on buccal mucosa, according to present results. About treatments, photobiomodulation in acupuncture points can be an alternative treatment in children with SB, because of bite force reduction, probably caused by a biostimulation, increased blood circulation, vasodilation, anti-inflammatory effects, and accelerate the healing of damaged tissues.

Low Level Laser Therapy In bone Growth In Periodontal Disease With Mercury Detox

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1. Introduction and Hypothesis

The effects of LLLT in long term is bone regeneration. In all cases, the laser irradiations group had results in the short term effects: antiinflammatory, hemostasis, painrelief, and long term, tissular regeneration, no recurence and use of medication.

2. Methods

RT-PCR analysis RNA was isolated by affinity chromatography using RNeasy Minikit (Qiagen Inc., Hilden, Germany) and was subjected to reverse transcription with oligo (dT) 12 and Superscript III (Invitrogen) being used for PCR. The PCR amplification was carried out with the Go Taq. The PCR products were separated by electrophoresis on 1.5% agarose gels.

3. Results Methods:

We made a PCR before using the laser and after. We used an infrared diode laser, wave length 830 nm, and red with the wave length of 630nm, with convergent beam, energy between 0,5 and 3 J, applied continuously or in pulses with a frequency of 4,68 Hz or 9,12 Hz. The parameters were adjusted automatically, depending on the necessary penetration deeps (2,5 – 12 mm). RNA isolation and RT-PCR analysis were made. In the first place,we detected the specific pathogens infect the periodontal sites of a patient. thoughout the developed genetic material amplification method called PCR (Polymerase Chain Reaction). Total RNA was isolated by affinity chromatography using RNeasy Minikit (Qiagen Inc., Hilden, Germany) and was subjected to reverse transcription with oligo (dT) 12 and Superscript III (Invitrogen), according to the protocols from the manufacturer. In this experiment, 1 µg of total RNA was used for RT in a final reaction volume of 20 µl, with 1µl being used for PCR. The PCR amplification was carried out with the Go Taq hot start kit (Promega, Charbonnières-les-Bains, France). The PCR conditions were as follows: initial denaturation for 3 minutes at 94 ° C followed by 35 cycles at 94 °C for 1 minute, annealing for 1 minute and elongation for 1 minute at 72 ° C, with a final extension of 10 minutes at 72 ° C. The PCR products were separated by electrophoresis on 1.5% agarose gels. At all stages, freshly prepared and cultured cells expressed Pax9, Dlx5, Lhx6, Lhx7, Msx1, Msx2, Bmp2, Bmp4. Statistic evidence show in all cases in the benefit of the use of LLLT

4. Conclusion

Immediate effects: short bleeding and pain duration; no post surgery complications (edema, inflammation, infection and pain); forming and maintaining the clot; maintaining the masticator function. There was no post surgery alteration, permitting the patient an un-interrupted social life Long term effects: rapid and esthetic scar; healing of the soft tissue; rapid recovery of a more compact bone tissue and fixation of the teeth; complete restoring and maintenance of the masticator and esthetic functions. The results depend on the age, general health and metabolic problems of the patient. Very good results were obtained for the diabetic patient. Recurrence rate is low.

We found that la pathogenesite of the bacterial site it is redused, that let place for regeneration of tissues. The use of PCR is a confirmation of the germ reduction value of the LLLT

Comparative Effectiveness Of Photobiomodulation And Manual Therapy Alone Or Combined In TMD Patients: A Randomized Clinical Trial

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1. Introduction and Hypothesis

Temporomandibular disorder (TMD) is a multifactorial disease. Therapeutic modalities expected to relief symptoms and improve function. The aim of the present study was to compare the effectiveness of photobiomodulation therapy (PBMT) and manual therapy (MT), alone or combined (CT) in pain intensity, mandibular movements, psychosocial aspects and anxiety symptoms of TMD patients.

2. Methods

Fifty-one TMD patients were randomly assigned at three groups. PBMT group (n=18) received therapy by a single professional using a continuous wave of GaAlAs diode laser (MMOptics Recover, São Paulo, Brazil), with a wavelength of 808 nm, in punctual contact, with a spot size of 0.03 cm^2, power output of 100 mW, irradiance of 3.33 W/cm^2, radiant exposure of 133 J/cm^2, 40-s exposure time per point, and 4 J of total energy per point. PBM was applied 12 times (3 times a week for 4 consecutive weeks) in 12 points (5 in the TMJ region and 7 in muscles.The protocol results in 48 J per point or 576 J per each side of the face after 4 consecutive weeks. MT group (n=16) for 21 minutes each session on masticatory muscles and TMJ and CT group(n=17) applied during twelve sessions. Seven evaluations were performed indifferent moments using visual analogue scale (VAS), RDC/TMD Axis I and II,Beck anxiety inventory (BAI).

3. Results

All groups demonstrated reductions in painimprovement in some jaw movements during the treatment and follow-up($p<0.001$). The assessment of psychosocial aspects of TMD comparing baselineand follow-up in all treatment groups revealed that treatment did not promote modification in intensity of chronic pain ($p>0.05$). However, depression symptoms showed reduction in PBMT and CT groups ($p\leq0.05$). All treatments promoted reduction in physical symptoms with and without pain and enhancement of jaw disabilities ($p\leq0.05$). MT promotes improvement in 5 functions, PBMT in 2 and CT in 1 ($p<0.001$). BAI analysis revealed that all treatments lead to a reduction in anxiety symptoms ($p\leq0.05$).

4. Conclusion

All protocols promoted pain relief, improve mandibular function, and reduce the psychosocial negative aspects and the levels of anxiety in TMD patients.

Statements: approval from the Human Research Ethics Committee (CEP/UFRGS 1.541.360 and CAEE protocol 52651416.1.0000.5347). ClinicalTrials.gov Identifier: NCT03454581.

Violet–Blue Laser Inactivation Of Microorganisms

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1. Introduction and Hypothesis

Antimicrobial resistance is one of the most serious global health problems. In this work, we evaluated the effect of violet-blue laser radiation on microorganisms and characterized the types of endogenous chromophores involved in mechanism of photoeradication.

2. Methods

The microorganisms were Staphylococcus aureus ATCC 25923, Escherichia coli ATCC 8739, Candida albicans ATCC 10231, all obtained from the American Type Culture Collection. The light sources were semiconductor lasers generating in CW mode at wavelengths of 405 nm and 445 nm. The power density of radiation was P = (50 ± 3) mW/cm^2. The time of irradiation was 0 – 180 min. Bacterial suspensions were prepared in sterile saline solution (0.9% NaCl) by serial dilutions using McFarland turbidity standard. A 3 ml of this suspension was transferred to the sterile cylindrical glass tubes with interior diameter of 1.4 mm and then the tubes were irradiated. After irradiation, 100 µl of test and control samples were immediately plated onto agar plates using standard microbiological plating methods and incubated at 37 °C for 24 h. The ratio of colony forming units (CFU) in experimental and control groups was used to evaluate the effect of laser radiation. To characterize the endogenous chromophores involved in mechanism of photoeradication the spectral-luminescent studies of bacterial cell extracts were carried out.

3. Results

The results show that E. coli and yeast-like fungi C.albicans are the most sensitive to radiation with λ = 405 nm: the inhibition of their growth by 90% in comparison with the control population is registered at dose of 99 J/cm^2. At the same time, complete inhibition of mentioned pathogens is observed at a dose of 135 and180 J/cm^2, respectively. S. aureus is the most resistant to the action of aforementioned factor: the inhibition of growth by 90% in comparison with the control population is registered at dose of 366 J/cm^2. When exposed to light with λ = 445 nm, C. albicans appeared to be the most sensitive to the photodamage – the inhibition of their growth by 90% is observed at dose of 366 J/cm^2, whereas for S. aureus and E.coli - 606 and 609 J/cm^2, respectively. The comparison of effects of laser radiation with λ = 405 nm and λ = 445 nm shows that doses of acting radiation with λ = 445 nm initiating the inhibition of viability of microbial cells by 90% (in comparison to the control population) exceed the corresponding doses of radiation with λ = 405 nm in 3.7–6.2 times. Spectral-luminescent studies of bacterial extracts confirmed that porphyrin and flavin type endogenous chromophores are involved in mechanism of photoeradication. The highest ratio of porphyrin/flavin concentrations was observed in C. albicans extracts, significantly lower in E. coli; for S. aureus extracts (flavin fluorescence is well detected), porphyrin fluorescence is poorly detected. The porphyrin fraction is mainly represented by uro- and coproporphyrins. For the first time, the fluorescence of flavin photosensitizers in E. coli extracts was discovered.

4. Conclusion

We show that violet-blue laser inactivation of microorganisms is highly-efficient non-antibiotic approach to overcome the drug resistance problem.

Photobiomodulation in Medication related Osteonecrosis of the Jaws

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1. Introduction and Hypothesis

Osteonecrosis is a significant side effect of long-term medication therapy. It affects the quality of life due to the usual presence of infection and pain of the lesions. Besides bone necrosis, the loss of weight, low immune system and depression are common characteristics of these patients. Consequently, we should strive for early diagnosis and treatments including laser which is minimally invasive and highly effective.

Osteonecrosis affects two growing groups in society: osteoporotic elderly and oncological patients. Dentists should be aware of photobiomodulation as a tool in clinical practice due to its antibacterial and biostimulant effect on soft and hard tissues.

2. Methods

Five patients were treated according to the protocol: twice a week with low power laser (Therapy EC, DMC Equipamentos, LTDA, São Carlos, SP, Brazil), with power of 100mW, CW irradiation mode, single probe, spot size of 0.028 cm^2 , 3.5 W/cm^2 and contact mode.

For the lesion area, photodynamic therapy tecnique was performed using methylene blue at 0,005% during 1 minute applied on the lesion and posterior irradiation of the red wavelength (660 nm), 90 seconds of irradiation per point (every 1cm x 1cm), Dose (9 Joules per point), total Energy Density of 315 J/cm^2.

For the distal area, infrared wavelength (830 nm) was used as stimulation for hard tissue. The perimeter 1 cm far from the lesion was considered. It was used 30 seconds of irradiation every 1cm of this distal perimeter, Dose (3 Joules per point), total Energy Density of 105 J/cm^2.

3. Results

All patients had similar lesions size (2.0 to 4.0 cm^2) which were completely healed after a mean of 4.4 laser sessions with the detachment of the bone sequestrum. Four patients reported relief in pain (VAS scale) from 10 to 7 after the second irradiation. Furthermore, ingestion of solid nutrients was feasible. One patient achieved VAS 7 after 5 irradiations owing to the fact that she was the oldest in the group and used a poorly adapted lower denture.

4. Conclusion

It is blatant that laser therapy promotes an effective result in medication related osteonecrosis of the jaws. Therefore, the dentist plays a major role in this scenario: early diagnosis for laser conservative management and treatment of dental diseases which is a well established risk factor for osteonecrosis.

How Can Laser Act In Halitosis Treatment?

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1. Introduction and Hypothesis

Halitosis is defined as an offensive breath to others caused by periodontal disease, bacterial coating of tongue, xerostomia, systemic disorders and different types of food. Halitosis is an unpleasant condition that causes social restraint. Studies worldwide indicate a high prevalence of moderate halitosis, whereas severe cases are restricted to around 8% of the populations. The etiology of halitosis relates to the presence of odoriferous substances in exhaled air such as volatile sulphur compounds produced by bacteria. The organoleptic diagnosis is the gold standard and clinical management includes oral approaches, especially periodontal treatment and oral hygiene instructions, including the tongue. Nevertheless, Laser is a tool that can be accomplish in all these treatment phases enhancing the quality and time of treatment.

2. Methods

Patients were treated according to the protocol: once a week with low power laser (Therapy EC, DMC Equipamentos, LTDA, São Carlos, SP, Brazil), with power of 100mW, CW irradiation mode, single probe, spot size of 0.028 cm^2, 3.5 W/cm^2, contact mode.

For the anti bacterial effect on the tongue, photodynamic therapy tecnique was performed using methylene blue at 0,005% during 1 minute applied on the surface of the tongue and posterior irradiation of the red wavelength (660 nm), 90 seconds of irradiation per point (every $1cm^2$), Dose (9 Joules per point), Energy Density of 315 J/cm^2. A total of 6 points were irradiated per tongue.

For xerostomia, infrared wavelength (830 nm) was used to stimulate saliva production. Four groups of salivary glands were irradiated:

a. Sub lingual Gland
b. Sub mandibular Gland
c. Parotid Gland
d. Minor Glands

For the first 3 groups: each gland (left or right side) received 40 seconds of irradiation divided into 2 points of 2 Joules comprising a total Energy Density of 70 J/cm^2. The last group (minor glands) received irradiation of the red wavelength (660 nm), 05 seconds of irradiation per point (every $1cm^2$), Dose (0.5 Joules per point). A total of 6 points per area: tissue of buccal mucosa, tissue of the labial mucosa, the soft palate, the hard palate and the posterior floor of the mouth.

For emotional strain, Intravascular Laser Blood Irradiation (modified technique) was applied following the protocol of: minutes of irradiation equals patient's weight divided by two. The irradiation was performed with red wavelength (660 nm) at the wrist of the patient; preferably at point P6 of acupuncture for anxiety and stress relief.

3. Results

All patients benefited from the tongue biofilm desinfection. No plaque was observed after 2 sessions of PDT. Moreover, they reported relief in mouth humidity after irradiation of salivary glands and less anxiety after blood irradiation.

4. Conclusion

Although literature is scarse on this theme, dentists should overview laser as a complete tool for halitosis treatment since we can treat physical causes (biofilm and xerostomia) as well as aid the reduction on anxiety and stress. These are growing common symptons in society and it is notorius that when stressed, we are in lower immunity level and with scarse saliva. Both, cause halitosis.

The Photo Bio-Modulation Effect Of Diode Laser On The Tooth Sensitivity After In-Office Bleaching; A Randomized Double Blind Clinical Trial

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1. Introduction and Hypothesis

The aim of the present study is to assess the effect of diode laser (940 nm) irradiation on the tooth sensitivity reduction induced by in-office bleaching.Bleaching is the most popular method requested by people aiming to reduce tooth coloring and achieve a more pleasant tooth appearance; the most common side effect of In-office Bleaching in vital teeth is tooth sensitivity.

2. Methods

This randomized double blind split mouth clinical trial study was conducted on 30 volunteers who satisfied the inclusion criteria of the study. The bleaching was carried out using 35% hydrogen peroxide gel at one session and three 15-minute steps. Subjects were assigned to control and test groups in a split-mouth study design after bleaching. The test site (Maxilla or Mandible) was randomly determined and was irradiated by a diode laser with specific characteristics (940 nm wavelength, 1 W power, tip diameter 400 µm, continuous mode, non-contact and defocused, sweeping motion, at a distance of 5 mm, and 30 s irradiation time). Tooth sensitivity was assessed at time intervals of 1 h, 24 h, 48 h, and 7 days after bleaching in accordance with the Visual Analog Scale (VAS). ANOVA repeated measures, pairwise T-test, and latent growth curve model were used to analyze the results ($p < 0.05$).

3. Results

The results of the present study indicated in the time interval one hour after bleaching the difference between the case and control groups was not significant ($p>0.05$). However, the difference became significant in time intervals of 24 h, 48 h, and 7 days after bleaching($p<0.05$).

Pairwise comparison of case and control groups at various time intervals

4. Conclusion

Conclusion: According to the results of study, the photo bio-modulation after in-office bleaching can relieve tooth sensitivity.

Statement: the authors would like to acknowledge Hamadan university of medical sciences for the financial support of the present project. There was no conflict of interest to declare. This study has received ethical approve and registration from the International Center for Iranian Registry of Clinical Trials (protocol no. IRCT2017010231732N1).

Time interval	Group	Mean	Std. Deviation	p-value
1 h after bleaching	Case	2.4333	1.50134	0.056
	Control	2.8667	1.85199	
24 h after bleaching	Case	1.3667	1.24522	0.005
	Control	1.7667	1.40647	
48 h after bleaching	Case	0.4667	0.73030	0.002
	Control	0.9333	0.98027	
7 days after bleaching	Case	0.1000	0.30513	0.010
	Control	0.4000	0.56324	

Photobiomodulation Therapy In The Management Of Oral Lichen Planus: A Case-Control Study.

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1. Introduction and Hypothesis

Photobiomodulation (PBM) has been used in the last years for many diseases, also in the oral mucosa. Erosive lichen planus (eOLP) is a chronic painful condition affecting mucosal surfaces, and its management may be very challenging. This study aims to investigate if PBM can be useful in the management of eOLP in terms of oral ulcers extension and in terms of pain.

2. Methods

A case-control study was carried out. Patients with erosive oral lichen planus visited at the Dental Clinic of Brescia from June 2017 to January 2018 were enrolled. Patients were randomly divided into two groups: group A received cortisonic topical therapy (betamethasone 4mg/ 2ml, two rinses a day for two weeks) associated to laser therapy twice a week for two weeks; group B received just cortisonic topical therapy. For each patient, the size of the largest erosive lesion was taken (i.e area of lesion) at T0 (first visit) and T1 (after two weeks). Pain assessment was evaluated using a Verbal Rating Scale (VRS) where 1=no pain, 2=mild pain, 3=moderate pain, 4=severe pain. Device specifications: the laser instrument used for this trial was a diode laser device (class IV, K-Laser Cube series, Eltech K-Laser, Via Castagnole 20/H, Treviso, Italy), a portable and easy to handle device. The following laser protocol was applied: 660 and 970 nm-combined wavelengths, 3.2 W peak power, 320 mW/cm^2 irradiance, 32 J/cm^2 fluence per point. The overall treatment time was 100 seconds, divided into 10 phases of 100 seconds (10 points) each with the following frequencies modulation: 2 Hz, 10 Hz, 50 Hz, 100 Hz, 500 Hz, 2,500 Hz, 7,500 Hz, 15,000 Hz, 20,000 Hz, continuous wave. The spot size was 1 cm^2 . Laser application was performed over the entire oral cavity through a rotatory motion (defocused, non-contact modality), by maintaining the tip orthogonally with respect to the lesion.

3. Results

A total of 20 patients were included in the study, divided into group A (n=10) and group B (n=10). The difference in the decline of the areas of the erosive lesions between the two groups resulted not statistically significative. A statistically significative difference in pain reduction was observed.

4. Conclusion

Photobiomodulation therapy has demonstrated to have a positive effect in relieving erosive OLP pain.

Avaliação do Efeito da Fotobiomodulação Nas Glândulas Salivares Maiores de Pacientes Com Diabetes Mellitus e Xerostomia.

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1. Introduction and Hypothesis

Diabetes patients generally develop several systemic chronic complications that can be that presents oral manifestations such as: gingivitis; dental caries; periodontitis; opportunist infections and xerostomia. The glycemic decompensation of some patients can aggravate such manifestations. Saliva is widely used in the diagnosis of a variety of oral and systemic diseases and it is an essential fluid in health oral. The success of any dental treatment of these patients is closely related to the quantity and quality of saliva they produce. Although the standard treatment of the diabetes is well established, there is a need for further studies in relation to the treatment of salivary changes. The laser has shown satisfactory results in the improvement of salivary flow and consequently in the quality of life of patients with Sjogren syndrome and those submitted to chemotherapy and radiotherapy. In this work, we present our preliminary results on the photobiomodulation of salivary glands of diabetes patients.

2. Methods

51 diabetic patients and diagnosed with xerostomia were used for this work. After signing the Term of Informed Consent, anamnesis, physical evaluation, and questionnaires of self-perception of oral health and symptoms related to the function of the salivary glands were submitted, the subjects were randomly divided into two groups: Photobiomodulation (PBM) (n = 29); had major salivary glands irradiated and placebo (PCB) (n = 22), which were submitted to a simulation, where the application protocol was repeated, with the laser turned off. Sialometries were performed before and after treatment with a duration of 5 min to compare the volume of saliva. The protocol established for this study was 3 extra oral bilateral applications in the parotid, submandibular and sublingual glands, and 3 bilateral intraoral applications, using a Diode Laser (DMC® SP - Brazil), wavelength of 808 nm, power of 100 mW, 3.2J, 32s, continuous mode of operation, in a total of 12 points. the laser was applied in contact and the total radiated area was 0.336 cm^2/session. The irradiance was 3571mW/cm^2 and radiant exposure of 114J/cm^2. Each subject underwent one session per week during a month (4 sessions total). The total energy for each session was 38.4J.

3. Results

The preliminary results suggest that there was an increase in the non-stimulated and stimulated salivary volume of the patients who underwent photobiomodulation of the salivary glands, when compared, the final salivary volume was higher in relation to the initial volume, both in the non-stimulated and stimulated saliva. The placebo group did not show statistical differences when comparing the initial and final volumes of both unstimulated and stimulated saliva.

4. Conclusion

This work shows that this protocol of photobiomodulation of the salivary glands significantly increased the flow with four laser applications, but more studies are needed to better understand its effect.

Protobiomodulation Associated With Carbon Biomaterial May Improve The Bone Healing Process

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1. Introduction and Hypothesis

Bone diseases such as fractures and bone defects may result from several reasons, where the repair process is normally long and painful. The most used therapies are based either on the implantation of a biocompatible prosthesis or through the insertion of a biomaterial in the local injury. However, those treatments involve extended and costly surgical intervention. Thus, the association of two low cost techniques such as the use of activated carbon as bone biosubstitute and the application of the low-level laser therapy in order to assist the bone repair can be an alternative to overcome those problems.

The aim of this study was to verify the use of photobiomodulation therapy (PBMT) by low intensity laser associated with carbon biomaterial (AC) in the process of bone repair in rat tibias, assessing biochemical, histological and biomechanical changes.

2. Methods

The study was performed by induction of a bone defect in rat tibias and their subsequent treatment with AC and PBMT. Five different groups of rats were studied: control (CTL), untreated Injury (NT), Injured treated with activated carbon (AC), Injured treated with laser therapy (PBMT – 810nm; 6J; 100mW) and Injured treated with association of AC and laser therapy (AC+PBMT). All groups were evaluated by histological and biomechanical properties of bone after the healing process and by phosphatase alkaline level (ALP).

3. Results

The NT group presented lowest values of stress at break, besides histological changes related to disorganization of the tissue. Gradually, the groups PBMT, AC and AC+PBMT showed to improve their mechanical properties in comparison to CTL group. The group AC+PBMT presented the highest value of stress at break, organized histological aspects and increasing the levels of ALP.

4. Conclusion

Thus, the Photobiomodulation therapy association with activate carbon seemed to assist the process of bone healing in experimental model in rats tibia.

Evaluation Of Pain And Clinical Repair In Patients Submitted To Frenectomy By Diode (808Nm) Or Er,Cr:YSGG (2780Nm) Lasers Or By The Conventional Technique.

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1. Introduction and Hypothesis

The aim of this study was to make a quantitative evaluation of the pain level in patients, using the Visual Analog Scale (VAS), as well as the quantitative symptomatology and clinical repair in patients submitted to three different surgery techniques to perform labial frenectomy: employing Diode laser, Er,Cr:YSGG laser and the conventional technique performed with a scalpel.

Diode Laser (DMC São Carlos- Brazil). l808nm, continuous mode, P:2 W - 120 mJ, DE: 60 - 90J/cm^2 and 300µm laser fiber. The Incision was performed with the fiber in contact perpendicular to the sweeping movements until completely removed. Application of local ice for 5 minutes. A power and energy meter model 841-PE (Irvine, CA - USA) was used.

Er,Cr:YSGG model waterlase laser (Milenio, Biolase San Clemente, CA USA) l2780nm, pulsed mode, P:2W 100mJ-20Hz, DE: 79.6J/cm^2. 11% air cooling and 7% water, and handpiece with 9-4-400µm coupled sapphire tip. Incision and removal of tissue was performed with the laser tip 1mm away, always in the perpendicular without touching the tissue until its complete removal, after the procedure was applied local ice for 5 minutes. A power and energy meter model 841-PE (Irvine, CA - USA) was used.

2. Methods

After approval by the Research Ethics Committee of FOUSP all patients signed the Term of Free and Clarified Consent (TCLE). Eighteen patients indicated for frenectomy were randomly distributed into three groups by lottery. Surgeries were performed and the patients were clinically and visually evaluated by means of photographic analysis, by 3 calibrated examiners. The parameters analyzed were good, average or poor tissue repair. The Visual Analog Scale (VAS) was used to grade the post-operative painful symptomatology. Post-operative follow-up was rated according to immediate pain, and at time intervals of 72h, 1 week, 15 days and 1 month after the surgical procedure was performed. In the immediate clinical results, there was intense bleeding in the control group, and after 2 weeks, clinical repair in all groups presented gingival tissue with a healthy appearance, at the stage of epithelialization.

3. Results

There was no statistically significant difference among the groups considering pain and clinical repair. Tissue repair was similar in all groups, presenting a small significant difference when the Control Group and the diode Group were compared.

4. Conclusion

All techniques were effective in frenoplasty.The authors confirm that this article content has no conflict of interest.

Dose & Mechanisms

Analysis Of Photobiomodulation Transmission At Wavelengths 660 And 830 Nm In Experimental Skin Samples

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1. Introduction and Hypothesis

Among photobiomodulation application methods, the contact technique presents advantages by providing more power density in the target tissue, as it maximizes irradiance by reducing reflexion and consequently increasing penetration into tissues. Some of the therapeutic targets can be several centimeters deep, such as the muscles, tendons, pheripheral nerve and cartilage. This study aimed to analyze the the power transmitted low-level laser therapy (LLLT) into different tissue samples of rat and pigs using different wavelengths.

2. Methods

Tissues with different thicknesses (08 samples with 1,2 a 2,3 mm) were analyzed and interposed between the laser emitter and the power analyzer sensor. The samples were divided into the: rat skin 660 nm; rat skin 830 nm; pig skin 660 nm and pig skin 830 nm. All samples received one LLLT intervention using the equipment Laserpulse (Ibramed Equipamentos Médicos®, Amparo-SP, Brazil), single probe, 660 nm, 30 mW, continuous beam of 0.06 cm^2, 0.018 W/cm^2, with fluency of 20 J/cm^2, energy of 1.2 J, and exposure time of 40 s and another with 830 nm, 30 mW potency, continuous beam of 0.116 cm^2, 0.348 W/cm^2,, 20 J/cm^2, energy of 2,32 J, and exposure time of 77 s. Radiation transmission was measured by a power analyzer connected to a laser emitter with wavelengths of 660 and 830 nm and mean levels of 35,34 (±1,03) and 32,40 (±0,70) mW, respectively, previously calculated. All samples had a circular shape with a diameter of 80 mm, which allowed their attachment to the metal ring. All measurements of the thickness of biological tissues were performed with a micrometer (DIGIMESS, São Paulo, SP, Brazil) and caliper (DIGIMESS, São Paulo, SP, Brazil). Statistics were provided by Shapiro-Wilk test followed by ANOVA with Tukey post hoc for the values collected in the power analyzer, with a significance level of 5%.

3. Results

The findings indicate that all wavelenghts presented attenuation when applied on rat or pig skyn, with statistical difference in the intergroup comparison for practically all tissue thicknesses. The 660 nm presented major attenuation (over seventy percent) when compared with 830 nm and also was observed that with the increase of the tissue thickness, the greater the attenuation of the LLLT for all samples. Thus, new studies are needed to verify and to compare their effects when associated at different application protocols. Additionally, new pre-clinical and clinical trials are needed with rodents and pigs to translate the effects of LLLT for the human.

4. Conclusion

Tissue sample present variations in the energy transmitted by LLLT, depending on their structure and on the radiation wavelength. The 830 nm, usually presents de minor attenuation in the tissue models. It is recommended that the fluence rate to be applied on the body segments be corrected in consideration of the loss of transmission that occurs in different anatomical structures.

The The effect Of Low Level Laser Therapy (LPLT) on Bone Mineral Densitometry (BMD) and Bone Turnover Markers (BTMs) in individuals Complete Thoracic Spinal Cord Injuries (C.T.SCI) with Osteoporosis (Op).

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1. Introduction and Hypothesis

Op occurs as a result of an unconformity between osteoclast and osteoblast activiy.C.T.SCI results in prolonged limitation of both the loading and the movement of the lower limbs, this leads to marked inhibition of the osteoblasts, activation of the osteoclasts, an inevitable bone loss.Several studies have reported that LLLT positively affects on bone cells, but the complexity of the parameters involved in LLLT such: wavelength, fluence(J/cm^2), fluence rate(W/cm^2),pulse or continuous wavelength(CW), has meant that a number of negative studies. We hypothesized that LLLT delivering 830nm CW with optimal energy 4J/cm^2 on bone tissue might increase the bone metabolic activity to repair the bone Loss in C.T.SCI.

2. Methods

The present work is a prospective interventional study in individual C.T.SCI with Op.After baseline screening interview and BMD test, 32(4W,28M) individuals were diagnosed Op and of whom 8(3W,5M) patients were eligible and willing to participate voluntarily.BMD(g/cm^2) by Dual Energy X-ray Absorptiometry (DEXA), were reported in T-Score≤ -2.5 and Z-Score≤ -2 SD, at baseline measurement and at the 14thand 21th(Session) of the treatment and as well as 45 days(d) follow-up after last treatment on the four specific anatomic sites:The proximal Femur(PFe), the Distal Femur(DFe), Proximal Tibia(PTib) and Forearm.

The patients were irradiated by a semi-conductor GaAlAs(Gallium,Aluminium,Arsenide).delivering 830nm with the single probe,CW,0.237cm^2, spot area at the specefic anatomic sites written above. The dosage were designated by Power variety and Distance value(D) (the approximate depth of bone tissue from skin surface in centimetre(cm) to be treated), which was measured by Sonography. Optimal Energy on bone tissue were determined to be 4J/cm^2 by receiving different doses from skin surface: 8 (J/cm^2),19 Second(S),100(mW) for D<1(cm) and 12,16,20 (J/cm^2), 19,15,19, 24 S, 200(mW) for D=1-2, D=2-3, D>3 (cm) respectively. With treatment schedule of 3 time per week, for total of 14 and 21(Session) and Covered area of 24(cm) in 3 rows x 8 cm longitudinal for each region. BTMs were assessed by serum measurements of Osteocalcin(OCN) and Bone Alkaline Phosphatase(BAP) to considered a screening method for Op diagnosis before treatment, subsequent to monitoring bone formation after treatment.

3. Results

The BMD number in g/cm^2 at the PFe, DFe and Forearm at the 14th and 21th Session of the treatment and 45(d) follow-up were statistically increased compared with baseline(P<0.05).Although the BMD at the 21thSession increased significantly compared with baseline but decreased compared with the 14thSession(P >0.05). There was no significant differences the Laser effects on BMD at the PTib compared to baseline(P >0.05). Despite within the normal range of OCN and BAP in Op patients at baseline, LLLT effects associated with they both were not significant changed compare to the after last treatment(P>0.05).

4. Conclusion

Our present work provides the potential efficacy of local LLLT and a positive bio-simulative effect on bone healing and a biphasic dose response has been observed where LLLT at the 14th had a much better effect on stimulating and repairing than 21th Session but the determination of BAP, OCN as BTMs perhaps not to be a reliable screening method for Op diagnosis following to useful in monitoring bone formation to SCI.

How To Determine Clinical Protocols With Low Power Laser

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1. Introduction and Hypothesis

The determination of the protocol to be used in the clinical practice of laser therapy is one of the greatest challenges for health professionals.The difference of the phototype, the type of tissue and its depth, the stage of the lesion, among other characteristics make it necessary to individuate the protocol. On the other hand, dosimetry is one of the most divergent issues between clinicians and researchers. In this way, trying to bring scientific information closer to clinical practice, we present 10 steps that will help the health professional to determine the initial clinical protocol, taking into account the individual characteristics of each patient.

2. Methods

This methodology was developed in 10 years of teaching the Laser Training Course at São Leopoldo Mandic University in Campinas, SP, Brazil and applied in 40 classes between the years 2008 and 2018.

3. Results

The 10 steps consist in initially having the diagnosis of the lesion and observe the patient's local and systemic characteristics such as phototype, fat index, immunity, diseases and medications used. Followed by assessing aspects such as: target cell type, lesion depth, stage of injury, and possible light absorbers that hinder the arrival of the photons in the desired region. The form of irradiation is also taken into account: contact, away, punctual, scanning and respectively the result of each option in intensity (W/cm^2). Characteristics of the laser equipment, such as: wavelength (nm), power (mW) and spot area (cm^2), and the dose: a table with the main objectives of irradiation (regeneration, modulation of inflammation and analgesia) and target tissue types with their respective dosimetric window in Joules, guide the clinician to determine the initial treatment protocol. Methods to assess treatment progress and to modify the protocol if necessary are addressed in the final steps.

Joules table, per point of irradiation (based on 1 point/cm^2):

Purpose of irradiation x Type of Tissue	Regeneration	Modulation of inflammation	Analgesia
Skin and mucosa	0,2 – 1 J	1-3 J	>3
Muscles, glands, lymph nodes	1-2 J	2-4 J	>4J
Bones, nerves	2-3 J	3-5 J	>5 J

Modified table from: Meneguzzo, Daiane; Ferreira, Leila. Low-Level Laser Therapy in Dentistry. In: Michael R Hamblin and Ying-Ying Huang. (Org.). Handbook of Photomedicine. 1ed.: Taylor & Francis, 2013, v. 1, p. 653-662.

4. Conclusion

The 10 steps are straightforward simple and easy to use even by beginner laser therapists. Furthermore the application of the 10 steps by health professionals allowed a line of logical and common reasoning based on scientific information that was translated into better clinical application.

Effect Of Photobiomodulation Therapy On The Extracellular Matrix Of Human Dental Pulp Cell Sheets

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1. Introduction and Hypothesis

Photobiomodulation therapy (PBMT) improves processes relevant to tissue regeneration. The technique of cell sheets (CSs) can generate large amount of cells organized in an extracellular matrix (ECM) produced by these cells. The constitution of CSs ECM could be of importance for tissue regeneration. Type I collagen, fibronectin and tenascin are ECM proteins already detected in CSs of human dental pulp stem cells. The aim of this study was to investigate the effect of PBMT on the structural and ultrastructural characteristics of the ECM of dental pulp stem cells CSs.

2. Methods

Dental pulp stem cells were isolated and characterized by the expression profile of the surface molecules using flow cytometry for MSC-associated (CD105, CD146, CD44, STRO-1, Nanog and OCT 3/4) and non-associated (CD45 and CD14) markers. The CSs were formed in 6-wells plates after 13 days in culture in clonogenic medium supplemented with VC (20µg/ml). The wells were allocated in 3 different experimental groups, as follows: Control: no further treatment; PBMT1 and PBMT2. PBMT was performed with CW red diode laser ((PhotonLase III DMC - Equipment, São Carlos, SP, Brazil). The general parameters were: 660nm, 20mW, 0,028cm^2 spot size and 0.71W/cm^2. The PBMT1 parameters were: 4s, 3J/cm^2 and 0,08J per point, and the PBMT2: 7s, 7J/cm^2, and 0.14J per point. The irradiations were done on alternate days throughout the experiment period, in a punctual mode (5 points / well) in contact at the base of the plate. After the CS formation, 13 days after plating they were submitted to histology, immunohistochemistry (IHC), Western blot, transmission electron microscopy and scanning electron microscopy analyses. Statistical comparisons were performed ($p<0.05$).

3. Results

IHC revealed the presence of all proteins studied (e.g. type I collagen, type III collagen, fibronectin and tenascin). The results revealed changes in the patterns of distribution of collagen amongst the groups. Western blot revealed a tendency to a higher synthesis of type I collagen in the CSs submitted to PBMT.

4. Conclusion

PBMT may influence in the composition and ultrastructure of the ECM of cell sheets of dental pulp stem cells. Thus, PBMT could be of importance in the determination of the mechanical quality of CSs, which may favor cell therapy by improving the CS transplantation approach.

Microcirculatory Response To Photobiomodulation Is Dependent On The Baseline Skin Temperature: On The Way To Personalized Protocols – A Randomized Controlled Study

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1. Introduction and Hypothesis

Photobiomodulation (PBM) was shown to increase blood flow in healthy and diabetic subjects. In a previous randomized controlled trial (RCT) we found that 5 minutes of PBM irradiation in

either red or near infrared (NIR) had an immediate stimulative effect on the microcirculatory blood flow that remained high during 20 minutes follow-up as measured with laser doppler flowmetry and photoplethysmography. While the irradiation was on the wrist, response was detected downstream on the palm of the irradiated hand, but also on the contralateral non-irradiated hand. The objective of the current study was to further characterize the difference between the irradiated and non-irradiated hand also with thermal imaging.

2. Methods

Twenty healthy non-smoking volunteers without any known vascular pathologies were randomized to receive either red or NIR light. The light source was the OmniLux New-U (Photomedex, USA), cluster of LEDs (4X6 cm^2) that emits continuous irradiation in either 633 nm or 830 nm with power density (as measured with a power meter) of 70 mW/cm^2 (total energy per session 21 J/cm^2) or 55 mW/cm^2 (16.5 J/cm^2) respectively. A single session of 5 minutes irradiation was performed in direct skin contact over the wrist area. Capillary blood flow was measured continuously using Laser Doppler flowmeters placed on the palms of both treated and non-treated hands. Thermal images of both hands were taken every minute. Measurements were collected before irradiation, during irradiation, and for 20 minutes follow-up.

3. Results

Both red and NIR increased capillary blood flow and skin temperature as measured on the palm of the hand during irradiation (stimulation of blood flow relative to baseline, mean±SD [95%CI]: Red: 30±5% [9,70]; NIR: 90±10% [10,170], p=0.10 and p=0.027 respectively by 1-sample ttest). This increase remained up to 20 minutes after irradiation (Red - 40±6% [10,90]; NIR – 120±20% [40,110], p=0.07 and p=0.018 by 1-sample ttest with Holm's correction for multiple comparison of time points). The treated and non-treated hands were highly correlated in both wavelengths (Pearson correlation coefficient r=0.90 and r=0.87 for red and NIR respectively). There was no response in subjects with baseline skin temperature below 33˚C. However, when analyzing results of subjects with baseline skin temperature above 33˚C, we found a negative correlation between the change in temperature in response to PBM and the baseline skin temperature (ΔTemp [˚C]= -0.41×(baseline_temp)+15.5, r=0.83, p<0.0001).

4. Conclusion

Both red and NIR non-coherent light sources caused a vasodilative effects that enhanced downstream microcirculatory response both on the treated and the contralateral non-treated hand showing neural symmetrical involvement. Using thermal imaging, we found that PBM has a normalization effect on the microcirculation that is dependent on the baseline skin temperature. This individual response to PBM may pave the way to personalized protocols. Further studies investigating this effect on patients that have altered thermoregulation (i.e. diabetes and Raynaud) are warranted.

Statement: This study received an approval from the institutional ethics committee (www.clinicaltrials.gov registration#NCT03357523) as required. Subjects signed informed consent forms before any procedures. All the authors do not have any conflict of interest.

Musculoskeletal and Sports Medicine

Effect of low power laser therapy on lymphedema post mastectomy

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1. Introduction and Hypothesis

Lymphedema is the formation of a protein-containing fluid that accumulates under the skin due to decreased capacity of lymphatic system, leads to swelling and decreased function of the upper limb. The only standard method to control this complication is Combined Decongestive Therapy. In some countries, low power laser therapy is also used as a tool for managing lymphedema. The purpose of this study was to review published studies related to the effect of low power laser therapy on lymphedema post mastectomy.

2. Methods

Published studies from 2000-2018 were searched on the Google Scholar, Medlib, PubMed, Science Direct and Scopus databases. These keywords were used: low power laser therapy, lymphedema, Combined Decongestive Therapy, mastectomy. From the related articles, 8 articles were selected: 7clinical trials and 1 systematic reviews.

3. Results

Laser therapy may be effective in reducing the circumference and volume of the arm, pain, and increasing the tendency of breast cancer survivals to continue their treatment. The effectiveness of this modality is more attributed to pain relief and increased mobility of the limb. Therefore, its use can be suggested as an adjunct treatment beside the standard methods.

4. Conclusion

The results about its parameters are controversial so studies with proper design are needed to determine the exact parameters of low-power laser in managing lymphedema.

The Effectiveness Of Low Level Laser Therapy In Healing Of Partial Tear Of Supraspinatus Tendon

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1. Introduction and Hypothesis

The shoulder is a complex, multi-joint structure in the human body. It plays a significant role in

activities of self-care, work and leisure. Within the broad complaint of shoulder pain, rotator cuff disease (RCD) is the most common condition. RCD consists of tendinopathy, partial-thickness tears or full-thickness tears of the rotator cuff tendons. Low level laser therapy (LLLT) has been successfully used in various musculoskeletal injuries including tendon injuries. Its application is supported by experimental evidence of biological effects including increase in (collagen synthesis, adenosine tri-phosphate production, cell function, protein synthesis), reduction in inflammation and angiogenesis. Our main purpose was to heal partial tear of tendon with LLLT to provide cost effective and non surgical treatment to affected clients.

2. Methods

In this Single blind RCT, 72 patients with confirmed diagnosis ofpartial tear of supraspinatus tendon through musculoskeletal ultrasound (MSKUS) were randomly allocated into two groups by using a computer generated random sequence table with 36 patients in the experimental group (LLLT + Routine Physical Therapy (RPT) and 36 patients in the control group (RPT alone) as per CONSORT guidelines. Baseline assessment for supraspinatus tendon thickness and tear thickness were recorded using MSKUS before treatment. Experimental group received LLLT through Omega XP Model (Omega Laser System Pvt. Ltd., United Kingdom), Single-direct in-contact probe, pulsed mode with wave length of 820nm, power of 200mW, frequency 2.5Hz, power density 222mW/cm^2, energy density 6.7J/cm^2, spot size of 3mm (0.9cm^2), energy of 6 Joules for 30 seconds duration on seven points in the front of shoulder followed by 46-cluster-direct in-contact probe, pulsed mode with wave length and power of (10x15mW=660nm, 10x15mW=950nm, 10x26mW=870nm, 0x25mW=880nm, 5x25mW=940nm and 1x15mW=820nm), frequency of 2.5Hz, power density 95mW/cm^2, energy density of 11.4 J/cm^2, spot size of 10cm^2, total energy of 114 Joules for duration of 120 seconds as per WALT guidelines. All the patients received 18 treatment sessions over a period of 6 weeks (3 sessions per week) and 12 further sessions from 6weeks to 12 weeks follow up (2 sessions per week). At the end of six weeks and 12 weeks, both outcome measures were assessed again.

3. Results

Repeated Measure ANOVA revealed within groups, significant differences were found in the mean improvement in tendon thickness and tear thickness in experimental group both at 6 and 12 weeks follow-up. Non-significant differences were found in control group in both outcome measures at 6 weeks and at 12 weeks follow-up. An independent t-test revealed between two groups, at 6 weeks, significant differences were found for the mean improvement in tendon thickness except non-significant for tear thickness, whereas, at 12 weeks, significant differences were found in mean improvement for both outcome measures.

4. Conclusion

The findings of this study revealed that LLLT with RPT was more effective than RPT alone in the treatment of partial tear of supraspinatus tendon. Hence, LLLT is strongly recommended as treatment of choice for healing of partial tear of supraspinatus tendon. Inclusion of Placebo group, large sample size, use of different parameters of LLLT, cluster versus pencil probes can be future clinical recommendations.

Photobiomodulation in Patients with Low Back Pain: A Case Control Series for the Effect on Depression

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1. Introduction and Hypothesis

Patients with low back pain (LBP) frequently suffer from threshold depression. When comorbid, depression is often associated with more intense pain[and worsens LBP prognosis. Depression is linked to decreased mitochondrial respiration in blood platelets[. Consequently, it's speculated blood cells could be targeted as a systemic therapy for depression; suggesting possible whole blood involvement, such as mediating effects on organs, including the brain. Photobiomodulation (PBM) boosts ATP production by near infra-red (NIR) or red light, via mitochondrial respiratory chain stimulation. This case series of incidental findings on two LBP patient groups: Group-1, with clinical diagnosis of depression, scored highly for depression severity and received NIR and red-PBM from LED sources; Group-2, had high depression severity scores, but no clinical depression diagnosis and no PBM. Both groups received concurrent physical therapy. The study aim was retrospective testing whether NIR and red-PBM, over large skin areas to the back and thighs, decreased depression's severity.

2. Methods

A case-control series of five outpatients with LBP and concurrent self-reported depression is presented. Each patient was treated over 4-weeks for their LBP with physical therapy (PT 5-sessions) augmented with PBM (last 3-sessions only). Each patient was retrospectively matched, according to clinical and demographic variables, by five controls treated with PT alone (5-sessions).

Device: Thor-UK DDII, LED-104 instrument continuous output; red and NIR integrated LED cluster-probe.

Wavelength/power values respectively: 660nm (56 probes emitting 10mW) and LED=850nm (48 probes emitting 30mW). The total power=2 Watts, ~75% NIR/25% red light. Spot-size =20cm^2 (single spot-size1/e2=0.2cm^2). Total area treated=240cm^2: 12 symmetrical bilateral sites (20 cm^2 site): eight thoracic four posterior-thigh. Average irradiance=100mW/cm^2 /fluence=3J/cm^2.

PBM sessions=6 min (30sec/site for a total of 12 sites); NIR and red light were delivered over 14-18 days for three treatments at direct skin contact. The dose per session was 720 J (60 J/site). Depression was assessed with a one-question depression-scale (Orebro Musculoskeletal Screening Questionnaire, OMSQ-12 item #6). Functional status was assessed with a computerized outcome measure (Advise-Rehab Global Scale-ARGS).

3. Results

The two groups had non-significant differences at baseline, except for higher functional status (ARGS) in the PBM-group (33.6±12.2 vs.18.6±3.6, t(8)=2.638,p=0.030). After treatment, the mean decrease in depression scores (OMSQ-12 item #6) was significantly larger in the PBM-group (43.0±22.0 vs. 8.0±5.7, t(8)=3.449,p=0.009). Improvement in functional status (ARGS) in the PBM-group was similar to the controls (42.0±13.5 vs. 43.4±11.1,t(8)=0.179,p =0.862); suggesting group differences in antidepressant effect were independent of functional status improvements.

4. Conclusion

This clinical case-series presents incidental findings on the effects of PBM-therapy on problematic LBP patients with concurrent depression. PBM to large areas of the skin might have beneficial effects as part of a multi-modal treatment approach specifically targeted to depressed patients. However, in this case-control pilot study, PBM cannot be identified as the single-agent producing the psychological benefit, due to the above limitations in the design, and the findings must therefore be considered preliminary. Prospective randomized controlled trials are necessary to better characterize the efficacy of PBM in the population of our study.

As an retrospective de-identified study the Harvard University Medical Ethics Committee decreed no formal Ethics approval or individual consent, apart from an approval to use data, was required.

Antinociceptive Effect Of Light Emitting Diode Therapy Depends On The Descending Inhibitory Control

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1. Introduction and Hypothesis

Introduction: There are few scientific studies about the mechanism of action of LEDT in pain control, especially with regard pain. Objective: To investigate the possible activation of descendants inhibitory systems of antinociceptive effect of LEDT, through the model of nociception-induced acute cinnamaldehyde.

2. Methods

Experiment was approved by the USP's CEUA (131/17). Male Swiss mice (n=8), 2 months (25-35g) were submitted to LED (Anodyne® device, infrared light 890nm, 20.8J/cm^2, 390mW, 17.3mW/cm^2, 468J, 22.5cm^2, pulsed energy: 292Hz, 20min) applications. The pad light-emitting diode was positioned below the acrylic testing platform (10×4.5×4cm), and infrared radiation was directly applied to the total ventral side of the animal without shaving. For all the experiments, single pretreatment was done and the time of paw licking and biting was evaluated. Pharmacological interactions were managed via intrathecal (5µL) and evaluated in the model of nociception induced by cinnamaldehyde in paw. Opioidergic system, pretreated with naloxone (a nonselective opioid receptors antagonist, 20µg/i.t.), CTOP (a selective µ-opioid receptor antagonist, 150pmol/i.t.), serotoninergic sytem WAY100635 (a selective 5-HT1A receptor antagonist, 10µg/i.t.), ketanserin (a selective 5-HT2A receptor antagonist, 10µg/i.t.), noradrenergic system phentolamine (a nonselective α-adrenoceptors antagonist, 1µg/i.t.), prazosin (α1-adrenoceptor antagonist, 20µg/i.t.) and yohimbine (α2-adrenoceptor antagonist, 20µg/i.t.), gabaergic system bicuculline (a selective GABAA receptor antagonist, 0,5µg/i.t) and phaclofen (a selective GABAB receptor antagonist, 0,5µg/i.t) and dopaminergic system haldol (a nonselective dopamine receptors antagonist, 1nmol/i.t.) or saline 5, 10, 15, 5, 5, 5, 5 and 15 min, before the application of LED, respectively. The animals were submitted to immunohistochemistry and immunofluorescence for the analysis of c-Fos protein in the dorsal horn of the spinal cord, periaquedutal gray matter (PAG), Raphe magnus nucleus (RMg) and Locus coeruleus (LC).

3. Results

LEDT reduced nociception caused by cinnamaldehyde ($p<0.0001$), however the antinociception caused by LEDT was significantly prevented by pretreated of mice with naloxone ($p<0.001$), CTOP ($p<0.001$), WAY-100635 ($p<0.0001$), ketanserine ($p<0.0001$), phentolamide ($p<0.001$), prazosin ($p<0.001$), yohimbine ($p<0.01$), bicuculline ($p<0.0001$), phaclofen ($p<0.01$) and haldol ($p<0.0001$). As to the expression of c-Fos protein, cinnamaldehyde promoted an increase in its expression in the dorsal horn of the spinal cord ($p<0.0001$), an attenuated alteration by treatment with LEDT ($p<0.0001$). LED promoted the increase in its expression in the PAG ($p<0.0001$), RMg ($p<0.0001$) and LC ($p<0.0001$).

4. Conclusion

Results obtained in the present study provide scientific evidence that some of its neurophysiological mechanisms are mediate by interaction of the main endogenous systems of pain control that contribute to explain its therapeutic potential.

Dose: 468J; Energy Density: 20.8J/cm^2; Power: 390mW; Power Density: 17.3mW/cm^2; spot size: 22.5cm^2, pulsed energy: 292Hz; wavelength: 890nm.

Photobiomodulation improves neck range, pain and function three years post cancer radiation and chemotherapy – an N=1 study

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Co-Authors: C.P. Gabel; Coolum Beach, QLD/AU

1. Introduction and Hypothesis

The determination of the effectiveness of any intervention on the symptoms and functional status of chronic neck pain (CNP) is particularly difficult, and Photo-Bio-Modulation (PBM) is no exception. The presence and impact of CNP on the daily lives of individuals is critically recognised as among the leading causes of global disease burden, however minimal progress has been made in the identification of effective intervention strategies. Investigations of monotherapy interventions through N=1 studies enables the provision and indications of the potential effectiveness of such interventions, one of which is PBM. The therapeutic effectiveness of PBM on CNP has been recognised by systematic reviews (Chow et. al LANCET 2010) in terms of pool effect and prospective studies. However these do not map and track individual progress or show the immediate effects at the clinical level nor which patient reported outcome (PRO) measures can provide the most effective quantification of change. This N=1 study assesses the effectiveness of PBM 3-years post neck/throat-cancer with chemo/radiation therapy and significantly reduced range and function. This loss had remained despite trialed manual therapy, massage and medication interventions. Trial PBM was sought as a 'nothing to lose' option.

2. Methods

Case-control, n=1, study, 63 year-old male. Chemo/radiation-therapy had left notable neck soft-tissue tightening with significant loss of range, function and subsequent pain. Four treatments over three weeks at day-1, -3, -8, -15 were provided with the Thor-UK:DDII, LED-104 Cluster-Probe near-infrared (850nm) and red (660nm) light, irradiance 100mW/cm^2 and fluence 3J/cm^2 on three sites of the anterior and lateral neck for 120 sec/site; followed cluster-probe 5x200mW 810nm Ga-Al-Ar 60-sec/site, 15 sites. The LED was used first for photo-bleaching. Assessment was made for rotation and lateral-flexion, function measured with five-outcomes: spine functional index short-form-10 (SFI-10), numerical rating scales for function (NRS-F) and pain (NRS-P), patient specific index (PSI) and Advise Rehab Global Scale (ARGS) software – this was the most accurate/sensitive and used for final functional status reports. The 'difference-between-means' statistic was used to assess change.

3. Results

Patient function and range was self-assessed as static over the preceding 2-years: rotation 40-degrees, lateral-flexion 5-degrees functional-status ~48%. Limited change occurred over the initial 3-days post treatment-1, improved notably by 1-week (post treatment-2 and 3) and continued till day 12 then regressed. Treatment at day-15 stopped regression, function and range were regained and improved within 24-hours. The 'difference-between-means' statistic showed statistically significant improvement of 200% in range and function.

4. Conclusion

This case-control, n=1, study demonstrates that PBM for neck/throat-cancer chemo/radiation therapy with chronic loss of range and function can be modified and significantly improved within 3-weeks and 4-PBM sessions. The statistical assessment indicates real change and a therapeutic effect. This supports known PBM effects for chronic-neck conditions management but higher PBM doses are required.

Statement: Patient written consent was provided and the data de-identified with all clinical aspects.

An N=1 Study Of Photo-Bio-Modulation As A Monotherapy That Resolved Low Back Pain In An Elite Master's Surfer

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1. Introduction and Hypothesis

Low back pain, particularly non-specific (NS-LBP), is among the leading causes of global disease burden, yet there is little progress in identifying effective intervention strategies. Investigations of monotherapy interventions through N=1 studies can provide indications of the potential therapeutic effectiveness of such interventions. Photo-Bio-Modulation (PBM) is one such intervention but is limited in quantifiable results, dose and wavelength specifics. The N=1 study initiates the evidence pyramid providing quantifiable data leading to future investigations. This N=1 Study investigated monotherapy PBM effectiveness on chronic NS-LBP in a specific demographic example.

2. Methods

A healthy 56-year-old male graphic-designer and surfer with chronic NS-LBP was an N=1 prospective investigation. Referred with GP-diagnosed NS-LBP of 2-year graded onset and worsening left-lateral LBP radiating to the buttock and upper leg. Symptoms affected lifestyle, work, sleep and particularly surfing so intervention was sought. XR showed degenerative changes at L3-4/4-5 left facets. Several interventions had provided temporary relief including activity/technique modification, strength and flexibility, manual therapy, acupuncture, electrotherapy and PRN medications. Initially PBM was sequentially introduced as part of multi-modal intervention approach using a Thor-UK:DDII, LED-104 Cluster-Probe near-infrared (850nm) and red (660nm) light, irradiance 100mW/cm^2 and fluence 3J/cm^2 on three sites of the anterior and lateral neck for 120 sec/site; followed cluster-probe 5x200mW 810nm Ga-Al-Ar 60-sec/site. The subject noted substantial improvement including an initial immediate analgesic effect and subsequent ongoing relief. Concurrent interventions of exercise, manual and other therapies were sequentially eliminated to leave only PBM. Symptoms were measured through a Computer Decision Support System (CDSS) using an Advise Rehab Global Scale (ARGS) of function (MDC90=5%), composed of an algorithm driven by scores from pain, activity and specific spine functions, on a percentage scale of ability ie 100%=Maximum/Normal function.

3. Results

baseline andretrospective quantification of status were consistent with the reported history (months 0-12). Status showed mild temporary improvements with various interventions over 4 weeks but was not significantly improved or sustained till PBM was introduced (month 13). Status increased as had occurred previously but to a higher level and for greater duration, with the latter being sustained as concurrent modalities were removed. Frequency of therapeutic PBM intervention was reduced from 3-2-1x weekly then fortnightly and monthly to 6-weekly, 13 treatments over 5 months, till discharge in April 2018. The status improvement was significant, exceeding MDC90 by 10 fold and was sustained in comparison to previous status responses to therapeutic intervention.

4. Conclusion

A healthy 56yo male surfer with an ongoing history of LBP, referral and significant lifestyle affected changes regained normal functional status over a 6 month period with 13-laser therapeutic sessions over 20 weeks as the main causal intervention. This quantified change was statistically significant, the PBM intervention was considered the sole specific affecting therapy and the 'settings' used can provide a starting point for further prospective investigations through cohort and eventual RCTs.

Statement: Patient written consent was provided and the data de-identified with all clinical aspects.

Comparing The Effects Of Low Level Laser Therapy And High Voltage Pulse Current On Pain And Effusion In Patients With Anterior Knee Pain

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1. Introduction and Hypothesis

Introduction: Anterior knee pain is one of the most common musculoskeletal disorders. Knee effusion occurs in the knee injuries and surgeries frequently.

Methods: 40 subjects randomly were assigned to two groups: low level laser therapy (LLLT) and high voltage pulse current (HVPC). Pain and effusion were recorded by VAS and tape measure respectively. All outcomes were evaluated before treatment and after sessions 5, 10 and 1 month follow-up.

2. Methods

Device specifications:

- Manufacturer, location and model number: CARCI,Brazil,4098 – Probe Design: single probe
- Wavelength/s: 905nm
- Power: 50mW
- Power Density: 263mw/cm^2
- Spot size or area of irradiation:.19 cm^2
- Pulsing or duty cycle if use: Pulsed
- Energy Density: 8J/cm^2
- Energy per point / area: 3.04J

Treatment specifications:

- Treatment Time (sec): 600s
- Frequency of treatments: Daily
- Total number of treatments: 10
- Technique used: Direct in-contact probe
- Area(s) treated: local.
- Location and number of points.2 points posteromedial aspect of knee and 8 points med/lat. knee

3. Results

Demographic and quantitative variables were not significant before treatment. (LLLT: age: 45.84±13.69, weight: 78.68±15, height: 161.68±8.76. HVPC: age: 51.96±11.53, weight: 76.00±10.66, Height: 159.43±7.172). The repeated measures ANOVA analysis (2*4) showed that interaction of group and time were not significant for pain and effusion (P>0/05). The main effects of group and time were statistically significant for pain and effusion (p <.001). Independent t-test revealed that there was significant differences between two groups at follow-up (P=0/02).

4. Conclusion

Although both LLLT and HVPC showed major short-term improvements in outcomes, the long-term effects of LLLT were better than HVPC in patients with with anterior knee pain.

Statements: The patients filled the consent form. There was no any Conflict of interest for the present study.

Level Of Pain, Muscle Strength And Functional Capacity On Association Of An Exercise Program And Photobiomodulation In Women With Knee Osteoarthritis

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1. Introduction and Hypothesis

Degenerative chronic diseases have been more frequency with the aging population, as the osteoarthritis (OA). About 10% of people with above 55 years old showed knee OA pain and inactivation, primarily women. In the context, no-pharmacologic treatments as exercise and photobiomodulation (PBM) showed efficacy. Thus, the aim of this study was to evaluate the effects of PBM and exercise program on pain, muscle strength and functional capacity in knee OA women.

2. Methods

A randomized double-blind study. Sixty-two participants with knee OA (with confirmed radiological diagnosis) were evaluated for this study. However, thirty-four women between 55 and 70 years old with knee OA (II and III grade) was considered eligible, and were randomized into two groups: EPPG - Exercise and PBM Placebo Group (n = 17) and EPAG - Exercise and PBM Active Group = 17), one participant was excluded of EPAG. The interventions were realized 2x/week in a period of 8 weeks. With an exercise program (warm-up, resistive exercises and stretching) and the PBM (Cluster Physio Lase; DMC®, São Carlos, SP, Brazil) with follow parameters: continuous wave 850nm, power 100mW, Direct in-contact probe, 7 points of the synovial region of the medial side of the knee and in 7 points on the lateral side, total 56J per knee, 40 seconds per application). The outcomes before and after intervention, West Ontario and the McMaster University Osteoarthritis Index (WOMAC), 1-repetition maximum test (1-RM) and Six minute walk test (6MWT), were used to analyze the effect of the treatments.

3. Results

When comparing groups, had a significant increase of the hip abductors 1-RM ($p = 0.005$) in EPAG. In intragroup analysis, a significant improve in pain WOMAC ($p = 0.001$), stiffness ($p = 0.001$) and function ($p = 0.001$), Hip Flexors 1-RM ($p = 0.001$), Hip Extensors 1-RM ($p = 0.001$), Knee Flexors 1-RM ($p = 0.001$), Knee Extensors 1-RM ($p = 0.001$), Hip Adductors 1-RM ($p = 0.001$) and 6MWT ($p=0.001$).

4. Conclusion

The exercise program used in this current study was effective in improve pain, enhancing muscle strength and functional capacity. Also, the exercise program associated with PBM intensified the strength gain of the hip abductor muscles and produced a clinical improvement for the other muscles evaluated and functional capacity. Thus, it is necessary to perform future studies to investigate the effects of different PBM parameters and it association with exercise programs on patients with OA.

The authors would like to inform that there was no conflict of interest. We would like to acknowledge São Paulo Research Foundation (2016/08503-0) for the financial support of this research.

Effectiveness Of Intra-Articular Triamcinolone Injection Compared With Laser Phototherapy In Treatment Of Temporomandibular Joint Disorders.

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1. Introduction and Hypothesis

There are various surgical and non-surgical treatment methods for Temporomandibular joint disorders(TMD). Successful use of Laser phototherapies with their bio stimulatory, analgesic and anti inflammatory properties, has attracted attention for their potential use as a non invasive treatment for TMDs. In this study the effectiveness of intra-articular Triamcinolone injection and 940nm diode laser therapy in the treatment of TMD were comparatively evaluated.

2. Methods

This study was a randomized clinical trial approved by the university's ethical commitee, 66 patients with bilateral chronic TMD, were randomly divided into two groups after signing an informed consent. One group received an intra-articular injection of 0.5 ml Triamcinolone acetonide (Bristol-Myers Squibb Co, Princeton, NJ, USA, Kenalog 40) in each side, and the other group received laser therapy on both sides using a 940nm Diode laser (Epic10, Biolase, USA). We used a novel combination protocol of high intensity laser irradiation in the first session and low intensity laser therapy in the following 8 sessions every other day for two weeks. The parameters were measured and applied as follows,first session: 4W, CW, 150sec, 600J in each side, using a single probe, therapy hand piece with 15mm spacer distance from skin and a spot size of 1.76cm^2 the handpiece was moved in a circular area of 3cm radius from the condylar head irradiating an area of 28.26cm^2 with an Energy density: 21.23J/cm^2. Flowing sessions:0.5W, CW, 50sec, 25J per point, using the therapy hand piece in contact with skin(0.78cm^2) Power density: 0.64W/cm^2 in five points on the condylar head and four directions around it for 50 sec in each point, Energy density per point:32J/cm^2. Patients' pain score(using visual analog scale), maximum mouth opening, click on opening and closing the mouth, and the amount of mandibular deviation from midline in the two groups were recorded at baseline,one week and one month after treatments. Data was analyzed by SPSS software version 21 at 95% confidence level($P<0.05$).

3. Results

In the Triamcinolone and laser therapy group, the mean and standard deviation of pain scores were 6.33 ± 2.19 and 5.36 ± 2.42,($P = 0.097$) at base line, 4.12 ± 2.60 and 2.27 ± 2.08($P = 0.002$) after one week and 2.69 ± 2.07 and 2.39 ± 2.14($P = 0.560$) after one month. Maximum mouth opening in the Triamcinolone and laser groups before and after the intervention were 21.42 ± 4.97 and 26.02 ± 6.80($P = 0.003$), 25.39 ± 5.11 and 30.58 ±5.73($P <0.001$) after one week and 27.81 ± 5.43 and 32.18 ± 5.57($P = 0.002$) after one month. Intragroup differences from base line and one week and one month were statisticaly significant for both($P<0.001$). There was no statistically significant difference between the groups regarding click sound and deviation from Midline. No side effects were reported.

4. Conclusion

Base on our results using a this protocole of laser irradiation can be as effective as Triamcinolone acetonide injection in reducing pain, improving maximum opening, reducing click sound and mandibular deviation from Midline. The decrease in pain after 1 week follow-up, seems to be higher in the laser group.

Comparison Of The Effectiveness Of Photobiomodulation (PBM) On Equine Muscle Soreness Between Class Iii And Iv Lasers And At High And Low Doses.

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1. Introduction and Hypothesis

PBM is an expanding field and recent human studies focus on its effects to reduce muscle soreness and delayed onset muscle soreness following exercise. From a previous systematic review, the author had no knowledge of such studies carried out in animals, specifically the equine species. This investigation aimed to compare two doses from Omega (3458, Essex, UK) Class III and a Celtics ASA Veterinary Orange Class IV (20987, Pembrokeshire, UK) devices to determine if PBM had any effect on equine exercise-induced muscle soreness (EIMS).

2. Methods

A randomised crossover Latin square design was used with five horses. Pressure algometry tested nociception of 5 points on both sides of the horse located across the biceps brachii, longissimus dorsi, and gluteus medius muscles. A baseline reading was taken prior to an underwater treadmill session as a controlled exercise protocol (CEP), 20 minutes with water to the level of the lateral styloid process. Treatment groups received laser intervention immediately before CEP whilst the control group received sham laser. A further four days of data collection followed the exercise day with recordings taken at the same time. A 2-week washout period was implemented between treatments.

A cluster probe (5 diodes) was used for the class III, and a single diode for the class IV, both in direct contact application. The class III used 820nm, 0.125cm^2, 200mw (total 1W), 250W/cm^2, 1000Hz at a low dose ([CL3_L] 8J, 25s, 40J/cm^2) and high dose ([CL3_H] 24J, 75s, 120J/cm^2). The class IV used 808±5nm and 905±7nm, 3cm^2, 1.2W, 600W/cm^2, 1000Hz, 75% intensity at a low dose ([CL4_L] 8J, 17s, 2.61J/cm^2) and high dose ([CL4_H] 24J, 50s, 7.69 J/cm^2). Device parameters were obtained from the manufacturers and dosages calculated. A two-way repeated measures ANOVA was used to test the significance of treatments, with studentized residuals to check for outliers.

3. Results

Points 1, 2 and 3 (gluteus medius) showed a significant 2-way interaction between time and treatment, F (16, 464) 2.506, ($p<.005$). At 24 hours post-exercise, all doses improved compared to control, however, only CL4_L ($p<.005$) and CL4_H ($p<.05$) doses showed a positive significant difference. Furthermore, at 48 hours post-exercise only the CL4_H remained positively significant ($p<.05$) compared to control.

4. Conclusion

Overall PBM has shown possible inhibition of equine EIMS in the gluteal region, with both class IV doses showing significance. There is speculation from this study that different doses and devices may be required in different locations in order to provide optimum results. This follows patterns in human studies, who also found increased performance following PBM, but this was not measured in this study.

There were limitations to this study as horse activity and coat colour varied (all had dark skin), with one horse clipped. No previous research of the effects of PBM on equine EIMS, dosages had to be speculated from human research, possibly affecting their efficacy.

PBM could be a treatment to inhibit equine EIMS, but more studies on action and dosage parameters are required.

Combined Intra-articular Laser and Platelet Rich Plasma (PRP) Injection Reduces Pain in Patients Who Had Failed Prior PRP Treatment

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1. Introduction and Hypothesis

Platelet Rich Plasma (PRP) injections reduce pain in most but not all arthritic patients.However, for patients who fail PRP treatment, no good alternative is currently available except total joint replacement surgery. Low level laser therapy (LLLT) on the surface of the skin has not been helpful for arthritis patients in our experience.However, we hypothesized that intra-articular laser treatment used together with PRP would be an effective augmentation to PRP injection alone and would increase the efficacy of PRP in patients who had failed prior PRP injection alone.

2. Methods

We offered Intra-articular Low Level Laser Therapy (IAL) in conjunction with repeat PRP injection to patients with OA whose joint had received no benefit from PRP alone. Each patient had 30 minutes of IAL treatment with two intra-articular laser probes. They represented the treatment group. There was no charge for the PRP or IAL for the first 30 patients while efficacy was being evaluated. Subsequent patients were charged only for the PRP but not the IAL. 39 patients (41 joints) were treated. 28 knees: 4 hips, 4 shoulder gleno-humeral joints, 3 first Carpometacarpal joints, one midfoot, and one ankle were treated. Each patient was evaluated prospectively at six months and 1 year follow-up.

Device specifications:

- Weberneedle® Combilaser (Lauenförde Germany) – Single probe
- Wavelengths: 405/635/810nm
- Power: 0.1W
- Power Density: 0.25 W/cm^2 (mfd)
- Area of irradiation: 4 cm^2 (mfd)
- Pulsing/duty cycle: None
- Energy Density: 0.000028 J/cm^2 (mfd)
- Total energy: 0.000112J (mfd)

Treatment specifications:

- Treatment Time: 10 min per wavelength or 30min total – Frequency of treatments: 1
- # of treatments: 1
- Technique: two intra-articular laser probes
- Area treated: local
- Location/# of points: 2
- Treatment pattern: Sequential
- Human treatment: Intraarticular

3. Results

No adverse events were seen. Six months post treatment, 31 of 41 patients (77%) were available for follow up. 15 of 31 (48%) had good outcomes at 6 six months.28 of 33 (85%) were available at 1 year. Of these, 7 had a good outcome (25%) at 1 year without further treatment in all but one patient. Patients were separated into 2 groups. Group 1 patients had severe bone on bone arthritis, group 2 had significant joint space remaining.. There were 15 patients in each group. 33% of Group 1 patients were improved at 6 months and 0% were improved at 1 year. 60% of Group 2 patients were improved at 6 months and 54% were improved at 1 year. There was a significant difference between the 2 groups at 1 year (p=0.005).

4. Conclusion

A single treatment of IAL in addition to PRP produced good results in almost half of patients who had failed prior PRP treatment alone for six months.Of the patients with mild or moderate OA. 60% had good results for six months and 54% had good results at one year. This is the first report showing clinical benefit from IAL treatment and the first to show augmentation of PRP effects by the addition of IAL.

Dose And Time Response For Photobiomodulation Of Chronic Low-Back Pain Patients: Randomized, Crossover, Double-Blind, Placebo-Controlled Clinical Study

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1. Introduction and Hypothesis

Chronic low-back pain can be defined as a continuous pain with the same intensity lasting for more than 3 months, also causing functional disabilities. More than 10% of the world's population suffer from low-back pain and make use of anti-inflammatory and painkiller drugs to alleviate its symptoms. However, prolonged drug use may cause adverse effects such as hepatotoxicity. Photobiomodulation therapy (PBMT) has been effective to control pain in several anatomical situations, but there are no studies reporting its dose and time effects to promote pain relief and reestablish functional capacity in chronic low-back pain patients. Thus, the aim of this study was to evaluate the effects of three PBMT doses on pain intensity and functional disability in chronic low-back pain patients during the 24 hours after application.

2. Methods

This randomized, crossover, double-blind, placebo-controlled clinical study enrolled 10 volunteers (6 women; 4 men; 39±12 years; 74±9 Kg; 26±3 Kg/m2) diagnosed with chronic low-back pain. Volunteers were assessed for pain intensity by visual analogue scale (VAS), functional disability by Oswestry Disability Index (ODI) and Roland Morris Disability Questionnaire (RMDQ). There were 3 regimens of PBMT (dose response): 1) Real PBMT with a low dose of light (50J; 1.2 J/cm^2; 37s); 2) Real PBMT with a high dose of light (500J; 12.5 J/cm^2 ; 365s) and 3) Placebo PBMT (0J; 0 J/cm^2; 100s). PBMT was applied in continuous mode using a cluster of 69 light-emitting diodes (LEDs; 1,370W; 34.25 mW/cm^2;40cm^2) containing 35 red LEDs (630±10nm; 10mW each) and 34 infrared LEDs (830±20nm; 30mW each) placed over the dorsal root ganglion on the lumbar 2 vertebra (L2) bilaterally in contact mode; delivering 100, 1,000 or 0 Joules per session. All volunteers were assessed at 5 time points: 1) pre-PBMT or placebo; 2) 1 hour later; 3) 3 hours later; 4) 6 hours later and 5) 24 hours after PBMT or placebo. All PBMT parameters were measured and calibrated by a power and energy meter (PM100D, Thorlabs).

3. Results

Data normality was assessed by Shapiro-Wilk test, and all treatments were compared by ANOVA with Tukey's post-hoc test. Regarding pain intensity, PBMT 500J significantly decreased pain ($p<0.01$) from 3 to 24 hours (-26±13 mm) compared to placebo (-5±4 mm), while PBMT 50 J significantly reduced pain ($p=0.01$) from 6 to 24 hours (-24±19 mm). PBMT (50J and 500J) significantly decreased ODI ($p=0.03$) by -9% compared to -2.5% (placebo), and RMDQ by -3.8% ($p=0.04$) compared to -1% (placebo) after 24 hours.

4. Conclusion

Both PBMT 500J and 50J promoted pain relief and improved functional capacity in low-back pain patients with a dose and time response compared to placebo therapy. PBMT 500J was slightly more effective to promote pain relief than 50J per site of irradiation. Statements: All procedures were approved by human ethics committee of the Sacred Heart University, Brazil (opinion n-2.402.414) and conducted in this university. Informed consent was obtained from all individual participants included in the study. This study was supported by research grant 2017/18722-3 from Sao Paulo Research Foundation—FAPESP. The authors declare no conflict of interest.

Low-Level Laser Therapy Can Reduce Knee Osteoarthritis Pain And Disability: A Systematic Review And Meta-Analysis Of Randomized Placebo-Controlled Trials

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1. Introduction and Hypothesis

Whether low-level laser therapy (LLLT) is effective in knee osteoarthritis (KOA) has been evaluated in other recent meta-analyses, but they included relatively few relevant trials and did not account for important differences between continuous and pulsed laser.

2. Methods

We performed a systematic review with meta-analysis of randomized placebo-controlled trials published in any language from database inception until 12th February in PubMed, Embase, CINAHL, PEDro, and, Cochrane Central, with KOA participants reporting pain, self-reported disability and/or quality of life assessments following LLLT. The trials were subgrouped using the World Association for Laser Therapy (WALT) guidelines for dosage per treatment spot (assumed adequate LLLT / assumed non-optimal LLLT). The review procedures are registered with PROSPERO (code CRD42016035587).

3. Results

Of 1827 publications, 19 trials were included (958 participants). Compared with placebo, significantly more pain was reduced by LLLT at completed therapy (14.51 mm VAS [95% CI: 7.04 to 21.97]) and at follow-up 2-12 weeks after completed therapy (16.32 mm VAS [95% CI: 5.74 to 26.91]). The subgroup analyses demonstrated larger differences in pain reduction significantly in favour of assumed adequate LLLT over placebo at completed therapy (19.1 mm VAS [95% CI: 9.16 to 29.03]) and at follow-up 2-12 weeks after completed therapy (26.24 mm VAS [95% CI: 11.75 to 40.73]). Compared with placebo, significantly more disability was reduced by LLLT at completed therapy (SMD = 0.57 [95% CI: 0.28 to 0.86]) and at follow-up 2-12 weeks after completed therapy (SMD = 0.57 [95% CI: 0.11 to 1.04]). The subgroup analyses demonstrated larger differences in disability reduction significantly in favour of assumed adequate LLLT over placebo at completed therapy (SMD = 0.72 [95% CI: 0.4 to 1.03]) and at follow-up 2-8 weeks after completed therapy (SMD = 1.32 [95% CI: 0.8 to 1.83]). Quality of life was only assessed following assumed non-optimal LLLT and was not improved. No adverse events were reported.

4. Conclusion

LLLT can reduce KOA pain and disability with doses per treatment spot recommended by WALT. The effect profile show the greatest pain reduction 4 weeks after completed therapy and that a perceptible pain relief is maintained even 3 months after completed therapy.

Neurorehabilitation

Photobiomodulation for Parkinson disease: from Preclinical Datas Toward A Clinical Trial

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1. Introduction and Hypothesis

Parkinson's disease (PD) is a neurodegenerative disorder due to the progressive death of dopaminergic cells. Nowadays, only symptomatic treatments are available, but they do not reliably slow the progression of the disease. Thus, there is a large need for new therapeutic strategies, particularly those that offer neuroprotection.

Photobiomodulation (PBM) has been reported to be effective in various PD animal models. It improves locomotor activity associated with a neuroprotective effect as determined by rescue dopaminergic cells. These data confirm a real potential for the development of light therapy as a novel neuroprotective strategy.

To this aim, we developed and qualified an intracranial implantable device delivering light. Here, we will present preclinical data supporting the hypothesis of intracranial PBM therapy for PD.

2. Methods

We used acute neurotoxine rodent and non human primates models of PD. Animals were illuminated extracranially using Quantum WARP 10 device, or intracranially using a specifically developed implantable device. The efficiency of PBM, and induced changes were analyzed on animal's behavior follow up, and histology. Depending on protocols, illumination was internal (tip diameter 300µm, targetting subtancia nigra compacta) or extracranial (full head illumination, unshaved). We used wavelength of 670 or 810nm, with a power density from 0.16mW to 10mW (depending of administration mode). Energy density was from 0.5J/cm^2 to 4J/cm^2. Illumination length was from 90 sec (once or twice a day) to continuous.

All experiments were approved by the animals ethics committee COMETH and the French ministry of research.

3. Results

We observed a neuroprotective effect of PBM, whatever the administration mode, in a dose dependent manner in the range of light treatment efficiency. We did not observed toxicity to brain tissue.

4. Conclusion

Within limitations of acute animal models of PD, our preclinical studies support the neuroprotective potential of PBM for PD. It helps surrounding translation to an imminent clinical trial.

Shining Light Into The Human Parkinsonian Brain: A Single Case Study Of The Short-Term Effects Of PBM On Non-Motor And Motor Outcomes

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Introduction:

Parkinson's disease (PD) is the second most common progressive neurodegenerative disorder with movement (motor) decline and non-motor symptoms such as cognitive effects and sleep disturbance. PD is not curable and the cause is not clear although it develops as a result of nerve degeneration in the substantia nigra. One hypothesis is that PD develops because of mitochondrial dysfunction. One proposed mechanism of photobiomodulation therapy (PBMt) is stimulation of mitochondrial action by the absorption of photons in specific transmembrane proteins (cytochrome c oxidase), resulting in a range of physiological effects that may be beneficial to cerebral function. We set out to determine whether PBMt might influence non-motor and motor effects in PD in the short term.

Methods:

A single case study design was applied to evaluate effects of PBMt delivered via home application device (Vie Light). A 74 yr old male volunteer with PD diagnosed (9 years) by a neurologist and stable on medications (Stalevo) with no other co-morbidities volunteered for this study. Non-motor and motor outcome measures were observed using the MDS-UPDRS tool (5-point scale) with four parts: 1. ''nonmotor experiences of daily living,'' 2. ''motor experiences of daily living,'' 3. objective ''motor examination,'' and 4. ''motor complications.'' Other objective measures were TUG, 10MWT, spiral drawing test, 9-hole peg test, and balance tests. All measures were evaluated in an "Off" stage of medication and collected by a trained/certified nurse and physiotherapist before and after intervention. PBMt intervention was the VieLight device: 1/daily (20min); 6 x/week; over a 4-week period.

Device specifications (as provided by manufacturer):

- VieLight Inc, Toronto, Canada; Neuro Gamma
- Probe: Single (nasal, posterior head x 3, anterior head x 1)
- Wavelength: 810nm LED
- Power: 25mW (nasal); 100mW (posterior); 75mW (anterior)
- Power Density: 25mW/cm^2; 100 mW/cm^2/diode; 75mW/cm^2
- Spot size: 1cm^2 per diode
- Pulsing: 40Hz; 50% duty cycle
- Energy Density: 15J/cm^2; 180 J/cm^2; 45J/cm^2

Treatment specifications:

- Treatment Time (sec): 1200
- Frequency of treatments: 6 days / week
- Total number of treatments: 24
- Technique used: Transcranial
- Area treated: Scalp - Default mode network
- Location and number of points: nasal x 1 point, posterior head x 3 points, anterior head x 1 point

Results:

The four UPDRS parts compared between beginning and end of the 4-week treatment phase demonstrated trends of improvement towards more normal scores in each part. Objective measures of TUG, 10MWT, spiral test, 9-hole peg test, dynamic standing balance did not show any significant difference. Self-reports suggested that changes were appearing in the final week of treatment.

Conclusion:

PBMt appeared to influence some aspects of non-motor and motor function in a 4-week program, however, this did not translate to objective improvements of function. Further testing of a longer time frame is planned and may establish if a threshold of dose is required to illicit substantive positive change.

Statements: Human Research Ethics Committee approval obtained from Griffith University (No:2017/1019). Participant provided informed, written consent. Purchase of the device used in this study was supported by a research discount from supplier.

Multi Organ Failure Inflammatory Response And The Potential Role Of Photo-Bio-Modulation

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1. Introduction and Hypothesis

Post-injury Multiple-organ failure (MOF) results from systemic hyper-inflammation. Prevalence has increased as critical care capacity and technology improved over the last four decades and patients no longer succumb to single-organ failure. The understanding of MOF syndrome from epidemiological and pathophysiological perspectives has progressed resulting in improved treatment, intervention strategies and significant subsequent reductions in mortality and morbidity. However MOF remains the leading cause of late post-injury deaths and extensive resource requirements. Currently there is no specific treatment available apart from supporting the failing individual organs. In contrast photo-bio-modulation (PBM) therapy through Near-Infra-Red (NIR) produced through light emitting diode (LED) and low level laser therapy (LLLT) sources has known effects on inflammation, lymphatic drainage, neural tissue and may positively influence MOF.

Hypothesis: That PBM would positively influences the MOF syndrome symptoms through subcellular to system effects.

2. Methods

This concept paper introduces a new and potentially life-saving use of PBM therapy for MOF syndrome.

3. Results

The PBM therapy may affect the known physiological contributors to MOF through potential positive modification of selectively targeting organ and cellular activity that is deficient or overactive. This includes full body skin exposure or blood irradiation that would target the blood, lymphatics and neural tissue as systemic therapy in the initial 48-72 hours post-trauma. This would potentially facilitate general tissue and cellular mitochondrial ATP production reducing tissue inflammation through actions on the cytochrome C-oxidase via the blood, lymphatics and neural activity centrally-peripherally.

The Dose Response Effects Of Low Level And High Power Laser Therapy On Motor And Sensory Nerve Conduction Velocity Of Median Nerve In Subjects With Moderate Carpal Tunnel Syndrome

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1. Introduction and Hypothesis

There has been few research about the effects of laser therapy on changes in the activity of neuronal cells. Some have reported changes in neuronal activity, and some have not shown any effect. The key to laser treatment is to pay attention to dosage.

2. Methods

98 subjects with moderate carpal tunnel syndrome(CTS) randomly assigned to 5 groups including: group A (GA): Usual physiotherapy+Exercise+LLLT(n=20, 50 mw, 8 j/cm^2) group B (GA): Usual physiotherapy+Exercise+LLLT(n=19, 50 mw, 20 j/cm^2), group C (GC): Usual physiotherapy + Exercise + HPLT(n=20, 1.6 w, 8 j/cm^2), group D (GD): Usual physiotherapy + Exercise + HPLT(n=20, 1.6 w, 20 j/cm^2), group E (GE): Usual physiotherapy + Exercise(n=19). Amplitude, latency and area of median motor and sensory nerve action potential were evaluated in all participants' before treatment and after 21 days of the last session by electromyography.

Device specifications:

- Manufacturer, location and model number (LLLT: Carci, CARCI,Brazil,4098. HPLT: Pagani, 60825, IEC)
- Probe Design – cluster / single probe (LLLT: Single probe, HPLT: Scanner) – Wavelength/s: 905 nm, 808 nm
- Power: (LLLT: 50 mw, HPLT: 1/6 w)
- Power Density: 263mw/cm^2, 160mw/cm^2
- Spot size or area of irradiation: (LLLT: 0/19cm^2, HPLT: 10 cm^2)
- Pulsing or duty cycle if used: (LLLT: 10 H, HPLT: 80 % DC)
- Energy Density: (LLLT & HPLT: 8, 20 j/cm^2)
- Energy per point / area (no. of areas) or total energy – Joules (LLLT: 9/6 and 24 j, HPLT: 160 and 400 j)

Treatment specifications:

- Treatment Time (LLLT: 32 and 80 s per points, HPLT: 100 and 250 s) – Frequency of treatments: 3/week
- Total number of treatments: (5 sessions)
- Technique used: Direct in-contact probe OR scanning technique: (LLLT: Direct, HPLT: Scanning)
- Area(s) treated: (LLLT: 0/19 cm^2, HPLT:10 cm^2)
- Location and number of points: (LLLT: 10 points, HPLT: Scan area) – Grid pattern/sequential treatment: (LLLT: contact, HPLT: scan)

3. Results

The mixed-model ANOVAs revealed a significant group-by-time (5*2) interaction (F = 34.03, p <.001) for latency and amplitude of motor and sensory nerve action potential. The main effects of group and time were statistically significant for all measures in laser therapy groups (p<0/05). There were not any significant differences in mentioned variables in usual physiotherapy group (p=0/46). The results of post-hoc bonferroni analysis showed that the significant differences in variables were in GC group (p=0/03).

4. Conclusion

Both LLLT and HPLT are effective in changing electromyographic parameters of median nerve in CTS patients. HPLT with low energy density is more beneficial in improving median nerve characteristics measured by electromyography. Statements: All patients filled the consent form. This project was supported by Guilan University of Medical Sciences.

4. Conclusion

Therapeutic PBM may induce physiological effects that enable blood targeted systemic therapy for MOF patients. This could be performed through techniques such as blood irradiation or skin exposure as achieved by whole body exposure at doses and wavelengths that can be speculated. This speculative beneficial PBM therapy may enhance the natural physiological effects that are overwhelmed, inefficient or downregulated in the MOF patient. Statements No ethics approval was required as this is a concept article, no conflict of interest is present for any author.

Effect Of Photobiomodulation In The Treatment Of Complex Regional Pain Syndrome - Type I: Experimental Model In Mice

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1. Introduction and Hypothesis

Complex Regional Pain Syndrome - Type I (CRPS-I) is defined as an extreme pain situation, associated with neurovegetative, sensory and motor disorders, in which there is no nerve damage. Among the electrophysical agents, the low level laser therapy (LLLT) is highlighted in the complementary treatment of CRPS-I. This study aimed to analyze the effect of photobiomodulation (LLLT) on Regional Complex Pain Syndrome - Type I, induced in an animal model of ischemia-reperfusion.

2. Methods

An experimental study (approved by the Ethics Committee of the Universidade Federal de Santa Catarina) composed of 24 Swiss mice, divided into: Naive, Sham, Control and 660 nm. CRPS-I was induced by an experimental model based on ischemia-reperfusion (IR). The animals were evaluated for mechanical hyperalgesia, thermal heat hyperalgesia, paw edema and spontaneous locomotor activity at baseline and after 4, 7, 14 and 21 days of the syndrome induction. The animals on Naive Group did not receive any type of intervention. The Sham Group animals were only anesthetized, whereas the Control Group was submitted to the experimental protocol of IR. The 660 nm Group was submitted to the experimental protocol of IR and treated with photobiomodulation using the diode Arsenide of Gallium Indium Phosphorus (Ibramed Medical EquipmentTM, Laserpulse, Amparo, Sao Paulo, Brazil), single probe, 660 nm, 30 mW, continuous beam of 0.06 cm^2, 0.018 W/cm^2, with fluency of 10 J/cm^2, energy of 0.6 J, and exposure time of 20 s. A single point on the the right hind paw dorsum was irradiated with direct contact from the point probe to treat the local area. LLLT irradiation was performed immediately after induction of CRPS-I and treated once daily for a period of 21 days, totalizing 12,6 J of treatment. The Two-Way ANOVA with post-hoc Bonferroni test was performed using Graphpad Prism version 6.01 (Graphpad software, Inc. La Jolla, California, USA) for data analysis. Significance values were defined as $p < 0.05$.

3. Results

In Mechanical Hyperalgesia, the 660 nm Group presented a significant improvement ($p < 0.05$) when compared to the Control, on the 7th, 14th and 21th evaluation days. In Thermal Hyperalgesia the 660 nm Group achieved a significant improvement on the 21th day in relation to Control group. Regarding edema, the 660 nm Group presented statistical significant reduction ($p < 0.05$) in the 14th and 21th evaluation days, when compared to the control. In the locomotor activity there was no statistical difference among the groups.

4. Conclusion

LLLT, in the used parameters, was effective in reducing hyperalgesia and edema in a type I CRPS model.

Laser Magnetic Implantation /LMPL/ In Spinal Cord Traumas - Fundamental Field For "Re-Creation" Of Neural Tissue Via Non-Surgical Means. Extended Clinical Results. Control Over The Process-Recreation-First Generation Apparatus. After WALT 2002, Japan, 4th World Congress.

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1. Introduction and Hypothesis

LMPL-in essence the positioning of the lesion (vacuum of particles carriers) in the range of a field (Laser, electromagnetic or combined) is Implantation of matter (rarefied to an uttermost degree) into another type of matter, leading to histological changes in the latter. The histological changes are a visual result of the visible partly energy-informational interactions. The lesion consist mostly of fields which exist separately from the particles carriers (the natural electromagnetic fields of the healthy conductivery tissue cease their dynamics after the trauma) ; they don'the have flow, cyclic functions and feedback..This in essence, is rarefied matter, comparative to vacuum. The interaction among the fields leads to their condensation and moving away from the previous degree of thinning out. Matter is re-created, but some is also destroyed. Other outside fields are absent(or we don't know about them) with the exception of the earth's gravity and the direction of its lines of force.

2. Methods

For a Laser effect Power-75-375mw, envelopmenot up to 9MHz, lambda -820-875nm -For a magnetic effect: 60000 A/m, frequency- 0-100Hz. -For a combined effect-their combination.

3. Results

a. Total number of cases-53
b. Grouping by diagnosis
    i. Group A- Contagious et compressio medullae spinalis, laessio partialis.
    ii. Group B- Contusio et compressio medullae spinalis, laessio totalis.

These groupsigns are divided into subgroups depending on

- the prescription of the trauma.
- the type of trauma (mechanics of the blow, damaged structures.)
- the histological changes at an early stage.
- the histological changes at a later stage.

4. Conclusion

The Laser and the magnetic field have to a high degree a similar effect over the neural tissue. Their combination leads to a greater effect compared to their individual use. The magnetic field allows for a more global treatment of the tissues and the organism and a more powerful attack on the secondary complications. The effect on blood circulation is powerfull. The Laser beam, with its valuable reflection when passing through differently optical tissues, can reach finely inside the micro spheres of the neural tissue and is almost a like in characteristice with the neural impulse.

Photobiomodulation Treatment On Facial Paralysis

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1. Introduction and Hypothesis

Dose 6J (3 J 808nm + 3 J 660nm), Energy density of 100J/cm,2 Power 100mW, Power density of 3,3 W/cm^2, Spot size 0,03 cm^2 Irradiation in continue mode, with a single probe and direct in-contact, aproximately 70 points of irradiation.

2. Methods

Methods: This clinical study is a placebo-controlled, randomized and triple-blind. Two groups, test (laser) and control (placebo), after ten session of placebo or photobiomodulation, were compared though measurement of some lines, before and after treatment: bipupilar line till eyebrown line; medium line face related to medium lips line, palpebrae aperture degree before and after treatment, distance between upper and lower lip on the palsy side. Patient asymmetries was analysed with a digital ruler, before and after, using Keynote (Apple Inc, California).The laser device used for irradiation, Therapy XC (DMC, São Carlos, SP, Brasil) was a diode. Spot size 0,03 cm^2, Power density of 3,3 W/cm^2, Energy density of 100J/cm^2; 3J of 606nm (100mW of power) and 3J of 808nm (100mW of power), so in total 6J at the same time each shot in a single probe for 30 seconds in continue mode and direct in-contact), on the facial nerve path, approximately 70 points. The treatment was twice a week, during 10 weeks. Placebo group received shots of a laser just with guide light (power off). At the end, control group received laser treatment.

3. Results

Test group had significant differences compared to controlled group.

Group		Media	Standart Deviation	p-diferences
Control (Placebo)	Before	2,950	,4970	,317
Control (Placebo)	After	3,117	,3371	,317
Test (Laser)	Before	2,950	,6124	,046
Test (Laser)	After	3,400	,5477	,046

Wilcoxon Signed Rank test*

4. Conclusion

The laser protocol of 6J (3J 808nm with 3 J 660nm) was effective on facial paralysis treatment.

Photobiomodulation on the Acute Stroke Setting

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1. Introduction and Hypothesis

Introduction: Intravenous Thrombolysis for Acute Stroke has been a problematic therapy since it's approval twenty years ago. The limited time for a therapeutic window, the availability of a stroke specialist and resources and the complexity of the eligibility criteria may be factors that can limit it's use. Photobiomodulation is a novel treatment which can be offer safely to an acute stroke patient due to the lack of adverse side effects. Here we present a small series of acute stroke patients who received photobiomodulation during the first 72 hours after an acute ischemic stroke followed with a treatment per week on each consecutive week after the treatment.

2. Methods

Methodology: An HNC Laser equipment from China was used. A probe with mixed therapeutic wavelengths, 11 laser diodes with 650 nm 5 mW and 4 laser diodes with 808nm 180 mW, with a total maximum power 775mW, with a power density of 9.87 mW/cm^2. Continuous cycle was applied transcranially at both transtemporal windows and the sub-occipital area at the base of the skull. Five treatments were offered to each patient; first two treatments inside the hospital, followed by one treatment per week for the next three weeks. Each treatment lasted 15 minutes.

3. Results

Results: Improvement was observed on the clinical neurological outcome (NIH Stroke Scale) and neuro-imaging of the four patients.

4. Conclusion

Conclusion: Acute ischemic stroke patients may benefit of photobiomodulation therapy with laser. A longer period of time than the calculated for the irradiated area can be required due to cerebral characteristics of the brain during ischemic stroke. Also, patients may benefit of an immediate photobiomodulation treatment during the first day of the acute stroke phase followed by other treatments during the subacute phase.

PBM Delivery

Welcome to the State of the Art, Dosage, Devices and Safety

Dr. J.C. Castel
Carewear Corp. Reno NV USA

Objective:

This presentation will consist of three sections. The first section will focus on a discussion of relevant Photobiomodulation parameters and terminology, as well as common errors and issues in reporting optical parameters associated with PBM treatment. The fact that researchers and clinicians rely on manufacturers for optical parameters often leads to incorrect reporting of dose. Power, Energy, Irradiance and Fluence must be correctly described as well as time domain parameters, surface area to be treated, treatment time, timing of the application, and application method. A discussion of measurement and reporting methods will take place during the session. Optical parameters relevant to PBM such as wavelength, reflection, refraction and scattering at tissue interfaces – and how they may impact treatment outcomes – will be presented. The dual effects of PBM including thermal and sub-thermal will be addressed, as well as the difference in delivering the same fluence in a long or short period with lower or higher irradiance.

The second section will focus on delivery systems for PBMT. This will address PBMT applications with point stimulation, cluster probes, light panel stimulation, percutaneous, transcranial delivery systems, and wearable light therapy. The third section will feature a discussion of the latest safety considerations and precautions relative to the clinical provision of PBM therapy.

The presentations will involve audience participation on an interactive basis.

PBM in Cancer Supportive Care

Three years of clinical routine use of PBM in the management of cancer-therapies' side effects at the "Centre de Haute Energie", Nice (France). Treatment parameters and clinical results for each type of side effect.

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1. Introduction and Hypothesis

In photobiomodulation, the body is locally irradiated by visible red light or invisible near-infrared. It might look like this, though the beam size (1mm2 - 32cm^2) and other parameters (wavelength, intensity, energy, number of sessions) vary a lot. The light is usually produced by a laser or LED device. Unlike common lamp light, in photobiomodulation light is monochromatic , consisting of one wavelength. Some of the most common wavelengths are presented below.

Common wavelengths in photobiomodulation

Visible red / Near-infrared (NIR). Near-infrared penetrates the tissue better than red light, so it's more commonly used for treating body parts that are under the skin (brain, glands, joints, muscles). Visible red light is more commonly used in the treatment of wounds or skin diseases.

2. Methods

Treatment parameters

A lot of photobiomodulation research focuses on the various parameters such as wavelength, energy density and treatment time. The following table provides the basic information about the most relevant treatment parameters. Low-to-moderate doses of light are often described as stimulating and high doses as inhibitory , because some markers that can be increased by low doses of light, have been shown to decrease with excessive light doses. The exact mechanism of biphasic dose-response is not known, but it might be related to excessive formation of reactive oxygen species (ROS).

3. Results

(1) Red light and near-infrared irradiation produce measurable changes locally in cells/tissues/organs. This form of light therapy is called photobiomodulation (PBM).

(2) Animal studies show that photobiomodulation therapy could be beneficial for over 90 different diseases.

4. Conclusion

Evidence from human studies is emerging in a fast pace. Over 2000 photobiomodulation papers have been published in PubMed, over 120 of which have a good impact factor. Research has been conducted in more than 40 different countries. We present data of 3 years of routine practice at the CHE (Nice France).

The effect of tissue thickness and skin colour on the penetration of 850nm LED light transmitted through the human cheek to the oral mucosa

Mr. Wayne J. Selting
Consultant (United States)

Mr. James D. Carroll
THOR Photomedicine Ltd. (United Kingdom)

Background:

Oral Mucositis, is the most frequent complication of radiotherapy, chemotherapy or HSCT treatment in cancer patients with an incidence in paediatric patients ranging from 52% up to 80%. To date, there is no standard therapy for mucositis management; the treatments are mainly supportive and palliative. There is growing evidence that Photobiomodulation is effective in both the therapy and prevention of mucositis.

Since lesions are located on the surface of the oral mucosa, the usual mode of application is intraoral. The ulcerations are extremely painful, and the simple task of retracting tissue to access the surface for treatment can be very painful.

Devices are now being developed to apply energy extra-orally requiring photons to pass through the skin and buccinator muscle of the cheek in order to reach the buccal mucosa. Reflection, scattering and absorption may make tissue thickness and skin colour significant factors affecting power density reaching the target tissue.

Objective:

To measure the irradiance of 850nm LED light transmitted through cheek to the oral mucosa in patients with different Fitzpatrick skin types and different cheek thickness.

Materials and Methods:

42 patients-of-record from a private paediatric and orthodontic practice (32 children age 8 through 18, ten adults age 19 through 60) were recruited assigned a score based on skin pigmentation using the Fitzpatrick skin type scale and tissue thickness was recorded at the center of the cheek and 5mm from the commissure. A THOR Photomedicine LED array consisting of 69 emitters (850nm, 65mw/cm^2) was applied to the external cheek. The power density of the energy passing through to the intraoral mucosa was recorded.

Results:

A total of 506 measurements were taken, 63% of applied power density never penetrated the tissue, the average cheek thickness was = 6.6mm, and percentage transmission at 850 nm = 13.4% at the buccal mucosa

Conclusion:

Penetration of therapeutic light is very strongly related to tissue thickness, and the relationship is logarithmic. Skin pigmentation did not significantly affect the power density of light transmission at 850nm and firm surface pressure decreases tissue thickness thereby enhancing light transmission to the buccal mucosa.

Effect Of Low Power Laser Therapy On Lymphedema Post Mastectomy

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1. Introduction and Hypothesis

Lymphedema is the formation of a protein-containing fluid that accumulates under the skin due to decreased capacity of lymphatic system, leads to swelling and decreased function of the upper limb. The only standard method to control this complication is Combined Decongestive Therapy. In some countries, low power laser therapy is also used as a tool for managing lymphedema. The purpose of this study was to review published studies related to the effect of low power laser therapy on lymphedema post mastectomy.

2. Methods

Published studies from 2000-2018 were searched on the Google Scholar, Medlib, PubMed, Science Direct and Scopus databases. These keywords were used: low power laser therapy, lymphedema, Combined Decongestive Therapy, mastectomy. From the related articles, 8 articles were selected: 7clinical trials and 1 systematic reviews.

3. Results

Laser therapy may be effective in reducing the circumference and volume of the arm, pain, and increasing the tendency of breast cancer survivals to continue their treatment. The effectiveness of this modality is more attributed to pain relief and increased mobility of the limb. Therefore, its use can be suggested as an adjunct treatment beside the standard methods.

4. Conclusion

The results about its parameters are controversial so studies with proper design are needed to determine the exact parameters of low-power laser in managing lymphedema.

Photobiomodulation Potentiates Cisplatin Toxicity On Epithelial Cell Lineages

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1. Introduction and Hypothesis

Cisplatin plays a central role in cancer chemotherapy, but drug resistance remains a major obstacle in the treatment response. This study investigates the effect of photobiomodulation therapy on the cisplatin treatment on oral keratinocytes (HaCat) and oral squamous (SCC25) and upper aerodigestive tract (HN12) carcinoma cells.

2. Methods

Cells were irradiated twice (T1 and T2) with a single probe diode laser (Photon Lase III, DMC LTDA, model #PL7092, São Carlos, Brazil) at 660nm; 60mW; 0.33J; 2.14W/cm^2; 11.7J/cm^{2}and

6s (one point/0.32cm^2) and treated with cisplatin (7.8µg/ml), according to the groups: C1L0 (cisplatin+ irradiation-), C0L1 (cisplatin- irradiation+) and C1L1 (cisplatin+ irradiation+). Firstly, cells were submitted to T1. Immediately after irradiation, cisplatin was added to the cultures for 24h. Then, cisplatin was replaced by regular medium and T2 was performed. Cell survival (1h, 12h and 24h after T2); expression of vascular endothelial (VEGF), transforming beta (TGF-β1) and endothelial (EGF) growth factors; as well as ki67 and caspase-3 protein expression were evaluated. Type of cell death and ATP quantification were assessed exclusively on SCC25 cells. Data was analyzed by ANOVA followed by Tukey's post hoc test at a significance level of 5%.

3. Results

Cells presented increased sensitivity to C1L1 treatments, particularly 24h after T2 ($p<0.05$). C1L1 treatments also decreased VEGF and TGF-β1 expression in HaCat cells ($p<0.05$). Cancer cell lineages presented no expression of VEGF and unaltered TGF-β1 and EGF expression profile in C1L0 and C1L1 groups in comparison to the controls. The cell cycle marker ki67 was increased in all cell lineages of C1L1 groups, as well as caspase-3, which also presented greater expression in the C1L0 group ($p<0.05$). SCC25 cell lineage data showed that C1L1 treatments led mostly to apoptosis, with greater consumption of ATP ($p<0.05$).

4. Conclusion

Laser potentiates the cytotoxicity of cisplatin possibly due to the increased cell cycle arrest and ATP bioavailability, culminating in significant cell death.

Photobiomodulation Therapy Prevents Severe Acute Radiodermatitis In Breast Cancer Patients (Transdermis trial)

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1. Introduction and Hypothesis

To investigate the efficacy of photobiomodulation therapy (PBMT) in the prevention of acute radiodermatitis (ARD) in breast cancer (BC) patients.

2. Methods

A randomized, placebo-controlled trial (RCT) with 120 BC patients undergoing RT was performed. Patients were assigned to the control (n=60) or PBMT group (n=60). PBMT or placebo was applied 2x/week, starting at the first day of RT. Skin toxicity was clinically evaluated by the Radiation Therapy Oncology Group (RTOG) criteria and objectively by biophysical skin measurements. Measures were collected at baseline, a dose of 40Gy, and end of RT (66Gy).

Device specifications

Manufacturer	ASA srl
Location	Arcugnano (VI), Italy
Model number	M6 MLS® laser
Probe Design – cluster / single probe	IR laser diodes Three emitters spaced 2 cm apart in a triangle pattern
Operating mode	Continuous pulsed wave mode
Wavelengths	Continous: 808 nm Pulsed: 905 nm
Power	3.3 W
Power Density	0.168 W/cm^2
Spot size or area of irradiation	19.625 cm^2
Duty cycle	50 %
Energy Density	4 J/cm^2
Total energy	78,5 J

Treatment specifications

Area(s) treated	Whole breast, inframammary fold, axilla
Treatment Time	Whole breast: ±420-720s Inframammary fold: ±103s Axilla: ±68 s
Frequency of treatments	2x/week

Total number of treatments	14 sessions
Technique used	Scanning modus
Grid pattern/sequential treatment	Sequential treatment

3. Results

At the end of RT, the incidence of ARD ≥G2 was significantly higher in the control than in the PBMT group (p=0.004, Fig.1). The objective skin measurements confirmed these clinical results by demonstrating that the mean percentage change from the baseline transepidermal water loss (TEWL), erythema, and melanin value was significantly higher in the control than in the PBMT group at the end of RT (Ps<0.05, Fig.2)

4. Conclusion

This is the first RCT demonstrating by a clinical and objective approach that PBMT is effective in preventing high grade ARD in BC patients.

Photobiomodulation therapy for the prevention of acute radiation dermatitis in head and neck cancer patients: preliminary results of a randomized controlled trial (DERMISHEAD trial)

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1. Introduction and Hypothesis

The purpose of this study was to investigate the effectiveness of photobiomodulation therapy (PBMT) for the prevention of acute radiation dermatitis (ARD) in head and neck cancer (HNC) patients undergoing radiotherapy (RT).

2. Methods

This is a preliminary analysis of a randomized, placebo-controlled trial with 34 HNC patients (n=17 in each group) who underwent RT with or without concomitant chemotherapy. Patients were randomized to receive PBMT or placebo from the first day of RT (2x/week). The severity of ARD was assessed by the criteria of the Radiation Therapy Oncology Group (RTOG) at baseline, dose of 40 Gy and end of RT (60-70Gy).

Device specifications

Manufacturer	ASA srl
Location	Arcugnano (VI), Italy
Model number	M6 MLS® laser
Probe Design – cluster / single probe	IR laser diode - handpiece
Operating mode	Continuous pulsed wave mode
Wavelengths	Continous: 808 nm Pulsed: 905 nm

Power	3.3 W
Power Density	0.168 W/cm^2
Spot size or area of irradiation	3.14 cm^2
Duty cycle	50 %
Energy Density	4 J/cm^2
Total energy	12,56 J

Treatment specifications

Area(s) treated	Head and (bilateral) neck region
Treatment Time	~300-600s
Frequency of treatments	2x/week
Total number of treatments	14 sessions
Technique used	Scanning modus
Grid pattern/sequential treatment	Sequential treatment

3. Results

At the end of RT, the number of patients with severe skin reactions (RTOG≥2) was significantly increased (p=0.046) in the control group. On the contrary, in the PBMT group the development of ARD remained stable (p=0.30). As such, there was a significant difference in skin toxicity between the two groups at the end of RT, with a higher percentage of patients presenting moist desquamation in the control group (70.6% vs. 29.4%, in the control and PBMT group, resp., p=0.038, Fig.1).

4. Conclusion

These preliminary results of the first RCT in HNC patients show that PBMT is an effective method to prevent the development of severe ARD.

Photobiomodulation in Oral Mucositis in Patients with Head and Neck Cancer: A Systematic Review

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1. Introduction and Hypothesis

Oral Mucositis (OM) presents as an abnormality resulting from the toxicity caused by cancer treatment, and is an inflammatory conditioncharacterized by pain and erythema in the oral cavity, which may progress to ulceration and pseudomembrane. The purpose of this study is to carry out a Systematic Review in order to gain knowledge about the scientific production related to photobiomodulation in Oral Mucositis, facilitating decision making and expanding the scope of its application in health services.

2. Methods

The studies were selected from the PubMed and MEDLINE databases. the studies that were published between 2007 and 2018, which are of the randomized clinical trial type. Patients in the sample were required to have a diagnosis of Head and Neck Cancer only.

3. Results

Following the criteria, 16 articles were selected. Within this context, low-level laser therapy has an anti-inflammatory and analgesic effect in addition to properties that contribute to tissue repair in OM. As observed in the studies included in this work, the radiant exposure used most often was 2.0J/cm^2 (17.64%), followed by 3.0J/cm^2 (11.76%) and 4.0J/cm^2 (11.76%). Of all the studies analyzed, eight applied the laser prophylactically, one therapeutically, and six studies applied the laser both for OM treatment and prevention.

4. Conclusion

Accordingly, photobiomodulation is a proposal for the effective treatment of OM, but it is important to make low-level laser therapy parameters available in publications for reproducibility and clinical application. Besides using adequate laser parameters, it is also necessary to consider the general state of health of the patient at all times and to analyze their individual needs in order for photobiomodulation to guarantee positive results and benefits for the health and quality of life of the cancer patient and to take place safely.

The Role Of Photobiomodulation On The Paraquat-Induced Pulmonary Fibrosis

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1. Introduction and Hypothesis

Pulmonary fibrosis (PF) is a chronic and progressive lung disease characterized by progressive lesion of the pulmonary parenchyma, inflammatory infiltrate and interstitial fibrosis. It is triggered by the excessive and disordered deposition of collagen and other extracellular matrix components, which results in severe changes in the architecture of the alveolus wall. Several factors can trigger PF among them exposure to chemical agents such as paraquat. Due to the absence of an effective treatment, the objective of the study was to investigate the effect of treatment with photobiomodulation on the course of PF.

2. Methods

Adult male C57BL6 mice were submitted to the induction of PF by the administration of Paraquat (10mg / kg, ip) and after 7 days of induction, the mice were treated during 7 days with Photobiomodulation (LED).

Device specifications: BioLambda Apparatus LEDsabr, São Paulo, Brazil; Probe Design, Single Probe; Wavelength: 660 nm; Radiant Power: 160 mW; Power Density: 38,5 mW/cm^2; spot area: 4,15 cm^2; Density of energy: 5,8 J/cm^2; Issuance: Continuous (cw); Total Radiant Emission: 24 J.

Treatment specifications: Exposure time: 152 s; Irradiated points: 1 point; Irradiation Method: Direct skin contact; Anatomical location: trachea and lungs; Irradiation rhythm: punctual; Number of treatments: 1 day, seven applications; Optical properties of tissue: Healthy tissue; Animals not shaved. These parameters were measured.

3. Results

We showed that photobiomodulation reduced Paraquat-induced cell influx into the bronchoalveolar lavage and elevates the level of resolvin D1 without alter the levels of IL-6, TNF-α, IL-10, and IL-17A in the lung homogenates. In addition, did not alter the tracheal responsiveness.

4. Conclusion

The reduced cell migration induced by photobiomodulation might be attributed, at least in part, to elevated level of resolvin D1. Thus, photobiomodulation although it did not alter some parameters, showed beneficial effects on the inflammation and more studies are needed.

Effects Of Photobiomodulation Plus Vitamin C In The Inflammatory And Fibrotic Parameters In Experimental Model Of Lung Fibrosis

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1. Introduction and Hypothesis

Paraquat (PQ) is one of the most herbicides used by several countries, although of their toxic effects in humans and animals. PQ exposition induces oxidative stress and can cause pulmonary fibrosis. Pulmonary fibrosis (PF) is a chronic and progressive lung disease characterized by progressive lesion of the pulmonary parenchyma, inflammatory infiltrate and interstitial fibrosis. Due to the absence of effective treatment, we aimed to investigate the role of photobiomodulation

2. Methods

Adult male C57BL6 mice were submitted to the induction of PF by the administration of Paraquat (10mg / kg, ip) and after 7 days of induction, the mice were treated during 7 days with Photobiomodulation (LED) and vitamin C (150mg/kg, ip).

Device specifications: BioLambda Apparatus LEDsabr, São Paulo, Brazil; Probe Design, Single Probe; Wavelength: 660 nm; Radiant Power: 160 mW; Power Density: 38,5 mW/cm^2; spot area: 4,15 cm^2; Density of energy: 5,8 J/cm^2; Issuance: Continuous (cw); Total Radiant Emission: 24 J.

Treatment specifications: Exposure time: 152 s;Irradiated points: 1 point;Irradiation Method: Direct skin contact;Anatomical location: trachea and lungs;Irradiation rhythm: punctual;Number of treatments: 1 day, seven applications;Optical properties of tissue: Healthy tissue; Animals not shaved. These parameters were measured.

3. Results

Our data showed that LED plus Vit C reduced the level of IL-6, IL-17A, TNF-α, TGF-β in the lung homogenates as well as reduced the collagen deposition into the lung. However, did not alter the level of MMP-9 in the lung homogenates

4. Conclusion

Our data showed that LED plus vitamin C might be an important tool to treat lung fibrosis. Thus, these results open the possibility for new studies and alternatives more efficient to treat lung fibrosis.

A Proposed Classification Detection for Melanoma Skin Cancer Spectrums

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1. Introduction and Hypothesis

There is a strong need for developing clinical technologies and instruments for prompt tissue assessment in a variety of oncological applications as smart methods. Elastic scattering spectroscopy (ESS) is a real-time, noninvasive, point-measurement, optical diagnostic technique for malignancy detection through changes at cellular and subcellular levels, especially important in early diagnosis of invasive skin cancer, melanoma. In fact, this preliminary study was conducted to provide a classification method for analyzing the ESS spectra. Elastic scattering spectra related to the normal skin and melanoma lesions, which were already confirmed pathologically, were provided as input from an ESS database.

2. Methods

A program was developed in MATLAB based on singular value decomposition and K-means algorithm for classification.

3. Results

Accuracy and sensitivity of the proposed classifying method for normal and melanoma spectra were 87.5% and 80%, respectively

4. Conclusion

This method can be helpful for classification of melanoma and normal spectra. However, a large body of data and modifications are required to achieve better sensitivity for clinical applications.

Comparative Study Between Photobiomodulation And Vitamin C To Treat Acute Lung Injury Experimentally

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1. Introduction and Hypothesis

The imbalance of oxidative and antioxidant species in lung tissue is an important event for the development of acute lung injury, which is characterized by rupture of the endothelium and alveolar injury resulting from an uncontrolled lung inflammatory response. The treatment is not effective resulting in high mortality. Thus, we investigated the efficacy of photobiomodulation in comparison with vitamin C to treat acute lung injury experimentally.

2. Methods

Adult male Bal/c mice were submitted to LPS injection (5µg/kg, ip, Salmonela abortus equi) and irradiated with LED or treated with vitamin C (150mg/kg, ip) 2 and 6 h after LPS injection. The parameters were investigated 1day after LPS injection. Device specifications:Bio Lambda LEDstar, Black Box Mini Model, São Paulo, Brazil; Probe Design, Single Probe; Wavelength: 660 nm; Radiant Power: 160 mW; Power Density: 38,5 mW/cm^2; spot area: 4,15 cm^2; Density of energy: 5,8 J/cm^2; Issuance: Continuous (cw); Total Radiant Emission: 24 J. Treatment specifications:Exposure time: 152 s;Irradiated points: 1 point;Irradiation Method: Direct skin contact;Anatomical location: trachea and lungs;Irradiation rhythm: punctual;Number of treatments: 1 day, two applications;Optical properties of tissue: Healthy tissue; Animals not shaved. These parameters were measured

3. Results

Our results showed that both treatments reduced the cell influx into the alveolar space as well as the blood cellularity. LED treatment, but not vitamin C restored the cell influx in the bone marrow. Moreover, LED treatment reduced IL-17, an important inflammatory cytokine, in alveolar lavage fluid, while vitamin C increased IL-10, an antiinflammatory cytokine. No differences were observed in catalase and superoxide dismutase activity between both treatments.

4. Conclusion

Our data showed that both treatments had beneficial effects in the acute lung injury, but by different mechanisms. Thus, we might assume that photobiomodulation seems to be more advantageous if we consider costs and side effects.

Effect Of Photobiomodulation On Apoptosis And Necrosis In Myoblast Cell Exposed To Snake Venom

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1. Introduction and Hypothesis

The envenoming caused by snakes of the Bothrops genus is considered a neglected tropical disease and is associated with severe local manifestations such as myonecrosis. The conventional treatment is the use of the antivenom serum, which has no effect on local reaction.

The aim of this work was to evaluate the effect of photobiomodulation on C2C12 muscle cells submitted to B. jararaca (Bjv), B. jararacussu (Bjsuv) and B. moojeni (Bmv) venoms on their mechanism of cell death (necrosis and apoptosis).

2. Methods

Myoblast cells were incubated with each venom (50 µg/mL) and immediately irradiated in the bottom of the plate with a Twin Flex Premier (MMOptics, Brazil) low-level laser in a CW mode at 660 nm (power= 10 mW, power density= 0.1 W/cm^2, energy density= 2.5 J/cm^2, area= 0.045 cm^2, energy per point= 0.1 J and irradiation time of 20 seconds). The cells that did not receive venom served as control. The cells were then incubated for 2 h and cell viability and flow cytometry was performed.

3. Results

Exposure of C2C12 cells to the venoms for 2 h significantly reduced cell viability by 35% compared to control group. Photobiomodulation was able to promote an increase in cell viability by 60%, 41% and 36% for Bjv, Bjsuv and Bmv, respectively. Bjv, Bjsuv and Bmv caused increased necrotic cell death by 18.7%, 21.9% and 15.2%, respectively, compared to control (4.4%). Bjv (14.9%) and Bmv (14.4%) increased cell death by apoptosis compared to control (6.3%). Photobiomodulation significantly decreased cell death by necrosis in all venom studied by 61%, 58% and 40% for Bjv, Bjsuv and Bmo, respectively, and by apoptosis for Bjv (76%) and Bmv (75%).

4. Conclusion

All venoms used are toxic to myoblast cells, photobiomodulation is effective to protect C2C12 cells against the studied venoms, increasing cell viability by decreasing cell death by necrosis and apoptosis.

Evaluation Of Photobiomodulation Combined With Extracts To Recover Keratinocytes Exposed To UVA

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1. Introduction and Hypothesis

Photoaging is induced by ultraviolet radiation due to the action of reactive oxygen species. Natural extracts present antioxidant activity, mainly due to the effects of polyphenols. For this reason, these compounds are used to stimulate cell renewal or inhibit deleterious processes induced by ultraviolet radiation in the skin. On the other hand, photobiomodulation (PBM) has been shown to be an efficient tool to induce cell renewal. The combination of antioxidant therapy with extracts and photobiomodulation seems to present an important possibility in reducing the harmful effects of UVA radiation.

2. Methods

Human keratinocytes (HaCaT) were seeded in 48 well plates (60,000 cells/well) and, after attachment were exposed to UVA (366 ± 10 nm, 2.5 mW / cm^2, 5400 sec), then treated with Fig or Nutwood extract (0.3% for 24 hours) and, finally, photobiomodulation (LED cluster, 640 ± 12 nm, 2.6 mW/cm^2, 420 sec). All the parameters presented here were measured. At the end of the treatments, cells were kept in the incubator for 48 hours, when the MTT colorimetric assay was performed.

3. Results

UVA (13.5 J/cm^2) caused damage to keratinocytes, reducing the amount of living cells to 80%. The PBM without previous damages had no effect on the keratinocytes. However, the use of PBM (1.0 J/ cm^2) after UVA damage promoted recovery (to approx. 92%), but did not reach the baseline levels. This recovery in cell viability may be the result of reduction of the cell death or activation of cell metabolism by photobiomodulation.The treatment of keratinocytes with Fig extract did not present any improvement in comparison to CT, when evaluating the cell viability: UVA caused reduction in cell viability and post treatment with Fig did not bring cell recovery; PBM after the exposure to Fig presented no changes in cell viability related to Dark (Fig extract was not toxic when associated to PBM) and finally, UVA+PBM associated to Fig treatment promoted recovery in relation to Fig UVA, however, with no difference regarding UVA+PBM (CT). Nutwood extract generated very different results from other treatments. PBM after Nutwood treatment was significantly different from the Dark CT, showing that Nutwood is photosensible in the red. The probable mechanism for the effect observed involves the red light absorption by the Nutwood extract, producing excited states that may generate reactive oxygen species and singlet oxygen which are well known cytotoxic agents. This sequence of events is the principle of the Photodynamic Therapy. Nutwood UVA+PBM was significantly smaller than CT UVA+PBM, showing that Nutwood treatment after exposure to UVA, and followed by the PBM does not bring improvements for cells, instead, it causes cell death.

4. Conclusion

The data showed that PBM seems to be an interesting tool to restore skin cells after UVA damage, however, the detailed mechanism and effects need to be better explored. Besides, the combination of PBM with NE may be a useful strategy however, the choice of the natural extract is challenging, since the concentration of use and other properties, such as photosensibility, may bring unwanted results.

Effects Of Photobiomodulation Using LED on The Analysis Of The Degree Of Muscular Atrophy After Sciatic Nerve Injury In Rats Wistar

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1. Introduction and Hypothesis

Introduction: Peripheral nerve lesions (LNP) do not clinically present a risk of death to the individual, but may result in motor and sensory disturbances altering the function of the affected limb. Phototherapy using low power laser (LBP) has demonstrated positive effects for the nervous and muscle repair process after different types of injury. The treatment with irradiation using Light Emitting Diode (LED) has demonstrated positive effects on the nervous tissue repair after peripheral nerve injury (PNI), however there is little description in the literature regarding the effect on muscle tissue.

Objective: to analyze photobiomodulation effects using LED on the degree of muscular atriphy after sciatic nerve injury of wistar rats.

2. Methods

85 Wistar rats were randomly divided into 5 groups: Control; Injury; Injury+LEDn (LED in the area of PNI); Injury+LEDmm (LED muscle); Injury+LEDn+LEDmm (LED in the area of the PNI and in the tibialis anterior muscle).

The LED irradiation was performed using the following parameters:

- LEDn consisted of 4 points during 20 seconds each one using an energy density of 0,8J/cm^2 and
- LEDmm consisted on 8 points during 10 seconds each one using an energy density of 0,4J/cm^2.

For both the length wavelength was 850nm, the area of the beam was 1cm^2 and the power density and total energy were 0,04W/cm^2 3,21J respectively. capturar1.jpg

After euthanasia of the animals at the different periods of analysis, the right and left TA muscles were carefully removed by resection of the tendon of origin and bone and clean insertion. The muscles were weighed in a semi-analytical balance and for each animal the muscle mass ratio was calculated using the following formula:

3. Results

The muscular atrophy index, in the 7-day period, all the groups treated with LED showed a decrease of the index in relation to the Control group. In 14 days, the LED groups showed an increase in relation to the Injury group. At 21 and 28 days, the injured groups showed a decrease in relation to the Control group. Only the LEDnm group showed a decrease compared to the Injury group. The LED induced an increase in muscle mass in relation to the animals that did not receive treatment in the period of 2 weeks after LNP.

4. Conclusion

We can conclude that LED induced an increase in muscle mass in relation to the animals that did not receive treatment in the period of 2 weeks post PNI.

Photon Absorption Of Primary Dressings Used In The Treatment Of Cutaneous Wounds

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1. Introduction and Hypothesis

There is a wide range of dressings and methods used in the treatment of cutaneous wounds. The choice of dressing varies according to the type of wound, size, location and even patient cost-benefit, with the overall focus being thedesired effect on the lesion bed. One method that has proven effective for wound repair is photobiomodulation (PBM). To apply the laser or LED to the lesion it is necessary to remove the dressing covering the wound, whether it be a primary or secondary dressing. The present study aimed to determine the photon absorption of primary dressings, commonly used for the treatment of cutaneous wounds, to verify the true necessity of their removal during photobiomodulation.

2. Methods

A spectrophotometer (USB 2000+, OceanOptics®, USA) was used with a quartz cuvette (z = 0.5 cm). A fragment of each type of primary dressing was inserted into thecuvette which was filled with saline 0.9%. It was inserted in such a way that the non-adherent side received the incident illumination, simulating the real application of the dressing being irradiated with photons. The baseline was measured with saline solution only. The primary dressings measured were Nu-derme®, Systagenix, United Kingdom; Dermazine®, Silvestre Labs, Brazil; Mepitel®, Mölnlycke Health Care, Sweden; Pielsana® Sachet, DBS, Brazil; Steri-StripTM, 3M, Germany; Opsite Post-Op®, Smith&Nephew, England; TegadermTM Film, 3M, Germany and AGE - SupriDerme®, Greenwood, Brazil. The absorbance of each dressing was measured between 400nm and 950nm.

3. Results

Among the dressingstested, the one that most absorbed photons, both in the red band of the electromagnetic spectrum as well as in the infrared spectrum, wasDermazine®. In descending order, Nu-derme®, Steri-StripTM, Pielsana® and Mepitel® also absorbedphotons in these ranges. The dressings with the lowest absorbance wasTegadermTM Film, AGE - SupriDerme ® and Opsite Post - Op ®, the latter two showingpractically noabsorption throughout the therapeutic window.

4. Conclusion

Se não houver perda na transmissão dos fótons ao passar pelo curativo primário, ou conhecendo-se a magnitude dessas perdas, torna-se possível alcançar maior efetividade do tratamento, seja com MPB ou farmacológico, reduzindo o desconforto e o custo de trocar curativos.

Effect Of Intravascular Laser Irradiation Of Blood (ILIB) In The Immunity Of Patients With Solid Maligance Tumors Submitted To Systemic Chemotherapy

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1. Introduction and Hypothesis

The most of drugs used in systemic chemotherapy have effect of the immune system, principally in the neutrophils, platelets and leukocytes,. Neutropenia may cause discontinuation of chemotherapy, compromising the control of tumor cells. Therefore, the aim of the study was to evaluate the action of intravenous laser irradiation of blood (ILIB) on cellular immunity in the patients with solid malignance tumors, submitted to systemic chemotherapy, comparing of two methods of ILIB application with control group.

2. Methods

A total of 21 patients with solid malignance tumors treated of the Oncology Ambulatory of Clinical Hospital of São Paulo State University (UNESP), Medical School, Botucatu, Brazil, April to July 2018, were divided into 3 groups. The group A (control group) patients submitted of chemotherapy without ILIB; group B1 (ILIB 30) underwent 30 minutes of daily of ILIB for 10 days; group B2 (ILIB 60) underwent 60 minutes every 2 days for 10 days. The course of the therapy consisted of two procedures with a twenty days interval between each procedure. Three blood samples were taken of each the patients for hematologic analysis: immediately before the first procedure, 10 days before the second procedure and 5th day following the last procedure. The ILIB method consisted in the placement of a bracelet on the right wrist with a fitting on the radial artery in which the equipment was attached. Irradiation was performed by a diode laser (model Therapy ILIB, DMC Equipamentos Ltda, São Carlos, SP, Brazil, SN 14093), wavelength 660 nm, power density 100 mW, and 0,028 cm^2 spot area. Modes IL 30 minutes and IN 60 minutes for groups B1 and B2, respectively.

3. Results

Preliminary results suggest an increased number of neutrophils in group B2 (ILIB60) in the blood sample 5th day following the last procedure when compared to the control and B1 groups. Clinically we have observed that after the start of the study, there was a significant reduction in discontinue chemotherapy by low neutrophil counts.

4. Conclusion

Although the study is at the beginning and small sample, the ILIB appears have an effect on increased immunity.

Low-Intensity Laser Therapy Inducing Vascular Reactivity And Response Of Blood Pressure To The Maximum Exercise In Military Policies

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1. Introduction and Hypothesis

Military police (PM) are exposed to a stressful environment, being submitted to a higher cardiovascular risk. Arterial rigidity, endothelial dysfunction, and exacerbated increase in blood pressure during exercise are markers of cardiovascular risk. Previous experimental studies have shown that low-intensity laser therapy (TLBI) promotes the increase of flow-mediated dilatation (DMF) and acceleration of angiogenesis, which causes temporary vasodilatation, an increase in the diameter of blood vessels

2. Methods

One group of PM underwent LTBI (PM / TLBI, n = 11)for 6 months, while a PM group matched for age and weight remained therapy and was characterized as a control group. TLBI (Model DMC Thera Lase) was applied using a single probe, Wavelength 830 nm, Power 50 mW, Power Density 6,0 J/cm^2 area of irradiation 0,1 cm^2 , used duty cycle Treatment Time 13seg in the sublingual region twice a week, with maximum intervals of three days between applications, scanning technique, Local Area treated Endothelial function was assessed by DMF of the brachial artery. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were analyzed during the cardiopulmonary exercise test.

3. Results

After 6 months, there was an increase in DMF in the PM / TLBI group, which did not occur in the PM / C group (increase Δ = 19.5 ± 2 and 1.5 ± 5%, respectively, P = 0.002). Interestingly, BP response to maximal exercise decreased only in the PM / TLBI group (pre vs. post, SBP = 198 ± 6 vs. 177 ± 4 mmHg, P =.02, DBP = 106 ± 2 vs. 90 ± 1 mmHg, respectively, P <0.001) and there was no change in the PM / C group (P = 0.19).

4. Conclusion

Our data demonstrate that TLBI can significantly increase vascular reactivity even in humans, which seems to explain, at least in part, the decrease in blood pressure response to exercise. In military police officers, who are exposed to high levels of stress, TLBI may be a therapeutic alternative to prevent cardiovascular risks.

Photodynamic Therapy Reverses The Negative Effects Of Periodontitis On The Uterine Microenvironment During The Gestation

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1. Introduction and Hypothesis

Periodontis (P) is one of the most common infetious disease that affects the periodontium and gradually destroys periodontal tissues. Among several systemic effects occasioned by P, alterations during the gestation have been studied. PDTIntroduction: Periodontitis (P) is one of the most common infectious diseases that affects the periodontium and gradually destroys periodontal tissues. Among several systemic effects occasioned by P, alterations during the gestation have been studied. PDT is characterized by the association of a light source with a photosensitizing agent in order to cause cell necrosis and microbial death. Thus, our objective was to evaluate the effect of PDT on the negative repercussions of periodontitis during pregnancy, mainly in the uterine microenvironment.

2. Methods

Methods: Ten days before pregnancy, periodontitis was induced by ligature technique, and subsequently the rats were caged over-night with a male. Pregnancy was confirmed by vaginal smear. The treatment with PDT was performed 15 days after the induction the ligatures. Pregnant rats non-manipulated were used as control. Pregnant rats were euthanized at day 18 of gestation and the uterus was removed in order to investigate the parameters. The photosensitizer methylene blue (0.005%, CHIMIOLUX, DMC, São Paulo, Brazil) was administered at the two sites (vestibular and lingual). After three minutes, the periodontal pockets were irradiated with a red laser (MM OPTICS; Wavelength 660 ± 10 nm; Radiant power100 mW; Exposure duration 90s; spot size 0.02827 cm^2; Radiant energy 9 J; Irradiance 3.5 W/cm^2; Radiant exposure 318 J/cm^2; Total radiant energy18 J).

3. Results

Results: We showed that PDT had an important impact on the uterine microenvironment reducing the gene expression of IL-6, COX-1, COX-2 and NOS in the uterine tissue of pregnant rats with periodontitis. We also observed that PDT reversed the decreased level of IL-10 in the placenta.

4. Conclusion

Conclusions: Thus, our data showed the important role of oral health during gestation as well as PDT is an effective therapy. These studies might be useful in providing an important indicator of risk for future obstetric complications considering the impact in the offspring.

Healing Mucositis And Dermatitis With Photobiomodulation At 660 Nm: Efficacy Of A New Woven Optical Fiber Device On Cell Proliferation And Migration

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1. Introduction and Hypothesis

Radiaotherapy- and chemotherapy-induced mucositis and dermatitis impair quality of life and cancer treatment efficacy of approximately 500,000 people worldwide. NeoMedLight is a French company currently developing a new woven optical fiber device for treatment and prevention of oral mucositis and skin dermatitis. The aim of this study was to evaluate in vitro the effect of photobiomodulation (PBM) with this new optical fiber device on cell proliferation and migration. This evaluation is done by measuring the proliferation and migration of representative cell lines at various illuminating doses.

2. Methods

NeoMedLight developed a PBM system using a woven optical fiber textile strip connected to high power led. Illumination was performed with continuous emission at 660 nm, using a 3*1,8 cm^2 square with a total surface irradiance of 21 mW/cm^2 (total irradiance 113 mW). Head and neck cancer cell line (SCC) and keratinocytes cell line (HaCaT) were cultured in vitro to evaluate this device. Cell proliferation and migration were studied at 3 illumination doses delivered once (0 J/cm^2, 3 J/cm^2 (treatment duration 139 seconds) or 6 J/cm^2 (treatment duration 278s)) and two conditions of cell irradiation (Control or 4Gy). Cell proliferation assay was assessed by the IncuCyte ZOOM® video microscope (Essen BioScience) measuring cell confluence during seven days. Cell migration was measured with a scratch-wound assay using the IncuCyte ZOOM® video microscope during two days. Normalized gap between conditions (with or without cell illumination) was calculated to measure the statistical difference.

3. Results

PBM significantly increased HaCaT and SCC proliferation in control conditions: the mean confluence reaches 82% for HaCaT and 25% for SCC at maximum. Normalized gap significantly increased until 72 hours in favor of illumination (18% for HaCaT and 16% for SCC). This confirms that the device is comparable to the ones in literature for proliferation rates.

In control conditions, illumination significantly increased HaCaT migration at $6J/cm^2$ (ratio 20%) as compared to $3J/cm^2$ (ratio 0%) after 24 hours. SCC migration was similar for the two illumination doses (ratio 10%).

After 4Gy irradiation, illumination seemed to have a lower effect on proliferation and migration for the two types of cells. HaCaT proliferation was slightly increased by illumination at $3J/cm^2$ (ratio of 10%).

4. Conclusion

This study demonstrates that PBM delivered by NeoMedLight's optical fiber device at a single dose is comparable to devices found in literature. PBM significantly increased proliferation of HaCaT and SCC compared to control group. PBM effect depends on cell type and stress conditions. If light parameters have to be cautiously controlled as the observed effect is dose-dependent, this device allows a simple, controlled and reproducible illumination.

The authors declare that they have no competitive interests.

Investigation The Effect Of Irradiation Of Laser Light Selected By The Monte Carlo Simulation In The Presense Of Gold Nanoparticles, On Reduction In Growth Of Murine Breast Adenocarcinoma Tumour

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1. Introduction and Hypothesis

In recent years, the tremendous development of nanotechnology has provided a variety of nanostructures with unique optical properties that are useful in biology and biomedicine applications. From the point of the view of cancer therapeutics, gold nanoparticles become very useful as agents for photothermal therapy on account of their enhanced absorption cross sections. Several groups have investigated destruction of solid tumors using hyperthermia with near infrared (NIR) lasers. To make the photothermal therapy of cancer cells highly effective, one needs to ensure a correspondence between three important factors: the laser wavelength, the maximal absorbance of the gold nanostructures being used as selective labels, and the spectral transmittance of the biotissues treated by laser pulses.

2. Methods

In this study, the murine breast adenocarcinoma tumor tissue is simulated by using Monte Carlo simulation (MCML has been coded in ANSI Standard C), and the possibility of influence of the laser beam with a wavelength of 540, 630, 650, 760, 810, and 830 nm in the center of the tumor was examined. By extracting the fluence of laser beam, appropriate wavelength was estimated. According to the maximum absorption of nanoparticles of different sizes, located in a specific wavelength region, type and size of the nanoparticle was estimated proportional to the wavelength of the selected laser. Accordingly, gold nanorods were synthesized by seed mediated growth method. To evaluate the photothermal treatment effectiveness of laser light with selected wavelength, on the tumors wich are containing nanorods, gold nanorods (≈ 37±5 nm length and 15±3 nm width) with peak optical absorption in 800 nm, were injected into the tumor interstitium of tumor bearing female Balb/c mice. Then tumors were illuminated with continuous laser radiation with a wavelength of 830 nm and a power of 100 mW, for 15 min. Then evaluation of the growth of tumors was performed by measurement of tumor volume and histological stusies.

3. Results

Significant difference between tumor volume in treated group and the other groups, was observed. But, histopathologic images indicated mass destruction with extensive necrosis in the treated tumor and confirmed the damaging effect of applying the treatment protocol. Also, the degree of tumor malignancy using Bloom-Richardson classification, showed redused tumor grade in treated group.

4. Conclusion

In treatment group, the use of laser with appropriate wavelength and gold nanorods with size, proportional to the selected wavelength, has resulted in thermal effect on tumors.

Simultaneous Effect Of Dual Frequency Ultrasound In Methylene Blue Photosensitizer Release From Nanopolymers In Breast Adenocarcinoma Treatment By Photodynamic Therapy Method

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1. Introduction and Hypothesis

According to high mortality rate due to cancer and side effects of invasive treatments, the noninvasive method such as photodynamic therapy for treatment of breast adenocacinoma is considerable.Encapsulation of sensitizer in nanoparticles can improve the accumulation of these agents in the tumor tissue and decrease its side effects. In this study, the application of dual (1 MHz and 40 kHz) frequency sonication for methylene blue sensitizer releasing from polymeric nanoparticles and its effects in treatment of breast adenocarcinoma with photodynamic therapy method in female Balb/C mice was investigated.

2. Methods

We have investigated the exposure parameters effects of 40 kHz and 1MHz ultrasound on cavitation production, by chemical iodide dosimeter. The effective protocol for enhancement of the inertial cavitation activity was determined. After preparation of methylene blue containing nanoliposomes, the drug release upon dual and single frequency sonication was checked and biodistribution of drug was studied in vivo. In treatment protocols, the animals were distributed in 15 groups (8 animals in each group) and encapsulated drug was intravenously injected. Then the animals were sonicated for 5 min. In some treatment groups, animals were exposed with laser for 2.5 min immediately after sonication. The tumor volume was measured for 1 month and animal survival was recorded. For confidence of treatment results, tumors in different groups were pathologically studied.

3. Results

Among different combinations, the combined ultrasound sonication in continuous mode can produce a more remarkable enhancement of the inertial cavitation activity (1.78 times) than other mode. Biodistribution study revealed that sonication with selected protocol after injection of encapsulated methylene blue, results in an increase in tumor drug uptake about 4.3 times compared to systemic drug injection ($P<0.05$). Statistical analysis of delay parameter showed that, treatment with laser irradiation after dual frequency sonication in the presence of encapsulated methylene blue, caused a significant reduction in tumor normalized volume compared to other groups ($P<0.05$). Also, animals survival is increased about 1.5 times compared to control group, which were pathologically verified.

4. Conclusion

It was concluded that, in breast adenocarcinoma treatment, combination of dual frequency sonication and laser irradiation in presence of encapsulated methylene blue were declined tumor growth.

Prevention Of Oral Mucositis In Bone Marrow Transplant Patients Using Red And Infrared Laser Simultaneously

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1. Introduction and Hypothesis

The incidence of oral mucositis in bone marrow transplant patients is very high.The presence of oral lesion is a gateway to microbial infections that may be the cause of death in these patients. Therefore, the search for effective protocols in the prevention of oral mucositis should be a constant goal for clinicians and researchers. An irradiation option not yet published is the use of two wavelengths (red and infra-red) simultaneously.The purpose of the association is to provide photons to the superficial mucosa as well as to the deep connective, acting more intensely in the modulation of the inflammation avoiding cellular apoptosis.

2. Methods

Five patients submitted to bone marrow transplantation were treated at Campinas Medical Center and submitted to the preventive treatment of oral mucositis according to the following protocol: daily irradiation with low power laser (Therapy EC, DMC Equipamentos, LTDA, São Carlos, SP Brazil), using simultaneously the red (660nm) and infrared (830nm) wavelengths, with 100mW each, CW, 0,028cm^2 spot size, 3.5W/cm^2, contact mode, 20 seconds of irradiation per point (every 1 cm^2), 4 Joules per point (2 J of each wavelength), 140J/cm^2 (70 J/cm^2 each wavelength) from the first day of chemotherapy to hospital discharge (an average of 20 visits per patient).

3. Results

Two patients presented punctual lesions, MO = 2 and three patients presented no lesion during treatment (MO = 0). All of them ingested fewer medicines and the mean number of days of hospitalization was reduced for two patients treated.

4. Conclusion

Laser therapy was effective in the prevention of oral mucositis in the described patients. Besides the improvement in the general health status of the patients, better mood due to not having complications and less drug intoxication, all the patients had lower risks of infections. The association of two wavelengths was effective in the prevention of Oral Mucositis suggesting a new therapeutic approach for hematological patients whose therapy is bone marrow transplantation.

Controlling Methylene Blue Aggregation: A More Efficient Alternative To Treat Candida Albicans Infections Using Photodynamic Therapy

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1. Introduction and Hypothesis

Methylene blue (MB) has been widely used in antimicrobial PDT (aPDT), however the delivery of MB should be considered a critical factor for therapy effectiveness, since depending on the physicochemical environment in which it is found, MB may aggregate, and its state of aggregation modulates the type of photochemical reaction that occurs, affecting therapy effectiveness. Thus, the objective of this study was to evaluate aPDT efficacy against C. albicans using MB in vehycles which may influence agreggation and present an oral formulation (OF) containing MB to be used in clinical aPDT procedures.

2. Methods

The most suitable experimental conditions were experimentally determined, evaluating MB concentrations, pre-irradiation time, and duration of irradiation. After that, the best parameters found were used in order to verify the efficacy of MB in different mediums. For this, the C. albicans suspension and the MB solutions were inoculated into microplates. After 5 minutes, they were irradiated for 30 minutes (4.68 J/cm^2)with an continous LED system that emitted light at 640 ± 12 nm, with 2.6 mW/cm^2, being measured at the surface of the wells. Following, an aliquot of each sample was taken, diluted and seeded onto Petri dishes containing the Sabouraud Agar Dextrose Culture Medium. The plates were incubated for 24 h at 37°C and the number of CFU/mL were counted. Based upon these analysis, an oral formulation (OF) containing MB in the most effective vehycle was tested in biofilms, previously grown by 48h. The biofilm treatment and analysis was performed according to the previously described procedures for planktonic assays. In paralel, MB dimer to monomer ratio was determined by UV-Vis absorption spectroscopy.

3. Results

MB presented an efficacy against C. albicans when applied in an SDS solution, achieving a complete inactivation in a planktonic assay. On the other hand, MB when it was applied in all of the other media, such as water, PBS, NaCl and urea, showed no differences to control (without the MB). The dimer to monomer ratio data suggested that values above 0.3 reduced the effects of the MB photodynamic treatments; while below 0.3, the values increased the efficacies of an aPDT. An oral formulation to control MB aggregation was tested in biolfim, and MB 50 mg/L was necessary to achieve some reduction in cell viability after treatment. In spite of OF with MB 50 mg/L caused statistical significant reduction in relation to control, total inactivation of C. albicans in biofilm was not observed. It would be possible to increase the microorganism inactivations by modifying the light exposure parameters. A new LED cluster was recenlty acquired to use higher irradiance.

4. Conclusion

The SDS solution was the most suitable vehicle to reduce MB aggregation and increase aPDT efficacy. Similarly, OF formulation showed to be an efficient strategy to control MB aggregation and increased the effectiveness of the therapy. The present research indicates that the development of formulations for the control of MB aggregation may result in more effective clinical protocols, however further studies are necessary to adjust the light parameters.

Efficacy Of Low Level Laser Therapy For Management Of Oral Mucositis In Oncology And Bone Marrow Transplant Children. A Pilot Study

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1. Introduction and Hypothesis

Oral mucositis (OM) is a prevalent condition associated with cancer therapy in children. Current

clinical management of OM includes palliative measures such as administration of analgesics, nutritional support and maintenance of good oral hygiene, prescription of topical agents to prevent infection and relieve symptoms. To date, no specific preventive or therapeutic interventions have been universally accepted for the clinical management of OM. To determine the response of oral mucosa treated with low level light therapy (LLLT) in children with cancer and undergoing bone marrow transplant (BMT) who are likely to develop OM.

2. Methods

Ethics approval was granted by The Royal Children's Hospital, Melbourne Human Research Ethics Committee (HREC Reference Number 33068A). Written and verbal informed consent was obtained for each patient by his or her parent/carer. Patient's over 14 years of age provided consent on his/her own accord. LLLT was applied extraorally to the facial skin over the cheek and buccal mucosa on one side of the face once daily for 7 days. A sham laser was also applied to the other facial side. LLLT was applied to the soft palate once daily for 7 days.

Patients had their mouth assessed daily except Sunday. Patients receiving chemotherapy were examined and OM scored during admission from 7 - 21 days. Bone marrow transplant patients were assessed from Day 1 of their conditioning regimen until 14 days after receiving BMT. OM was assessed using three indices: Oral Mucositis Assessment Score (OMAS), WHO oral mucositis score and the Children's International Mucositis Evaluation Scale.

Device specifications:

- Manufacturer: THOR Photomedicine LTD, Chesham, Bucks, HP51HQ, UK Model number: MO396
- Probe Design: cluster
- Wavelength/s: 34 x 660 nm 10mW, 35 x 850nm 30mW LEDs
- Total Power: 1390 mW
- Power Density: 50mW/cm^2
- Spot size of irradiation: 30.2 and 0.5cm^2
- Pulsing cycle at 2.5 Hz pulse frequency
- Energy Density: 3 J/cm^2
- Energy per point or total energy – 90.6 and 1.5 Joules

Treatment specifications:

- Treatment Time: 60 sec per site
- Frequency of treatments: Daily
- Total number of treatments: 7
- Technique used: Direct in-contact probe technique
- Area(s) treated: local extraoral and intraoral, split mouth Location and number of points. Bilateral cheeks and palate

3. Results

In all cases, there was noticeable improvement on the treated side compared with the non-treated side. Only one case exhibited minor deterioration of the treated side during LLLT. Children with a lower baseline OMAS score were noted to have higher scores on the control side compared with treatment side over the time period. OMAS increased on all the control sides for children with baseline OMAS scores less than four on day 1. For those patients with higher baseline OMAS score (four or more), progressive scores decreased over the time period, but change was more apparent on the treatment side compared with the control side.

4. Conclusion

LLLT reduced the prevalence of OM in the majority of BMT and in several oncology children. When OM was evident, all patients demonstrated less severe oral mucosal lesions and improved healing time on the treated side compared with the sham side.

The Effects Of Single Or Daily Photobiomodulation In Oral Squamous Cell Carcinoma Cellular Viability

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1. Introduction and Hypothesis

Oral squamous cell carcinoma (OSCC) accounts for more than 90% of the cases Head and Neck cancer. The conventional treatment for OSCC is surgery associated with radio/ chemotherapy, both associated with oral mucositis. Some studies have demonstrated that Photobiomodulation (PBM) can act preventing the development of mucositis as well as reducing pain and promoting wound healing, mainly when applied daily in oral mucosa. However, some studies demonstrated that PBM can promote tumor progression by acting in neoplastic cells. Thus, the aim of this study was to evaluate in vitro the effects of different dosimetric parameters as well as single or daily PBM in cellular viability of OSCC cell lines.

2. Methods

OSCC cell lines (SCC9, Luc4 and CA1) were cultivated in DMEM/F12 with 10% FBS, 1% antibiotic, 400 ng/ml hydrocortisone and RM+ supplement. 1x104 cells were seeded in 96 wells plates and divided according to the following treatments: no irradiation (Control), single irradiation (LED1) and daily irradiation (LED3, three consecutive days of irradiation). Cells were irradiated using the LEDbox (BioLambda, São Paulo, Brazil) in direct contact mode, cluster probe, wavelength 660nm, power 80mW, power density 25.5mW/cm^2, energy density of 1.5, 3 and 6J/cm^2 with 60, 120 and 240sec of irradiation and total energy of 4.8, 9.6 and 19.2J, respectively. Cellular viability was assessed in Control and LED1 groups after 24h and in Control, LED1 and LED3 groups after 72h by the MTT assay. After irradiation and incubation times, cells were incubated with MTT (5mg/ml) for 3h at 37°C and the formazan crystals were solubilized by adding isopropanol. All experiments were independently repeated three times. To verify data distribution, normality test was calculated by D'Agostino & Pearson and Shapiro-Wilk normality tests. Significance difference between groups was calculated using T-Test and Mann-Whitney test. P value < 0.05 was considered as significant.

3. Results

After 24h of irradiation, SCC9 cells treated with LED1-1.5J/cm^2 showed a significant decrease in cellular viability when compared to Control. The CA1, Luc4 and SCC9 cell lines treated with LED1-6J/cm^2 presented reduced cellular viability in relation to Control. After 72h, Luc4 and SCC9 cell lines showed increased cellular viability when treated with LED3-1.5J/cm^2. All cell lines demonstrated higher cellular viability in relation to control when treated with LED1-3J/cm^2. However, a significant decrease in cellular viability was observed in CA1 treated with LED1-6J/cm^2 or LED3-6J/cm^2 and in SCC9 treated with LED3-6J/cm^2, with a pronounced inhibitory effect when the irradiation was applied daily.

4. Conclusion

PBM with 1.5 or 3J/cm^2 and single or daily irradiation was associated with an increase in the cellular viability of OSCC cells. Moreover, PBM with 6J/cm^2 (dose used to treat mucositis) was able to reduce cellular viability more effectively when irradiation was performed daily, demonstrating a negative effect in OSCC cells. Additional studies investigating the biological effects of different dosimetric parameters and PBM treatments are necessary to understand its role in OSCC cells.

Laser Therapy In The Treatment Of Oropharyngeal Side Effects Caused By Cetuximab And Docetaxel

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1. Introduction and Hypothesis

New chemotherapy and clinical oncology protocols reflect on varied and challenging side effects in oropharynx. In addition to promoting stomatitis some chemotherapies accentuating the fragility of the oral mucosa. In this work we present three clinical cases whose drugs used were docetaxel and cetuximab, both with challenging oral effects that required new clinical approaches by the dental team.

2. Methods

For all cases, two protocols were used, one to treat lesions (0.5J, 660nm, 17.5J/cm^2, 3.5W/cm^2, scanned every 1 cm^2, for 5 seconds) and another to prevent injuries, using simultaneously the red (660nm) and infrared (830nm) wavelengths, contact mode, 20 seconds of irradiation per point (every 1 cm^2), 4 Joules per point (2 J of each wavelength), 140J/cm^2 (70 J/cm^2 each wavelength). The equipment used was Therapy EC (DMC Equipamentos, LTDA, São Carlos, SP Brazil, 660nm and 830nm, 100mW each, 0,028cm^2 spot size, CW). Moreover, all patients were instructed in oral hygiene and the use of related products (chlorhexidine, nystatin, vitamin E, water with bicarbonate, etc.). First patient, female, 54 years old, intestinal cancer with metastasis in the lung, chemotherapy with Cetuximabe, started laser therapy after severe oral mucositis. Dental anatomical problems were provisionally softened with a protective silicone plates to avoid trauma to the mucosa. Late stomatitis were detected and laser therapy protocol was changed to the daily format up to 15 days after the end of the chemotherapy. From the use of the laser, the initial grade 3 oral mucositis changed to 0 and 1 with few episodes of grade 2. Second patient, female, 69 years old, liver cancer with metastasis in breast, treatment with docetaxel. She was hospitalized with grade 4 mucositis, and laser therapy was performed throughout the hospitalization period that lasted 12 days. In addition to laser therapy, protective silicone plates were also used against occlusal trauma. From the second day of irradiation the mucositis was to grade 3, and after 6 days of irradiation to grade 2 until hospital discharge. And third patient, male, 54 years old, oropharyngeal cancer. Using weekly cetuximab concomitant to 33 sessions of local radiotherapy, and 3 sessions of docetaxel and cisplatin at monthly intervals. Laser therapy was performed throughout the radiotherapy, being 6 days a week which kept the patient free of mucositis, but with mild palate alteration. However, the presence of radiodermatitis was intense, and the presence of late oral lesions (grade 2 and grade 3 mucositis) required the continuation of laser therapy daily for another 20 days after the end of radiotherapy and chemotherapy.

3. Results

In all cases, laser therapy was important for the recovery of patients' oral health.

4. Conclusion

However, some chemotherapeutic agents, like cetuximabe and docetaxel, require a greater number and a higher frequency of low-power laser irradiation to maintain its effectiveness in the prevention and treatment of oral side effects.

Evaluation Of Periodontal Treatment With Photodynamic Therapy In Systemic Parameters Of Inflammation In Experimental Model Of Periodontitis And Asthma

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1. Introduction and Hypothesis

Periodontitis (P) and asthma (A) have high prevalence in the world population which implies high economic and social cost. Evidence suggests that P may be able to modulate the systemic immune response [1,2]. As the standard periodontal treatment (PT) may not have full efficacy over periodontal pathogens in deep pockets, photodynamic therapy (PDT) has been used with promising results, but the cellular mechanisms involved are still unclear. Objectives: To evaluate if PT associated with PDT is capable of interfere in systemic parameters of inflammation in an experimental model of asthma and periodontitis in Balb/c mice.

2. Methods

After CEUA-Uninove approval (#020.2017), sixty-four Balb/c male mice, 2 months years-old and 25 g were divided into 8 groups (n = 8): B-BASAL; P; P + PT; P + PT + PDT; A; A+P; A+P+PT; A+P+PT+PDT. Periodontitis was induced with ligation technique. After 15 days, PT was performed. For the PDT, it was used methylene blue Chimiolux® (0.005%, 0,05mg/ml) for 3 minutes, pre-irradiation. The irradiation was performed only once by direct in-contact probe with red diode laser (Therapy XT® DMC, São Carlos, Brazil, ANVISA 80030810157, single probe, λ = 660nm duty cycle, radiant power of 100mW, 35,38mW/cm^2 of power density, energy density of 6,369 J/cm^2, two irradiation points, inside the mouth, by buccal and lingual surface of the lower left first molar, with 0,0028cm^2, 9J per point, for 90s). After 43 days, all mice were euthanized. Total and differential blood-cells counts were performed, as well as the platelet count, femoral bone marrow cells count and the level of inflammatory cytokines (IL-4 and IL-10) in lung homogenate was analyzed. Histological analysis of the mandible was made to characterize the P. For the statistical analysis one-way ANOVA followed by the Student-Newman-Keuls test was used.

3. Results

There was an increase in the number of blood circulating eosinophils in group A when compared to group B ($p < 0.01$) that characterizes experimental model of asthma. There was no difference in total and differential blood circulating cells, total platelet count and femoral bone marrow cells, lung edema and inflammatory cytokines (IL4 and IL10) in lung homogenate for all analyzed groups.

4. Conclusion

These data have contributed to elucidate that periodontitis and asthma associated or not with periodontal treatment with PDT is not able to interfere in systemic parameters of mice Balb/c. Further studies are needed to understand the systemic regulatory process of these pathologies.

Statement: Approved by the animal ethics committee of UNINOVE, CEUA 020.2017. This study doesn't contain any conflicts of interest.

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Evaluation Of The Efficacy Of Antimicrobial Photodynamic Therapy In Treatment Of Peri-Implantitis: A Controlled, Randomized, Blinded Clinical Trial

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1. Introduction and Hypothesis

Elimination of pathogenic microorganisms from peri-implant systems is one of the milestones for success of treatment of peri-implantitis (PI). Photodynamic antimicrobial therapy (aPDT) is a resource that consists in the use of red laser to inactivate bacteria. The photosensitizer PapaMBlue® was used in this trial as a mediator of this therapy. We have performed a controlled, randomized, blinded clinical trial to evaluate the effectiveness of aPDT with this photosensitizer in treatment of PI.

2. Methods

Implants were randomly divided into two groups: group I received only conventional treatment; group II received conventional treatment and photodynamic therapy (aPDT) with PapaMBlue®. Both groups received individually oriented oral hygiene and removal of calculus deposits from surfaces of implants by curette scrapping and washing with sterile saline. APDT with photosensitizer was carried out in PI pockets deeper than ≥ 5 mm. The PapaMblue® photosensitizer was applied on the peri-implant pockets and a pre-irradiation time of 1 min was adopted. We have used laser device (Therapy EC, DMC, São Carlos, Brazil) emitting wavelength of λ = 660 nm and power of 100 mW for 2 min at each site, 30 J / cm^2 radiant exposure and power density I = 250 mW / cm^2 on mesio vestibular surfaces. We have collected microbiological samples of both groups before and immediately after treatments.

3. Results

Data showed that aPDT associated with PapaMblue® decreased bacteria concentration in PI by 99.9%. Control group did not have reduction on the amount of bacteria after conventional peri-implant curettage treatment.

4. Conclusion

For the treatment of peri-implantitis, our results demonstrate that aPDT with photosensitizer PapaMblue® reduces the amount of bacteria.

A Mapping Of Skin And Mucosal Areas At High Risk Of Toxicity To Guide Prophylactic Photobiomodulation In Head And Neck Cancer Treated By Radiotherapy

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1. Introduction and Hypothesis

Prophylactic photobiomodulation (PBM) has proved to be effective in the prevention of high grade (HG) mucositis, in patients treated with radiotherapy (RT) for head and neck cancer (HNC). In the department of RT of Institut Curie, HNC are irradiated using Tomotherapy, a rotational intensity modulated RT which provides both optimal conformation to planning target volumes (PTV), and organs at risk sparing. Moreover, most patients experiment HG mucositis and epidermitis with curative RT.To implement PBM, we acquired THOR intra-oral visible red (660 nm, 75 mW) laser probe, and mixed red and infrared LED Cluster probe (34x660 nm, 10 mW LEDs and 35x850 nm, 30 mW LEDs, with a total power of 1390 mW). Prophylactic intra and extra-oral PBM requires beforehand the clear identification of areas at risk (AAR) for HG mucositis and epidermitis ; this work aimed at determining a systematic method to report AAR of HG toxicity.

2. Methods

The volumes and dosimetry of six HNC (oral cavity and oropharynx) treated by exclusive or postoperative RT +/- chemotherapy were reviewed. PTV were constructed from clinical target volumes (CTV) with 5 mm margins in all directions excluding the skin with 3 mm. IMRT was prescribed with simultaneous integrated boost delivering respectively 70/63/56Gy in 35 fractions in PTV high/intermediate/low risk for exclusive RT, and 66/59,4/54Gy in 33 fractions or 60/54Gy in 30 fractions for postoperative RT. A mean dose inferior to 30 Gy was recommended if possible for the volume [oral cavity – PTV]. We considered the dose of 60 Gy or more to be clinically relevant to determine the AAR of HG toxicity.

3. Results

The skin surface where the 60 Gy isodose encompassed the first two millimeters of skin, could be visualized in 3D view, giving an accurate skin mapping to be treated preventively.The mucosal surface encompassed by the 60 Gy isodose could be determined from the projection of the 60 Gy isodose in 4 CT scan slices (median sagittal, and transversal through the top of the tongue, palatine arch and base of the tongue) ; these informations could be reported on an anatomy drawing of oral cavity and oropharynx with open mouth, resulting on mucosal mapping. THOR intra-oral laser probe should be prescribed to deliver preventively 2 joules per point in the selected areas of tongue and soft palate, and LED Cluster probe, to deliver preventively 3 Joules/cm^2 in selected areas of cheeks, lips and the skin.

4. Conclusion

A mapping of skin and mucosal areas encompassed by the 60 Gy isodose could be established from the dosimetry, to guide accurate prescription of prophylactic PBM in HNC treated by RT. This method should be tested in routine practice.

Antimicrobial Photodynamic Therapy For Infected Oral Lesions Of Cancer Patients: Report Of Some Clinical Cases

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1. Introduction and Hypothesis

Introduction: Cancer treatment can myelosuppress the patient, increasing the risk of infections and bleeding. The antimicrobial photodynamic therapy (aPDT) is a promising therapy for oncologic patients by reducing bacterial, fungal or viral contamination, in addition to be an atraumatic, easy, safe, non-invasive technique and effective against many species of pathogenic microorganisms.

2. Methods

Methods: Thus, the purpose of the present study is to report some successful clinical cases of aPDT for treating infected oral lesions of cancer patients, such as periodontal disease, infected oral mucositis, herpes simplex virus and angular cheilitis. Methylene Blue 0.01% was applied to the lesions 3-5 minutes before irradiation with a red diode laser (660 nm). Two different lasers were used, one presenting 0.04 cm^2 of spot area and, the other one, 0.028cm^2. The power used ranged from 40 to 100 mW, the energy from 4 to 5 J per point, the time from 30 to 120 s and the energy density from 107.1 J/cm^2 to 178.5 J/cm^2. The power density ranged from 1 to 3.6 W/cm^2 and the frequency of application was usually one to three aPDT sessions per patient. The irradiations were applied in contact and perpendicular to the lesion.

3. Results

Results: All patients presented an improvement in pain symptom immediately after aPDT and there was a progressive decrease of the lesions diameter until they were completely healed.

4. Conclusion

Conclusions: Based on the clinical improvement observed by these patients after aPDT, we would like to suggest aPDT as an effective treatment to control infection and, consequently, for stimulating the wound repair of infected oral lesions of cancer patients. However, controlled studies are necessary to confirm these findings.

Analysis Of The Effects Of Photobiomodulation In Cardiac Fibrosis In Experimental Model Of Myocardial Infarction: Study Of The Profile And Control Of Gene Expression

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1. Introduction and Hypothesis

Myocardial Infarction (MI) is an irreversible damage resulting from prolonged ischemia resulting from total or partial occlusion of one or more coronary arteries. Due to ischemic necrosis, in the acute phase of MI, a reabsorption of the cellular components and the extracellular matrix (MEC) is involved, which is the beginning of the tissue repair process. From this period, the deposition

of the components of the new ECM, mainly collagen, in the infarcted tissue and in the transition zone into the viable tissue, culminates in the formation of the infarct scar characterizing the cardiac fibrosis, occurs. Recently, photobiomodulation (PBM) has become a therapeutic alternative by modulating various biological processes depending on the wavelength, dose and condition of the irradiated tissue. Thus, temporal changes in the molecular mechanisms that occurred in the myocardium reminiscent of coronary occlusion-induced infarction (CAO) and submitted to PBM were evaluated.

2. Methods

An in silico analysis was performed using Bioinformatics tools for the verification of genes and microRNAs of the MEC composition involved in the formation of myocardial fibrosis. After searching the databases, 14 genes - Col1a1, Col3a1, MMP-1, MMP-2, MMP-9, TIMP-1, TIMP-2, TGF-β1, TNC, CT-1, Gal-3, NGAL, SPARC and OGN and 4 microRNAs - miR-1, miR-21, miR-29a and miR-133 were associated with post-MI myocardial fibrosis. Coronary occlusion was performed in anethetized rats, briefly, the hearts were exposed after thoracotomy, and photobiomodulation was performed using a laser of Aluminum Gallium Indium Phosphorus - AlGaInP - with wavelength of 660 nm, CW mode, single irradiation, 15mW of power, energy

density 22.5 J / cm^2, 60 seconds of application, irradiated area 0.785 cm^2, dose 1,1 J (Twin Laser - MM Optics ®). Irradiation was performed 60 seconds after coronary occlussion. Ethical committee 034/2015.

3. Results

The Myocardial Infarction Group (MI), and the Infarction + Laser Group (IM + Laser), when compared to the control group (Sham) presented differentially expressed genes, mainly after 3 days of coronary occlusion. In analysis of gene interaction network, we demonstrated associations in the regulation of target genes and microRNAs. The results found in this work suggest that photobiomodulation was able to reduce the formation of myocardial fibrosis especially by the modulation of ECM components genes in cardiac remodeling, opening perspectives for additional investigations on antifibrotic therapies for cardiovascular diseases.

4. Conclusion

Thus, knowledge about the molecular processes involved in cardiac alterations post-insult verified in this study allows characterizing these markers as key genes and enables a more global understanding of the molecular dynamics of cardiac remodeling post-infarction.

Photodynamic Therapy with Phenothiazinium Photosensitizers: Mechanisms of Cell Death

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1. Introduction and Hypothesis

Phenothiazium dyes are a family of molecules that present interesting properties for Photodynamic Therapy. Recently, it was shown that their efficacy is dependent on aggregation, however none is known regarding the cell death mechanism. Autophagy is a pathway related to promotion of cell homeostatis, however, it was already reported that the parallel damage to mitochondria and lysosomes may lead to a destructive outcome. In this study, three methods for cell viability measurement were used in order to predict autophagic cell death in vitro through a rapid screening after photodynamic therapy treatment using phenotiazinium dyes.

2. Methods

HeLa cells were seeded at 48 wells plate (30000 cells/well). After 24 h, the cells were exposed to Azure A (AA), Azure B (AB) and Methylene Blue (MB) at 10 mmol/L in DMEM 1% Fetal Bovine Serum for 3 h at the incubator (37 C and 5% CO2). After incubation, the wells were washed with phosphate buffer saline and irradiated using a continuous LED system (Biolambda, Brazil) 660 ±10nm, 9.5mW/cm^2, 7.0J/cm^2 (740s irradiation). Following irradiation, the cells were kept in the incubator in DMEM 10% SFB for 3, 24 or 48h, when the cell viability assays MTT, Neutral Red (R) and Cristal Violet (CV) were performed, following the literature procedures.

3. Results

The data showed no reduction in viability by MTT 3h after the irradiation for all the compounds used, when both NR and CV methods showed 60% cell death by MB, and 20% by AA and AB. This cell death presented in a short period after treatment is usually reported as necrosis. Analysing data 24h post-treatment, MTT showed 60% of reduction in viability induced by MB, and 20% by either AA or AB. By NR method, MB was the most efficient photosensitizer reaching 80% cell death, followed by AB (60%) while AA was the less eficient (50%). A suchlike behavior was observed in CV method. Similarly, 48h post-treatment MB was the most efficient compound (60% cell death), and no difference was observed between AA and AB (30%) by MTT method. By NR method, MB reached 80% cell death, AB 50% and AA 30%. Finally, by CV method, again MB was the most efficient photosensitizer (60% cell death), pursued by AB and AA (50% death). The combined data determined by the three methods produced AAU (autophagy arbitrary units) values below 1 for all the phenothiazinium dyes at all the timepoints analysed. Except for AA at 48h, which was 1.1, indicating the possibility of any kind of autophagy related cell death.

4. Conclusion

All the methods performed showed that MB is the most active photosensitizer in the series, followed by AB and AA is the less effective. Although this no promissing result, AA seems to be the only photosensitizer in the series to exhibit of autophagy related cell death, which has been considered a more effetive mode to decrease cell proliferation. Further studies are needed to confirm the autophagy-associated cell death induced by AA.

The Effect Of Low Level Laser Therapy On Chronic Lung Inflammation In An Experimental Model Of Asthma.

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1. Introduction and Hypothesis

Asthma is characterized by chronic inflammation in the airways. It presents high prevalence, economic and social cost. Several models have been proposed aiming the discovery of new therapies. Low Level Laser Therapy (LLLT) is relatively new and effective, of very low cost, with no side effects. In this sense, the objective of the present study was to evaluate the effect of LLLT on chronic lung inflammation in an experimental model of asthma induced by House Dust Mite (HDM).

2. Methods

We used Balb/c mice, divided into 4 groups: Basal, HDM, Laser (3J) and HDM+Laser (3J). The LLLT used was diode (660 nm, 100 mW) and used 30s in three points: trachea, left lobe and right. For the experimental model, the animals received orotracheal administration of 100ug/animal HDM on days 0, 14, followed by 3 weekly administrations by day 56. After 24 hours, we studied functional and structural parameters, such as pulmonary inflammation through bronchoalveolar lavage fluid (BALF), quantification of macrophages (CD11b), neutrophils (LY6G), eosinophils (Syglec F), CD3+, CD4+ and CD8+ in the lung, the percentage of 7AAD and ANEXINA V in BALF by flow cytometry, cytokines in BALF (IL-4, IL-5, IL-10 and IL-13) by ELISA, morphometric analysis of eosinophilic peribronchial infiltrate (LUNA), mucus (PAS), collagen (PSR), bronchoconstriction index, bronchial and muscular thickening (HE), pulmonary mechanics (pulmonary elastance) were analysed.

3. Results

Results showed that LLLT was able to modulate observed pulmonary inflammation by reducing the number of cells in the BALF, as well as reducing the percentage of neutrophils, eosinophils and T lymphocytes (CD4+ and CD8+). In addition, it decreased apoptosis and cell necrosis. On the other hand, laser therapy increased the percentage of macrophages and IL-10 and reduced levels of IL-4, IL-5 and IL-13 in the BALF. LLLT was able to reduce mucus production. Regarding the structural alterations, we observed a significant reduction in the quantification of peribronchial eosinophils, collagen deposition, bronchoconstriction index, bronchial and muscular thickening in the airways, after LLLT treatment. Finally, in functional analysis, the evaluation of pulmonary mechanics presented a decrease in all groups submitted to laser therapy.

4. Conclusion

We conclude that the use of laser therapy in the treatment of chronic inflammation of the airways attenuated the inflammatory process, functional parameters and pulmonary structure. We emphasize in general that the 3J laser presented better results. Thus, photobiomodulation can be considered a promising tool for the treatment of chronic pulmonary allergic inflammation observed in asthma.

Efficacy of microneedle patches containing salicylic acid or EGCG on acne vulgaris

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1. Introduction and Hypothesis

Dissolving microneedle technology is an emerging system which makes it easy to deliver medications through skin barrier. It is expected to be effective on acne lesions using a microneedle system coated with a known topical acne medications. The purpose of this study is to evaluate the efficacy and safety of salicylic acid (SA) and epigallocatechin-3-gallate (EGCG) containing microneedle patches on facial acne lesions.

2. Methods

A prospective, split-face study was performed for 4 weeks. A total twenty adult acne patients were conducted to assess the treatments. The participants applied the different types of patches (SA, EGCG and control) on each quadrant area of the face every other day. Clinical improvement was assessed by lesions counting using photographs, investigator grading analysis score, sebum excretion, erythema index, and patients' subjective assessment of satisfaction.

3. Results

At week 4, both SA and EGCG containing microneedle patch showed clinical improvement on each assessments. SA had a superior efficacy than EGCG and control patches, especially on lesions counting of non-inflammatory acne lesions which were showed a statistically significant difference. No adverse effects were noticed.

4. Conclusion

Almost none statistically significant difference was seen among SA, EGCG and control microneedle patches, except for non-inflammatory acne lesions. But still SA and EGCG containing microneedle were shown to be clinically more efficacious than controls.

Analysis of Decontamination of Pressure Injury Through Blue Light - Randomized Trial Clinical Study

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1. Introduction and Hypothesis

The present study was to analyze the effects of photobiomodulation using the Light-emitting Diode (LED), operating at wavelength 420 +/- 20 nm (Violet-Blue) in pressure injury decontamination.

2. Methods

The sample consisted of 36 patients, 24 of whom met the inclusion criteria and were randomized into 3 treatment groups, where three different photobiomodulation. Device: Cosmedical® LED plate Cicatrillux; containing 36 LEDs, 420 +/- 20 nm, optical diameter 10 mm

+/- 2, optical output 2-5 mW, device energy 106J, radiant exposure 3.8 J / cm^2, irradiance 6.4

mW/cm^2. The total energy (Joules) was applied directly to the lesions by means of the LED plate in each group, as follows: 53J (5 min), 106J (10 min) and 159J (15 min), respectively.

3. Results

The analysis of the results was based on the counting of Colony Forming Units (CFU), as well as characterization of the lesions using the National Pressure Ulcer Advisory Panel and severity by the Pressure Ulcer Score Healing scale. The mean age of the study patients was 72 years, most of the pressure lesions were in the sacral region (70%), 62% female patients, 79% of the lesions were in the sacral region and 54% were stage III. The results showed a slight reduction in the CFU count, especially in the treatment group with 159 Joules.

4. Conclusion

We conducted this randomized clinical trial with the objective of verifying if the transposition of the in vitro and preclinical studies translates into an effective clinical application of blue light in the bacterial inactivation of pressure injury. The results showed that the photobiomodulation of lesions at wavelengths of 420 nm to reduce contamination, despite a slight decrease in CFU count in the time of 159J, was not effective in the doses applied in the three groups studied, since no there was a statistically significant reduction in none of them.

Repercussion Of Periodontitis During Pregnancy On The Development Of Allergic Lung Inflammation In The Offspring: The Role Of Photodynamic Therapy

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1. Introduction and Hypothesis

Periodontitis (P) is one of the most common infectious diseases that affects the periodontium and gradually destroys periodontal tissues. The local inflammatory response of P causes systemic effects due many inflammatory mediators to be released in the blood. Alterations during the gestation occasioned by P as well as its repercussions in the offspring have been studied, and the link between P and pregnancy is inconclusive. PDT is characterized by the association of a light source with a photosensitizing agent in order to cause cell necrosis and microbial death. Thus, our objective was to evaluate the effect of P during pregnancy on the development of allergic lung inflammation in the offspring and the effects of photodynamic therapy.

2. Methods

Ten days before pregnancy, periodontitis was induced by ligature technique, and subsequently the rats were caged overnight with a male. Pregnancy was confirmed by vaginal smear. The treatment with PDT was performed 15 days after the induction the ligatures. Pregnant rats non-manipulated were used as control. After 30 days of birth, the offspring was submitted to allergic lung inflammation by ovoalbumin administration. The inflammatory parameters were evaluated 24 hours later. The photosensitizer methylene blue (0.005%, CHIMIOLUX, DMC, São Paulo, Brazil) was administered at the two sites (vestibular and lingual). After three minutes, the periodontal pockets were irradiated with a red laser (MM OPTICS; Wavelength 660 ±10 nm; Radiant power100 mW; Exposure duration 90s; spot size 0.02827 cm^2; Radiant energy 9 J; Irradiance 3.5 W/cm^2; Radiant exposure 318 J/cm^2; Total radiant energy18J).

3. Results

We showed that pregnant rats with periodontitis had an increased influx of leucocytes in the blood as well as elevated levels of IL-6 in the gingival homogenates and PDT reversed these responses. No differences were observed among groups of pregnant rats in relation to weight gained during gestation. We also observed important impact of PDT in the offspring parameters. Our data showed low birth weight in the offspring from periodontitis mothers as well as increased development of lung inflammation and PDT was capable to rescue partially low birth weight, besidesreduced lung inflammation.

4. Conclusion

Our data showed the impact of periodontitis in the offspring and the important effects of PDT. Thus, our data showed the important role of oral health during gestation as well as PDT is an effective therapy.

Efficacy Of Phototherapy To Treat Facial Ageing When Using A Red Versus An Amber Led

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1. Introduction and Hypothesis

The term photoageingis is used to characterize the aging of the skin caused by solar radiation. Clinically, the skin becomes more flaccid, while there is an early appearance of wrinkles and changes such as skin cancer. One of the treatments used to combat photoaging is phototherapy, which uses light emitting diodes (LEDs). The objective of this study will be to evaluate the percentages of reduction in the volume of periocular wrinkles when treated with red and amber LEDs.

2. Methods

The study included women aged 40 to 65, 37 subjects received through photobiomodulation red LEDs (660nm) and amber (590 nm) in the periocular region, each color in a hemifacial. The face side to be treated with each color was randomized. The equipment used was the Cicatrillux BionextLED boards Cosmedical (Maua, Brazil), in contact with skin. Each board features 36 LED units around 10cm x 12cm area. Each LED has 5mW of power, 6.4mW / cm^2 and the final radiant exposure is 3.8J / cm^2 (10 minutes per session). The complete treatment consisted of 10 sessions, 2-3 sessions per week, within 1 month. The volume of periocular wrinkles (crow's feet) was measured by a VisioFace (CK Eletronic) device before and after 10 treatment sessions. To assess the impact of the treatment on the participants' quality of life, two Skindex-29 and Melasquol adapted questionnaires were applied.

3. Results

A statistically significant reduction of approximately 20% in the volume of wrinkles was observed in the two treatments used, and no difference in treatment efficacy was observed in relation to this factor. The results of quality of life questionnaires showed less dissatisfaction of participants with skin condition after treatment.

4. Conclusion

The results of this clinical trial confirmed the effectiveness of phototherapy in reducing periocular wrinkles. There was no difference in the efficacy of treatments in relation to the reduction of wrinkles.

The Effects Of Low Level Laser And Light Therapy On Range Of Motion In Patients With Total Knee Arthroplasty

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1. Introduction and Hypothesis

Low Level laser therapy (LLLT) has been proven to be effective in pain control. Reduction of swelling and tissue repair after TKA surgery. The aim of this study was evaluation the effect of low level laser and light therapy on range of motion in patients with total knee arthroplasty.

2. Methods

This study is a single blinded randomized placebo controlled trial and we evaluated 45 cases of total knee arthroplasty in Imam Khomeini hospital for three months. The patients were under went in three approaches intervention (LASER, LIGHT and CONTROL group) in order to improve range of motion and reduce rehabilitation period in all groups. forty-five randomized patients were enrolled in this study; they were undergoing primary total knee arthroplasty.

Device specifications:

REIMERS & JANSSEN GmbH, 79297 Winden/Germany single probe; 810 nm, 500 mW; 0.005 W/cm^2 0.01 cm^2 ; 5 J/cm^2; 2 Points / 10 J

Treatment specifications:

10 s; 5 times; 3 treatments; In-contact Local H&D acupuncture points at Knee Sequential Per day; shaved.

3. Results

ROM in LASER and LIGHT groups were changed significantly (p value<0/00001) There was significant difference ROM between control group and intervention groups, It should be noted ROM in the LASER group changed more than LIGHT group. Knee ROM after knee arthroplasty in laser group improved significantly (p<0.0001).

4. Conclusion:

The result of the present trial research showed using LL-Laser therapy and Light therapy can reduce the rehabilitation period and improve range of motion in patients with total knee arthroplasty.

Photobiomodulation Therapy On The Pain In A Collagenase-Induced Model Of Tendinitis In Rats - Molecular And Functional Aspects

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1. Introduction and Hypothesis

Tendinopathies are alterations in tendon health, where the most commonly used treatment is the pharmacological treatment for pain relief with unsatisfactory results due to its side effects in prolonged use. The search for non-pharmacological therapies in the treatment of these diseases assumes a prominent role in the medical area. Low level laser therapy (LLLT) has being a promising therapy in the modulation of acute and chronic inflammation with no adverse effects.

The objective of this study was to study the effect of LLLT on the gene expression of COX-2, neurokinin 1; MPO and on the improvement of functional parameters.

2. Methods

Male Wistar rats weighing between 150 and 200g were used, from the UNINOVE Animal Ethics Committee AN0037. The animals were separated into 4 groups: Control, with healthy tendon (CTL), untreated tendinitis (NT) and Tendinitis treated with Sodiun Diclofenac (DIC) or LLLT (L3J) in the following irradiation parameters: (Laser CW, 830nm, 107.14J / cm^2; 3J; 100mW and beam diameter = 0.028cm). In order to induce tendinitis, the animals of the NT, DIC and L3J groups were anesthetized and received transcutaneous injection of collagenase (100µg / animal) in the posterior region of the paw in the calcaneus tendon. The treatments started immediately after induction of tendinitis and continued daily until the 7th day. The animal paw compression test (Randall & Selitto) was performed until the 7th day and then the animals were euthanized and the tendon was removed for analysis.

3. Results

Animals of the NT group showed increased expression of COX-2 and NK1 (223.260100 ± 10.692710 UA) compared to the CTL group (100 ± 4.0251 UA). Both DIC and L3J groups presented a reduction in the expression of COX-2 and NK1 (88.656130 ± 11.444890UA and 56.871650 ± 32.277470UA), respectively, compared to the NT group, and L3J group showed reduction of MPO compared to the NT group. The L3J group presented improvement in the functional parameters of the paw compression (1.56667 ± 6.908208g), with similar values to the control group (-0.8 ± 3.051119g) when compared to the NT group (-24.04 ± 12, 89178g).

4. Conclusion

LLLT modulated the expression of the COX-2 inflammatory enzyme by controlling the painful process by reducing neurokinin expression and improving certain functional parameters.

Evaluation Of The Treatment Of Halitosis With Photodynamic Therapy In Bronchiectasis Patients

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1. Introduction and Hypothesis

Halitosis is an unpleasant odor that emanating from the mouth. Bronchiectasis is a lung disease that are among the extra-oral causes of halitosis. To date, no studies have evaluated its treatment in adult population with bronchiectasis. The aim of this randomized, controlled clinical trial was to treat oral halitosis in bronchiectasic adults with photodynamic therapy after periodontal treatment.

2. Methods

Thirty bronchiectasis patients were randomized into 2 groups: G1- treatment with photodynamic therapy; G2- treatment with tongue scraping). Methylene blue was used as photosensitizer (0.005%) irradiated with THERAPY XT® laser (DMC, São Paulo, Brazil) at 660 nm, continuous wave, 9 J,6 points in contact in the tongue, 90 s per point,100 mW, 3537 mW/cm^2 and320 J /cm^2. Halitosis were evaluated measuring volatile sulfur compounds using gas chromatography. After the treatment, a second evaluation were performed if the halitosis persists, participants received periodontal treatment. Comparisons were made using the t Student test, with the level of significance of 5 % ($p < 0.05$).

3. Results

Thirty-nine bronchiectasis patients were evaluated, and thirty was halitosis positive. After aPDT both groups significantly reduced the levels of halitosis ($p<0.05$).

4. Conclusion

The PDT and scraping treatment was effective in the immediate.

Effects Of Photobiomodulation On Nitric Oxide Synthesis And Viability In C2c12 Cells Cultivated In A Presence Of M1 Macrophages-Conditioned Medium

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1. Introduction and Hypothesis

The macrophages have a great influence and importance to the skeletal muscle regeneration process, since the products secreted by them can influence the satellite muscular cells in their different stages of differentiation. Photobiomodulation (PBM) has demonstrated in the literature the ability to modulate the viability and the inflammatory process in different cell lines. In the present study, the aim was to evaluate the effects of PBM on cell viability and synthesis of nitric oxide (NO) using the same irradiation parameters to treat macrophages and satellite muscle cells.

2. Methods

Myoblasts C2C12 were cultivated in proliferation medium (DMEM+10% Fetal Bovine Serum-FBS) and with differentiation medium (DMEM+2% Horse Serum-HS-for 72h) and after received the M1 macrophage-conditioned medium (M1MM) from irradiated and non-irradiated macrophages. For the activation to M1 profile, J774 macrophages were incubated with interferon-γ and lipopolysaccharide for 2h. The evaluated groups were (a) Proliferation condition (FBS): (1) C2C12+FBS, (2) C2C12+non-activated MM, (3) C2C12+M1MM non-irradiated, (4) C2C12+PBM+M1MM non-irradiated, (5) C2C12+M1MM irradiated, (6) C2C12+PBM+M1MM irradiated; (b) Differentiation condition (HS): (7) C2C12+HS, (8) C2C12+non-activated MM, (9) C2C12+M1MM non-irradiated, (10) C2C12+PBM+M1MM non-irradiated, (11) C2C12+M1MM irradiated and (12) C2C12+PBM+M1MM irradiated.

Cells from each experimental group were centrifuged and the pellets were exposed to laser irradiation (the beam was placed in contact at the bottom of the tube). The irradiation was performed once using an aluminum-gallium-arsenide (AlGaAs) diode laser (Twin Laser®, MM Optics, São Carlos, SP, Brazil) continuous wave, a wavelength of 780 nm, output power of 70 mW, power density of 1.75 W/cm^2, area of 0.04 cm^2, and energy density of 17.5 J/cm^2 for 15 seconds, totaling 1 J. The conditioned medium from J774 cells was collected 24h after the irradiation and also for the macrophages non-irradiated. The C2C12 cells were seeded in 96-well plates after the irradiation and received 50% of the MM (from irradiated or non-irradiated macrophages). After C2C12 were incubated in at 370C, 5% CO2 for 24h and at the end of this period the viability and the NO synthesis were assessed by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and Griess method, respectively.

3. Results

The C2C12 cells from proliferation groups showed an increase in cell viability after the PBM when incubated with M1MM without irradiation ($p<0.05$) and it was observed a reduction in the NO production in cells that received the irradiated M1MM ($p<0.05$). This reduction was also more evident in the group which that both cells were treated with laser ($p<0.01$).

The C2C12 cells cultivated in the differentiation condition that received untreated M1MM showed an increase in cell viability after PBM in comparison to the group that both cell lines received the irradiation ($p<0.05$). The NO synthesis showed a significant decreased in the C2C12 cells treated with PBM that received the untreated M1MM in comparison to the C2C12 group no-irradiated ($p=0.001$) and when both cells were treated with PBM ($p=0.001$).

4. Conclusion

In conclusion, PBM using the same laser parameters, was able to modulate the viability and NO synthesis in C2C12 cultivated in different conditions and in the presence of M1 macrophage-conditioned medium from irradiated and non-irradiated cells.

Use Of Photobiomodulation To The Muscles To Control Glycemia In Type 2 Diabetes Patients: Randomized, Crossover, Double-Blind, Placebo-Controlled Clinical Study

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1. Introduction and Hypothesis

Diabetes mellitus type 2 (DM2) is a metabolic disease with impaired function of the beta-cells of the pancreas, poor insulin production, leading to insulin resistance and hyperglycemia, triggering systemic problems that increase mortality risk. The most common treatment for DM2 is systemic pharmacological therapy, which may lose effectiveness, and sometimes causes sudden hypoglycemia and hepatotoxicity. Photobiomodulation therapy (PBMT) has shown improved insulin resistance in animal models via increased energy metabolism in skeletal muscles, which consume large amounts of glucose. The objective of this study was to evaluate the effects of three PBMT doses on blood glucose levels in DM2 patients during 12 hours after application to body muscles.

2. Methods

This randomized, crossover, double-blind, placebo-controlled clinical study enrolled 10 volunteers (8 women; 2 men; 63±8 years; 78±15 Kg; 32±4 Kg/m2) with a medical diagnosis of DM2. There were 3 regimens of PBMT (dose response): 1) PBMT 100J per site (25 clusters of 4J; 5.7J/cm^2; 50s; 800J total body); 2) PBMT 240J per site (25 cluster of 9.6J; 13.7J/cm^2; 120s; 1,920J total body); 3) Patient's diabetes control drugs plus PBMT placebo [(D+P); 0J per site; 0J/cm^2; 30s; 0J total)]. PBMT was applied in continuous mode through a prototyped flexible array (684cm^2) with 100 light-emitting diodes (LEDs), arranged into 25 clusters each containing 4 infrared LEDs (830±20nm; 80mW each; 114mW/cm^2), totaling 2W, applied to eight separate anatomical sites including quadriceps femoris, hamstrings, triceps surae, and ventral region of the arms and forearms muscles bilaterally. At each session all volunteers were assessed for capillary blood glucose through a glucose meter (Roche) at 5 moments (time response): 1) 1 hour after consuming standardized breakfast (300 Kcal); and 2) 30 minutes, 3) 3 hours; 4) 6 hours and 5) 12 hours after the PBMT session. A 1-week washout was applied after each intervention. All PBMT parameters were measured and calibrated previously by a power and energy meter (PM100D, Thorlabs).

3. Results

Data normality was assessed by Shapiro-Wilk test, and all treatments were compared by ANOVA with Tukey's post-hoc test. Increments in blood glucose were very similar after breakfest for all treatments ($p>0.05$). PBMT 100J decreased blood glucose (mg/dL) significantly compared to PBMT 240J at 30min (-54±14 versus -7±57;$p=0.02$), 3 hours (-86±20 versus -41±50;$p=0.04$), 6 hours (-73±29 versus -26±43;$p=0.04$) and 12 hours (-67±39 versus -12±37;$p=0.01$). There was no significant difference between PBMT 100J and D+P at the same time points (-27±22,$p=0.27$; -68±41,$p=0.28$; -62±48,$p=0.07$; -49±36,$p=0.08$; respectively). Finally, there was no significant difference ($p>0.05$) between PBMT 240J and D+P at all time points.

4. Conclusion

PBMT 100J was efficient to reduce and control glycemia in DM2 patients with a clear time response peaking at 3 hours and a biphasic dose response without side effects, being similar to pharmacological treatment. Statements: All procedures were approved by human ethics committee of the Sacred Heart University, Brazil (opinion n-1.959.414) and conducted in this university. Informed consent was obtained from all participants included in this study supported by research grant 128549/2017-3 from Brazilian Council of Science and Technology Development—CNPq. The authors declare no conflict of interest.

Neuropathic Pain & Photobiomodulation

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Diabetes Mellitus (DM) is a group of metabolic disorders causing a serious international health concern affecting approximately 425 million adults across the globe). By 2045 India is emerging to be the diabetic capital of the world. According to International Diabetic Federation, 72.9 million cases were reported in India in 2017 and 57.9% those currently undiagnosed. The prevalence of DM in India varied from 4.3 % - 10% with an overall prevalence of > 9% . DM leads to both microvascular (neuropathy, retinopathy, and nephropathy) and macrovascular complications (atherosclerosis, stroke, peripheral arterial disease). Long term association of these complications leads to negative impact in patient quality of life.

Diabetic Peripheral Neuropathy (DPN) is one of the most common complication associated with long term diabetes. DPN has a life time prevalence of 50%. Diabetic neuropathy affects all peripheral nerves including pain fibers and 40-50 % of patients with DPN develops Painful Diabetic Peripheral Neuropathy (PDPN). Long-standing peripheral neuropathic pain is seen in one of six diabetic subjects associated with peripheral neuropathy. Painful DPN is associated with functional limitation & poor quality of life. Non-pharmacological symptomatic treatments have also been suggested, including near infrared therapy, and electrotherapies, transcutaneous electrical nerve stimulation (TENS). The efficacy of most conservative treatment options for painful diabetic neuropathy is still need to be established. Therefore, focus of the presentation is to highlight the effect of photo bio modulation on pain and quality of life in type 2 diabetes mellitus with neuropathy.

Stem Cells and Regenerative Medicine

Cell Sheet Of Human Dental Pulp Stem Cell, Associated With Photobiomodulation Therapy For Bone Regeneration Of Diabetic Rats Sections

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1. Introduction and Hypothesis

The bone repair impairment caused by Diabetes Mellitus (DM) demands for new therapeutic strategies. Cell therapy associated with photobiomodulation therapy (PBMT) could improve bone regeneration. One modality of cell therapy is based on transplant of cell sheets (CSs) of stem cells (SCs) that are cultures that preserve cell-cell contact, structural organization, and stem cell phenotype (SCs). The objective of this study was to evaluate the effect of the use of CSs of human dental pulp SCs, associated or not to PBMT, on the regeneration of bone defects in the calvaria of rats with DM.

2. Methods

The study comprised in vitro and in vivo approaches. For analyzing the potential of human dental pulp stem cells (hDPSCs) for maintaining their undifferentiated status and osteogenic differentiation capacity when arranged in cell sheets (CSs), the CSs were formed after being induced for 10-15 days by clonogenic medium containing additional vitamin C (20 µg/ml). Then, the cell viability of hDPSCs in the CSs was assessed by the Live/Dead® assay. Cells dissociated from the CSs were compared with the original hDPSCs. The two cell types were characterized immunophenotypically by flow cytometry using specific mesenchymal stem cell-associated markers (CD105, CD146, CD44, STRO-1, and OCT3/4) and non-associated markers (CD34, CD45 and CD14). Osteogenic differentiation was analyzed with the Alizarin red assay. DM was induced in 72 rats using Streptozotocin (60mg/kg). The diabetic rats received standardized critical size bone defects on the parietal bone, which will then be treated according to the following experimental groups (n=12 per group): DM: with no additional treatment; CS: transplant of CS; LCS: transplant of CS followed by PBMT; PBMT: only PBMT; M: placement of commercial swine collagen membrane (BioGideTM); LM: Placement of BioGideTM followed by PBMT. Healthy rats were used as positive control (NC). PBMT was applied with a single probe diode infrared laser (PhotonLase III DMC - Equipment, São Carlos, SP, Brazil) in the following parameters: 780 nm, 40 mW, 1W/cm^2, 0.04cm^2 beam area, CW, 3s, 3J/cm^2, 0.12J per point, immediately, 48 and 96 hours after surgery. The irradiations were made in contact to the shaved skin of the animal at the site of the defect in punctual mode, at 3 points (one central and the others equidistantly around the defect). Four and eight weeks after surgery, the animals were euthanized, the skulls dissected, fixed and submitted to the analysis by computerized microtomography. The following data were collected: bone volume, relative bone volume, number, thickness and separation of trabeculae, density connectivity and model structure index. The data was treated statistically ($p \leq 0.05$).

3. Results

The preliminary results showed differences in the percentage of bone formation amongst the groups, mostly in 60 days after treatment. The most promising results were those of cell sheet group that showed bone formation similar to that of healthy rats. The PBMT did not interfere in the bone regeneration.

4. Conclusion

The cell sheets retained their stemness and their osteogenic differentiation potential. The association of cell sheet technique and PBMT seems promising as cell therapy to improve bone regeneration of diabetic rats.

Veterinary

Result Of The Class Iiib Laser On Wound In Cat Due To Pharmacodermia After Antibiotic Application

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1. Introduction and Hypothesis

A female cat, 3 months of age, presented an acute wound in the thoracic dorsal area, 1,8cmx1,6cm, due to pharmacodermia after 2 subcutaneous applications of antibiotic doxycycline to Rhinotracheitis. The cat has a great tendency to form abscesses in the subcutaneous tissue and great elasticity of the skin which favors the formation of extensive wounds with a long time of cicatrization and secondary infection. The treatment with the Physiolaser Olympic (RJ-Waldekirch-Germany-1717224), super pulsed, 904nm, 300 Watts, 5 x60watts- probe, dose 15 joules per cm 2, 3,3 minutes, twice a week for 2 weeks was performed to complete healing.

2. Methods

Before the irradiation in the clinic it was performed local cleaning with chlorhexidine solution 0,5% and drying with gauze. The wound was initially 1,8cm width and 1,6cm length and the Physiolaser Olympic, super pulsed, 904nm, 300 Watts, 5 x 60watts- probe had a plastic film protection to irradiation direct contact over the wound, dose 15 joules per cm 2, 3,3 minutes, twice a week for 2 weeks.

3. Results

1 th Application - 5th June - width 1,8cm and length 1,6cm

2 th Application - 8th June 2017 –width 0,8cm and lenght 1cm

3 th Application - 12th June 2017 – width 0,7cm and lenght 0,6cm

4th Application - 14th June 2017- 0,6cm 21th June - complete healing

4. Conclusion

The dose of 15 j/cm^2 twice a week for 2 weeks it was satisfactory for the kitten that presenting a deficient immune system and wound healing without intercurrence.

Result Of Auxiliary Treatment With Laser Acupuncture In Atopic Dermatitis Of A Dog

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1. Introduction and Hypothesis

Canine atopic dermatitis is a inflammatory skin desease that usually demanding multimodal treatment, genetic origin and characterized by intense and generalized pruritus.The dog reported was a female, 13years old, presented itching and alopecia at dorsal region, paws and face, that received auxiliary treatment with low level laser therapy, Physiolaser Olympic(RJ-Waldekirch-Germany-1717224), super pulsed, 904nm, 300 Watts, pen 90watts 1cm^2, 20 joules per point, 1 minute, once a week, 3 weeks, at some acupuncture points, large intestine 4, heart 7, gallbladder 31 and 39, lung 7, stomach 36, was applied to stimulate immunity and reduce itching recovering hair and skin.

2. Methods

The low level laser therapy applied was a Phyolaser Olympic, super pulsed 904nm, pen 90watts 1cm^2, 20 joules per point, 1 minute, once a week, 3 weeks, at some acupuncture points, large intestine 4, heart 7, gallbladder 31 and 39, lung 7, stomach 36, was applied to stimulate immunity and reduce itching.

3. Results

The itching was reduced to a third, hair and skin were completely recovered.

4. Conclusion

The dose of 20j / point, once a week for 3 weeks in the acupuncture points large intestine 4, heart 7, gallbladder 31 and 39, lung 7, stomach 36, presented a satisfactory outcome of hair and skin to atopic dog due to a chronic disease.

The Effect of Photobiomodulation on Healing and Pain Relief of Quadriceps Muscle Contusions

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1. Introduction and Hypothesis

Following a blow to the muscle, patients often get contusions. This could lead to hematoma, loss of activity, or decreased ADL. We believe that Photobiomodulation using pulsed blue 450 nm and red 630 nm light with a printed flexible LED light patch and hydrogel interface, can have a positive impact on this type of injury.

2. Methods

24 subjects were randomly selected for the treatment or sham groups. The treatment group received Photobiomodulation for 30 minutes every day for five days at a fluence of 5 j/cm^2 and

irradiance of 3 mW/cm^2, pulsed at a 33% duty cycle at a frequency of 33 KHz, using blue 450 nm and red 630 nm, using a printed LED substrate. The sham group received a mock treatment. A photo was taken of the quadriceps muscle. Using a tennis ball-serving machine, subjects were hit with a tennis ball in the quadriceps muscle. The ball traveled at 136 kmh. Each subject then performed 10 squats and filled out a VAS for pain. Subjects returned to the lab where a follow-up photo was taken, followed by imaging ultrasound. Each subject received either placebo 30-minute Photobiomodulation treatment or actual treatment at the parameters listed. Subjects returned to the lab for four days where they were treated with either placebo protocol or treatment protocol.

3. Results

We observed a more rapid decrease in pain, improved acceleration of healing based on the color transition of the bruise and a reduced muscle hardness on the subjects treated with the blue-red light patches as compared to placebo. We are continuing the study and will provide statistical analysis as part of our presentation.

4. Conclusion

The use of a LED light patch, which conforms to the body, using blue 450 nm and red 630 nm, provides a promising therapy for the immediate treatment of pain, acute injury and contusion.

Photobiomodulation Ameliorates Lung Inflammation In Sepse-Induced Acute Respiratory Distress Syndrome

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1. Introduction and Hypothesis

Acute respiratory distress syndrome (ARDS) is characterized by rupture of the endothelium and alveolar injury as result by an uncontrolled lung inflammatory response causing gas exchange impairment. Among the main causes of ARDS, sepsis is highlighted. The restoration of normal lung function is very complicated and the treatment of ARDS is still a clinical health problem, so new therapies are needed. It is known that light-emitting diode (LED) treatment displays anti-inflammatory effects, and here we studied the effects of LED treatment on ARDS induced by sepsis.

2. Methods

Adult male Bal/c mice were submitted to LPS injection (5µg/kg, ip, Salmonela abortus equi) and irradiated or not with LED 2 and 6 h after LPS injection. The parameters were investigated 1day after LPS injection.

Device specifications: Bio Lambda LEDstar, Black Box Mini Model, São Paulo, Brazil; Probe Design, Single Probe; Wavelength: 660 nm; Radiant Power: 160 mW; Power Density: 38,5 mW/cm^2; spot area: 4,15 cm^2; Density of energy: 5,8 J/cm^2; Issuance: Continuous (cw); Total Radiant Emission: 24 J.

Treatment specifications: Exposure time: 152 s; Irradiated points: 1 point; Irradiation Method: Direct skin contact; Anatomical location: trachea and lungs; Irradiation rhythm: punctual; Number of treatments: 1 day, two applications; Optical properties of tissue: Healthy tissue; Animals not shaved. These parameters were measured.

3. Results

We showed that LED treatment reduced LPS-induced neutrophils influx, decreased the levels of IL-1β, TNF-α, IL-17A and enhanced the levels of IFN-gamma in the bronchoalveolar fluid. We also observed reduced levels of resolvin D1 and E2 after LED treatment, and no differences were found in lipoxin A4 levels. Moreover, the tracheal hyperresponsiveness was reduced after LED treatment.

4. Conclusion

Our data showed the beneficial effect of short treatment with LED on ARDS caused by sepsis, and suggest that LED is a promisor tool to treat ARDS.

Effect of Photobiomodulation on Lower Urinary tract dysfunction in Rat Cystitis model

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1. Introduction and Hypothesis

It has been reported that photobiomodulation (PBM) controls activity of sensory nervous system associated with pain transmission. Sensory nervous system is also important for storage and voiding function of lower urinary tract and its abnormality is associated with lower urinary tract dysfunctions such as interstitial cystitis and overactive bladder. In this study, we examined the effect of PBM on lower urinary tract dysfunction in rat cystitis model, and determined the power density at the lumbosacral area in order to verify the light dose and efficacy.

2. Methods

Rats were randomly divided into three groups, sham-, control- and laser-group. Cystitis was induced as follows; bladder fistula was prepared for all groups, then acetic acid were injected intravesically through the fistula in control- and laser-group. The next day of cystitis induction, parameters of lower urinary tract function including voiding interval, voiding volume and bladder pressure were evaluated. In laser-group, 830-nm laser was irradiated for 3 minutes on the skin above each side of L6 lumbosacral intervertebral foramen at 10 W pulse mode (10% pulse duty, 20 ms pulse width, 5 Hz frequency, 1.5 cm^2). To determine the PBM dosage at lumbosacral area, photodiode-sensors were implanted near the lumbosacral nerves and laser was irradiated transcutaneously to the sensors.

3. Results

After laser irradiation, voiding interval of laser-group tended to be longer compared with control-group. In sub-group analysis in the animals with short voiding interval (<6min), laser irradiation improved voiding interval and voiding volume statistically ($p<0.05$). On the other hand, detrusor contraction was almost unchanged among all three groups. Power density near lumbosacral nerves was determined as 23.2 mW/cm^2 on this experimental condition.

4. Conclusion

These results indicate that transcutaneous laser irradiation may reach lumbosacral nerves in rats and improve urine storage function without impair of voiding function, particularly in severe urinary frequency.

Effects Of Red Laser On Skin Graft In Rats

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1. Introduction and Hypothesis

A skin graft is commonly used to cover open wounds in orthopedic and plastic surgery. However, the skin graft may cause important complications and consequently result in partial or complete necrosis of the graft. Recently, more innovative therapeutic approaches have been developed aiming to avoid and to reduce necrosis and enhance safety and viability of skin grafts. Among the innumerable range of interventions, the positive effects of photobiomodulation.In this context, it was hypothesized that the Laser may optimize healing process and stimulate the skin graft survival in rats was raised. Thus, the aim of this study was to evaluate the effectiveness of red laser on collagen expression using an experimental model of skin graft in rats.

2. Methods

20 adult Wistar rats (Rattus norvegicus) were used. After animals anesthetized, a incision of 3x5-cm rectangle was centrally made. Once the grafts were harvested, the panniculus carnosus muscle was dissected from the overlying dermis. The previously procured skin grafts were sutured onto the dorsal recipient beds using nonabsorbable material. Animals were randomly divided into: Control group (CG) and Laser group (LG). A laser continuous wavelength (660 nm), 0,04 cm beam diameter, 40 mW, 60 s, 2.4 J, 1.0 W/cm^2, and 60 J/cm^2 was used. Laser irradiation started immediately after the surgery at 12 transcutaneous point, above and surrond the site of the injury, and it was performed with an interval of 24 h between each session, totaling sevem sessions. On postoperative day 7, the animals were again anesthetized, and the skin grafts were removed.

3. Results

The morphometric evaluation of the density of collagen fibers results demonstrated that the percentage of collagen fiber was significantly higher in red laser treated group compared to control group.

4. Conclusion

These partial results suggest that laser was efficient in promoting skin graft survival in rats and enhancing the collagen synthesis.

Effects of Low Level Laser Therapy on the prognosis of Split Thickness Skin Graft in Type 3 Burn of Diabetic Patients: A case series

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1. Introduction and Hypothesis

Significant populations in burn centers are diabetic burn patients. Healing process in these patients is complicated. Split-thickness skin grafting (STSG) is widely used to treat burn ulcers but in diabetic patient due to impaired tissue perfusion some of this grafts fails and rate of amputation is high. The technique of Low level laser therapy improves tissue perfusion and wound healing. The purpose of this case report is introducing a new therapeutic method for accelerating healing with better prognosis in these patients.

2. Methods

Diabetic type 2 patients with grade 3 burn ulcers, candidate for amputation, were enrolled to the study. We used Low Level Laser Therapy (LLLT) by red, 650 nm laser light, 150 mW, radiation area: 0.25 cm^2, power density: 0.6 W/cm^2, 2 J/cm^2, continuous mode, 16-20 point, 10 sec each point, (Canadian Optic Laser Center, COL laser, Canada) direct in-contact probe. To avoid contamination a sterile, transparent cover was used. Output laser power after passing through the cover was calculated using dosimeter for bed of the ulcer, and 6 J/cm^2 for the margins along with intravenous laser therapy, before and after Split Thickness Skin Graft (STSG) for treating grade 3 burn ulcers in 13 diabetic ulcers.

3. Results

All 13 ulcers had complete healing in at last 8 weeks

4. Conclusion

In this case series, we present 13 cases of diabetic ulcer with type 3 burn wound, that were healed completely using Low Level Laser Therapy (LLLT) and Split Thickness Skin Graft. This is the first time that these two techniques are combined for treatment of burn ulcer in diabetic patients. Using LLLT with STSG might be a promising treatment for burn victim especially diabetic patients.

Effect of Low Level Laser Therapy on the Healing Process of Donor Site in Patients with Grade 3 Burn Ulcer after Skin Graft Surgery (a randomized clinical trial)

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1. Introduction and Hypothesis

Background: Skin graft is standard therapeutic technique in patients with deep ulcers but managing donor site after grafting is very important.

Low Level Laser Therapy (LLLT) has been used in several medical fields, but there is not any report of using this method for healing of donor site in burn patients. In this study for the first time we evaluate the effects of LLLT on the healing of donor site in these patients.

2. Methods

Materials and Methods: The protocols and informed consent were reviewed according to Iranian Registry of Clinical Trials (IRCT2016020226069N2). 18 donor sites in 11 patients with grade 3 burn ulcer were selected. Donor areas were divided into 2 parts, for laser irradiation and control randomly. Laser area was irradiated by red, 650 nm laser light, 150 mW, radiation area: 0.25 cm^2, power density: 0.6 W/cm^2, 2 J/cm^2, continuous mode, 16-20 point, 10 sec each point, (Canadian Optic Laser Center, COL laser, Canada) direct in-contact probe. To avoid contamination a sterile, transparent cover was used. Output laser power after passing through the cover was calculated using dosimeter. Treatment was done on day 0 (immediately after surgery), 3, 5, 7 and 9 (5 sessions). Dressing and other therapeutic cares for both sites were the same. Patient and the person who analyzed the results were blinded.

3. Results

Results: The size of donor site reduced in both groups during the 7 days study period ($P<0.01$) and this reduction was significantly greater in laser group ($P=0.01$).

4. Conclusion

Discussion: In the present study for the first time we evaluate the effects of LLLT on the healing process of donor site in burn patients. The results showed that local irradiation of red laser light can accelerate wound healing process significantly.

Effect of Low-Level Laser Therapy (Ga-As laser, 904 nm) on the Serum Vascular Endothelial Growth Factor (VEGF) and Wound Closure in Diabetic Foot Ulcers

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1. Introduction and Hypothesis

Diabetic foot ulcer is known to be resistant to conventional treatment of wound healing. This study was conducted to evaluate the efficacy of low-level laser therapy (LLLT) with 904 nm Ga-As laser, on the serum vascular endothelial growth factor (VEGF) and the wound closure in diabetic foot ulcers.

2. Methods

30 volunteered patients with type II diabetes and grade II of diabetic foot ulcer (DFU) enrolled in this study. The patients were randomly divided into two Ga-As laser (n=15) and placebo (n=15) groups. Ga-As laser (Physiolaser Olympic Version 1.5, Germany) was applied two j/cm^2 and 90mW for 3days/week, every other day, and 4 weeks (12 sessions totally). In placebo group, the probe was set like to the laser group, but the power was off. In both groups, patients received similar conventional therapy, including debridement, cleaning of the wound with saline, and dressings. At the first and twelfth treatment sessions, blood sample was taken before and after LLLT to determine the levels of serum VEGF. Wound surface area. (WSA) was measured at the first, sixth, and twelfth sessions.

3. Results

The results showed after twelve sessions of laser therapy, VEGF decreased significantly compared to the placebo group (P=0.04).The percentage of decrease of wound surface area (%DWSA), in the LLLT group was significantly greater than the placebo group at 12th session (P = 0.005).

4. Conclusion

The result suggest Ga-As laser is effective to angiogenesis through control of the VEGF expression. It seems that LLLT is effective to fast decrease of wound surface area in DFU.

Effect Of Low-Level Laser Therapy In The Treatment Of Accidental Extravasation Of Medications

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1. Introduction and Hypothesis

Extravasation in the administration of some medications by intravenous infusion remains an accidental complication that may result in serious damage to patients. The symptoms vary according to the amount and concentration of extravasated drug, and the location of the vein where extravasation occurs.. Pain and erythema, induration and skin discoloration progresses over few days and weeks, and may progress to blister formation. Blister or necrosis can lead to invasion and destruction of deeper structures how tendons, nerves, and joints. The aim of this study was to evaluate the effect of Low-Level Laser Therapy (LLLT) in the treatment of accidental extravasation of chemotherapy, sodium bicarbonate and glucose

2. Methods

We will report three most serious cases of extravasation in our service, all the patients were treated in Clinical Hospital of São Paulo State University (UNESP), Medical School, Botucatu, Brazil, the ambulatories of Oncology, Neonatology and Renal Transplant, respectively.

Case 1: N.E.R, female, 4 year-old, in treatment for rhabdomyosarcoma,of left nasal cavity, presented with a blister on the back of right hand due to accidental extravasation of vincristine. The protocol of treatment was blister breaking with insulin needle for secretion drainage, LLLT and curative with essential fatty acids around the injured. The protocol of irradiation was punctual irradiation by contact, energy 1J, 10 s irradiation time, per point in six points around and one point central in the injured, every other days per one week. After 10 days the injured presented healed.

Case 2: A.C, male, 6 days of life, premature birth, presented with a ulcer on the back of right foot due to accidental extravasation of sodium bicarbonate. The protocol of treatment was LLLT and curative with essential fatty acids in the ulcer. The protocol of irradiation is been punctual irradiation by contact, energy 1J, 10 s irradiation time, per point in six points around and one point central in the injured, every other days, with progressive reduction of the lesion.

Case 3: J.C.A, male, 57 year-old, was submitted to kidney transplantation, presented with blisters on the back of left foot due to accidental extravasation of glucose concentrate. The protocol of treatment was blister breaking with insulin needle for secretion drainage, LLLT and curative with essential fatty acids and hyaluronidase. The protocol of irradiation was punctual irradiation by contact, energy 2J, 20 s irradiation time, per point in eleven points around and 4 points central in the injured of major blister, diary per 10 days. After the patient leaving the hospital the LLLT continue to be performed once a week, due the impossibility of the patient to return daily. Irradiation was performed by a diode laser (Therapy XT, DMC Equipamentos Ltda, São Carlos, SP, Brazil, SN 8975), wavelength 660 nm, power density 100 mW, and 0,028 cm^2 spot area.

3. Results

We observed that the evolution of wound healed was more rapid compared with the protocol previously used without LLLT.

4. Conclusion

The inclusion of LLLT in the protocol of accidental extravasation of medications accelerated the healing process as well as reduced secondary infections.

Comparison Between 830 Nm And 660 Nm Laser On Integration Of Full-Thickness Graft In Rats

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1. Introduction and Hypothesis

The skin graft is one of the most widely used techniques in reconstructive plastic surgery, being able to restore the structure and function of cutaneous lesions. There are controversies regarding the parameters of the therapeutic resource used in skin grafting, among them the wavelengths are extremely important due to their physiological related effects. Objective is to compare the effects of light intensity (LBI) with different wavelengths (830 nm and 660 nm) in the integration of full-thickness grafts.

2. Methods

Fifteen Wistar rats were used, were divided into 3 groups of 10 animals: Group 1 (sham) – subjected to skin-grafting surgery; Group 2 – subjected to skin-grafting surgery, followed by 830-nm laser irradiation; Group 3 – subjected to skin grafting, followed by 660-nm laser irradiation. The grafts were demarcated with the standard measurements of two areas of 4 cm^2 (2x2 cm) in the dorsal region of the animal, two grafts were performed, one cranial located just below the lower angles of the scapulae and a flow 3 cm below the cranial graft. The application of laser therapy (DMC®) occurred on the third day after removal of the dressing and for seven days thereafter. The energy density of 10 J / cm^2, at wavelengths of 830 and 660 nm, continuous emission mode, average power of 30 mW, cross-sectional area of the beam of 0.028 cm^2, application time of 9.34 seconds, total energy of 3.64 J. The application was perpendicular to the skin graft, being applied in 13 points, being 8 points in the external region of the graft and 5 points in the internal region.

3. Results

On the 10th postoperative day, a sample was collected for evaluate the gap area formed between the graft and its bed, through hemotoxylin-eosin. The average gap area of the group 1 was 6.94 µm, group 2 was 1.80 µm and group 3 was 2.46 µm.

4. Conclusion

The low-intensity laser at both wavelengths (830 and 660 nm) improved integration of the skin graft and laser 830 nm promoted a smaller gap between the graft and the receptor bed.

Epidermal Thickness In Skin Graft After Application Laser 830 Nm In Rats Submitted To Nicotine.

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1. Introduction and Hypothesis

The survival of the graft in studies decreases when these are applied in compromised recipient beds, as in the case of smokers, being need to investigate therapeutic resources that increase the viability of the grafts. Purpose: Evaluate the epidermal thickness in skin graft submitted to

nicotine after laser 830 nm application.

2. Methods

Fifteen Wistar rats were used, were divided into 3 groups of 10 animals, were submitted to nicotine in 28 days in the preoperative: Group 1- submitted only to the surgical technique for obtaining skin graft, Group 2- stimulated to nicotine and Group 3 - stimulated with laser 830 nm. The grafts were demarcated with the standard measurements of two areas of 4 cm^2 (2x2 cm) in the dorsal region of the animal, two grafts were performed, one cranial located just below the lower angles of the scapulae and a flow 3 cm below the cranial graft. The application of laser therapy (DMC®) occurred on the third day after removal of the dressing and for seven days thereafter. The energy density of 10 J / cm^2, continuous emission mode, average power of 30 mW, cross-sectional area of the beam of 0.028 cm^2, application time of 9.34 seconds, total energy of 3.64 J. The application was perpendicular to the skin graft, being applied in 13 points, being 8 points in the external region of the graft and 5 points in the internal region.

3. Results

On the 10th postoperative day, a sample was collected for evaluate the epidermal thickness through hemotoxylin-eosin using Image J® software. The average epidermal thickness of the group 1 was 1.13 µm, group 2 was 0.93 µm and group 3 was 1.41 µm.

4. Conclusion

The laser 830 nm increased the epidermal thickness of skin graft in rats submitted to nicotine.

In Vivo Dose Response Study Of 532nm Cw Laser On Rat Skin

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1. Introduction and Hypothesis

Green spectrum visible lasers are routinely employed in numerous medical and defence fields such as treatment of vascular pigmented lesions, tattoo inks, skin toning, dazzling target and mob dispersal. With expanding utility, various accidental and targeted injuries have also been reported in occupational settings. Such green laser associated occupational hazards remain uncharacterized. Thus, our study is aimed at investigating the extent of damage imposed by green laser, monitoring its effect at different time intervals to determine safe exposure limit and to develop methods to ameliorate laser-inflicted injuries.

2. Methods

Male Sprague-Dawley rats (180±20 g) were used. The dorsal surface of each rat was shaved, divided sequentially into 5 rows before irradiating a circular spot of 10 mm diameter (0.786 cm^2) at 0.1, 0.25, 0.5, 1 and 1.5 W/cm^2 (1, 2.5, 5, 1, 1.5 J/cm^2 respectively) using a single probe 532 nm CW laser (Shanghai Dream Tech, China; SDL-532-15000MFL) for duration of 10 sec (single exposure). An infrared thermal imaging camera (VarioCAM, Jenoptik) was used to measure temperature of irradiated skin surface. The skin tissues were collected at different intervals post exposure and investigated for expression of heat shock proteins, inflammatory markers like cyclooxygenase 2, TNFα and DNA damage and apoptosis markers like PARP 1, p53, CAPNS1, caspases etc by immunoblotting to evaluate the biological effects of green laser. Damage to skin tissue and collagen fibres was assessed by histopathology and Masson's trichrome staining.

3. Results

We found significantly increased level of HSPs ($p<0.05$) concomitant with histopathological observations showing up regulated inflammatory response at higher fluences (above 0.25 W/cm^2) in exposed rats compared to non-irradiated controls. Consistent with these findings, higher dose of green laser was found to trigger an elevated expression of calpain subunit, PARP 1, p53 and Caspase 3 indicating laser-induced apoptosis. However, low-intensity green laser irradiation (0.1 W/cm^2) resulted in elevated calcium release and activation of pAkt pathway along with no change in PARP 1 and Caspase 3 expression with respect to control skin.

4. Conclusion

Our study suggests that irradiation with low-intensity green laser followed by pAkt activation may instigate a stimulatory response whereas higher intensities may lead to activation of calpains followed by DNA damage which might lead to apoptosis. The observations were found to be consistent with histopathological evaluation showing neutrophilic debris accumulation and acute inflammation at higher doses, whereas no change was observed at lower doses with respect to non-irradiated skin. This study outlines the effects produced by green laser irradiation on skin and its utility in choosing safe laser dose for skin-based applications and evolving methods to ameliorate laser-related injuries.

Statement: All experiments conducted on rats were approved by Institutional Animal Ethical Committee, DIPAS, India. Authors declare that they have no conflict of interest whatsoever.

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Fournier's Gangrene: Clinical Presentation

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1. Introduction and Hypothesis

Fournier's gangrene (FG) is a fulminant form of infective necrotising fascitis of the perineal, genital, or perianal regions, which commonly affects men, but can also occur in women and children. Fournier's gangrene is associated with acute pain and progressive necrosis of the affected tissue. Necrotizing cellulitis is secondary to anaerobic germs as well as Gram negative bacteria. Thus, associated with high morbidity da mortality. Despite advanced management mortality is still high and averages 30%. Considering the characteristics of Fournier's gangrene, laser is an extremely appropriate tool in order to enhance wound healing as well as an anti microbial effect.

2. Methods

Female Patient, 40 years old, with diabetes mellitus and amputation of the left inferior member urged for treatment of a necrotizing infected lesion situated on the left gluteus measuring 40 x 10 cm. She was treated according to the protocol: three times a week with low power laser (Therapy EC, DMC Equipamentos, LTDA, São Carlos, SP, Brazil), with power of 100mW, CW irradiation mode, single probe, spot size of 0.028 cm^2, 3.5 W/cm^2, contact mode (wound edge) and scanning mode (wound bed).

For the wound bed (lesion area), photodynamic therapy tecnique was performed using methylene blue at 0,005% during 1 minute applied on the lesion and posterior irradiation of the red wavelength (660 nm). The lesion was divided into four quadrants. Each quadrant received 90 seconds of irradiation, Dose (9 Joules per quadrant), Energy Density of 315 J/cm^2 per quadrant.

For the wound edges (distal area), infrared wavelength (830 nm) was used. The wound edge perimeter was irradiated in 8 points, considering a distance of 5cm from one point to the other. It was used 10 seconds of irradiation, Dose (1 Joules per point), total Energy Density of 280 J/cm^2 for the total wound edge.

After 1 month of treatment (12 sessions), the laser sessions were reduced from three time to once per week. Total of 30 sessions.

3. Results

After 12 sessions, there was a significant reduction on the dimensions and the wound bed tissue was viable. There was no longer exsudate, dark color on the wound bed, irregular wound edges or irregular aspect of the lesion. Moreover, the depth of the wound reduced completely. Consequently, laser sessions were established once a week and the total restablishment of a healthy tissue was accomplished with 30 laser sessions.

4. Conclusion

Laser effect on wound healing, modulation on inflamation, analgesia and antimicrobial effect are well established on literature. Therefore, its use in devastating wound like Fournier's Gangrene is mandatory. Laser is a tool that is capable of reducing the morbidity and moratlity of these complex wounds.

The Low-Level Laser Therapy In The Treatment Of Steven Johnson Syndrome/Toxic Epidermal Necrolysis

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1. Introduction and Hypothesis

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are variants of the same condition. It is a rare, acute, and potentially fatal skin reaction.. STS/TEN is classified by the extent of the detached skin surface area: STS less than 10%, STS/TEN 10% to 30% and TEN more than 30% body surface area. STS/TEN is estimated to affect two to seven million people each year, SJS being three times more common. It can affect anyone with a genetic predisposition, it is more common in older people and women. Medications are causative in over 80% of cases. The aim of this case report was to show the effect of Low-Level Laser Therapy (LLLT) n the control of pain and healing of oral lesions in children with STS and STS/TEN treated in Clinical Hospital of São Paulo State University (UNESP), Medical School, Botucatu, Brazil.

2. Methods

Case 1: I.K.P, female, 10 year-old, she arrived in the emergency room with papules in the abdomen, back, inguinal region and lower limbs that evolved rapidly with conjunctival hyperemia, chest and tumble blisters, exulcerated lesions in lips and genital. She had been using for five days prednisone, dipyrone and ibuprofen for bronchospasm. Diagnosis was STS/TEN. Patient was intubated, sedated and administered electrolytes and immunoglobulin for 3 days and hydrocortisone. Lesions stopped evolving. The LLLT was used in labial lesions. The protocol of irradiation was punctual irradiation by contact, energy 1,5J, 16 s irradiation time, per point in 4 points around and 2 points central in the injured in the upper and lower lips, every other days, during 30 days, until wound healing. The irradiation was performed by a diode laser (model Flash Laser II, DMC Equipamentos Ltda, São Carlos, SP, Brazil, SN 169), wavelength 660 nm, power density 1,2W, and 0,028 cm^2 spot area.

Case 2: M.V,S.M male, 10 year-old, with history of after 2 days using benzathine penicillin for sore throat and fever, started with red and bullous lesions in the body and oral cavity. He was medicated with amoxicillin + ibuprofen + paracetamol with progressive worsening of the lesions when he was referred to the hospital. The diagnosis was SJS. Prednisone was administered with lesion regression. The LLLT was used in labial lesions. The protocol of irradiation was punctual irradiation by contact, energy 1J, 10s irradiation time, per point in 4 points around and 2 points central in the injured in the upper and lower lips, every other days until during seven days, until wound healing. Irradiation was performed by a diode laser (Therapy XT, DMC Equipamentos Ltda, São Carlos, SP, Brazil, SN 8975), wavelength 660 nm, power density 100 mW, and 0,028 cm^2 spot area. Prior to LLLT session the scabs were removed with physiological saline.

3. Results

we observed improvement of pain and a faster healing of oral lesions after the sessions with LLLT.

4. Conclusion

LLLT can be included in the treatment protocol of patients with STS e STS/TEN, with the aim of relieving pain and accelerating healing.

Healing After Photobiomodulation In Pressures Injuries

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1. Introduction and Hypothesis

Pressure lesions (PL) are one of the most prevalent complications in hospitalized patients, constantly challenging health professionals. A study conducted at a US hospital found an averagetreatment cost of US$129,248.00forpatients with PLs over the course of 29 months. A Brazilian study saw a monthly cost of R$8,899.63 in hospitalized patients. Both studies evidence the high cost of this adverse event. Among the resources used for the treatment of PL, photobiomodulation (PBM) has been shown to be an efficient therapy in wound healing.To evaluate healing after PBM with red LEDs on PL patients in stages 3 and 4,admitted to a public tertiary level hospital in Brazil.

2. Methods

This was a randomized controlled clinical trial, using a convenience sample, totaling 15 in-patients. In the conventional group (CG) the dressings were made daily with physiological solution, hydrogel of sodium and calcium alginate and covered with cellulose membrane. In the LED group (LEDG) the dressings were made daily with physiological solution and irradiated with a cluster of red LEDs (Linealux Rosso®, Cosmedical, Brazil). The parameters used were$\lambda = 664 \pm 20$ [nm], P=15.0mW, irradiance 4.8W / cm^2, area of irradiation10X13 cm, radiant exposure 2.9J / cm^2, E = 9.0J and t = 10min, applied daily until discharge of the patient after 15 days of treatment. The PUSH scale was used for evaluation of the lesions. The resultant scores were analyzed using the Mann-Whitney test corrected by Fisher, with $\alpha = 0.05$.

3. Results

From the 6th dressing session on, 86% of the LEDG achieved a 14% reduction on the PUSH scale, while in the CGonly 37.5% of the patients achieved this. This result evidences the improvement in the quality of the wound bed andin the borders,as well asthe decrease inthe exudate and area, primordial characteristics for a good evolution in cicatrization.

4. Conclusion

PBM with LED was as effective as the conventional treatment for PL, with advantages in practicality, cost and quality of the healing process.Further studies, with larger samples, will be required before this therapy can become a standard procedure in the hospital setting.

Mechanism Of Action Of Laser Radiation And Magnetic Field On Sperm

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1. Introduction and Hypothesis

It is generally believed that the joint (simultaneous) effect of laser radiation and a constant magnetic field is characterized by a synergistic effect and underlies the method of magneto-laser therapy. However, the biophysical mechanisms that are in the basis of this phenomenon have not been studied well.

2. Methods

To assess the equivalence of effects of laser radiation and constant magnetic field, the determination of penetration depth of laser radiation with wavelength of 543 nm into biological tissue at power density of 10 mW/cm^2 in the absence and presence of external magnetic field with induction of 50 mT was carried out. The velocity of curvilinear motion of control and irradiated by laser spermatozoa after their activation by water was studied using television control (in the field of view of microscope). The lasers and LEDs with wavelength of 630 nm at power density of 3 mW/cm^2 were used. The exposure time was 15-600 s.

3. Results

It is shown that the application of constant magnetic field affects the depth of penetration of laser radiation into the multilayered tissue of living spermatozoa. Such an influence of the magnetic field is absent when controlling the depth of penetration of laser radiation into dead muscle tissue. The modifying effect of the magnetic field on the depth of penetration of laser radiation into the tissue of spermatozoa can be due to a change in the structure of cells under the action of this physical factor.

It is established that the application of magnetic field with induction of 50 mT changes the motion dynamics of spermatozoa: alterations in the velocities of straight line and curvilinear motion induced by magnetic field and in the nature of trajectories of motion as well as a pronounced effect of the magnetic field on the distribution of cells according to the velocity of motion are observed. This effect is a confirmation of the liquid crystalline nature of the structure of spermatozoa.

The maximal stimulating effect on the functional and biochemical characteristics of sperm is observed when exposed to linearly polarized radiation; the photobiological effect induced in the same dose interval by natural light (i.e. unpolarized) is much less pronounced. The magnitude of the stimulating effect of circularly polarized radiation has an intermediate value. The biological effects induced by linearly polarized radiation of monochromatic laser and quasi-monochromatic LED sources are practically identical.

4. Conclusion

The results obtained point to the synergism of the action of laser radiation and magnetic field. Among the photophysical processes of resonant and non-resonant nature (the orientational effect of light, the action of gradient forces, dipole-dipole interactions, thermo-optical processes), capable of causing photobiological effects which are dependent on such laser-specific characteristics as polarization and coherence, the determining role in the processes studied in this work belongs to the orientational effect of light on structures with liquid crystalline ordering character. The presence of weak absorption enhances the sensitivity of these systems to structural transitions induced by the orientational effect of polarized radiation.

Effect of Photobiomodulation in Cell Death, Oxidative Stress and Expression of Biomarkers in Huvec Cells Submitted to Experimental Hypoxy

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1. Introduction and Hypothesis

Studies about the applicability of laser therapy are increasing because their satisfactory results in clinical and experimental research. It is known that in vitro laser irradiation is capable of improving cell viability, increasing proliferation and decreasing death. However, there is no description in the literature about the use of laser in endothelial cells as a pretreatment. These cells have promising angiogenic potential for revascularization therapies in cases of atherosclerosis and ischemia. Therefore, laser is able to modulate the cellular metabolism becomes a therapeutic alternative in these cases. OBJECTIVE: The objective of the present study was to analyze the effects of photobiomodulation on endothelial cells submitted to experimental hypoxia.

2. Methods

Human Umbilical Cord Endothelial Cell (HUVEC) groups were irradiated (single irradiation) with a 660nm wavelength laser (Twin FLEX-LASER apparatus, MMOptics Ltd, Brazil), 10 mW, 1.5 J/cm^2, CW mode, irradiated are 0.04 cm^2 for 6 seconds (Laser and Laser + Hypoxia groups). Subsequently, groups were submitted to hypoxia for 24h (Hypoxia and Laser + Hypoxia groups). In sequence, cell viability analyzes for apoptosis (Propidium Iodide) and necrosis (Annexin V), leukocyte adhesion molecule (CD11b) and reactive oxygen species (ROS) were performed by flow cytometry. Cells and supernatants were collected and processed for analysis of VEGF expression by real-time PCR and ELISA, respectively.

3. Results

Hypoxia decreased cell viability in HUVEC cells. Therefore, laser-treated group submitted to hypoxia did not show significant differences in cell viability, CD11b expression and ROS values. However, VEGF mRNA expression increased significantly ($p<0.01$, ANOVA) after laser irradiation in cells submitted to hypoxia. Increased VEGF expression was not detected by ELISA in culture medium of this group.

4. Conclusion

We demonstrated that laser pretreatment was effective in increasing VEGF mRNA expression of HUVEC cells after hypoxia protocol.

Analysis Of The Effect Of Low Intensity Laser Irradiation On Vein Popliteal And Nitric Oxide-Generating Enzyme Modulation Induced In Patients With Subacute Deep Venous Thrombosis.

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1. Introduction and Hypothesis

Venous thromboembolism (VTE) is a disease with high morbidity and mortality which includes deep vein thrombosis (DVT) and pulmonary embolism (PE). It is an important and common condition it is characterized, by unspecific symptoms. The disease's clinical conditional depends upon the affected veins and extension of the thrombus. The presented signs and symptoms are: pain, and muscle tenderness, which are the most frequent, leading edema, cyanosis and increased dilation of the superficial veins, also occur. The most clinical applications for diagnosis, it is the vascular ultrasound, noninvasive test and without side effects. Nitric oxide (NO) modulates inflammatory or anti - inflammatory responses, depending on cell type and stimulus, it is released further arteries than in veins. Photobiomodulation (PBM) exerts significant anti -inflammatory effects in the initial processes of wound healing, decreasing chemical mediators, cytokines, reduced the inflammatory cells migration and increased growth factors contribute directly to tissue remodeling.

2. Methods

We used two groups of patients (n=10 each) with subacute thrombosis in femoropopliteal territory, and analyzed the effect of PBM in relation to the diameter of femoral, popliteal, medial and lateral gastrocnemius and short saphenous veins and also through iNOS (induced nitric oxide synthase) messenger RNA expression (mRNA) in the blood before and after the laser application. We used a cluster of the brand Multi Radiance Medical's GameDay model, composed of 2 diodes, one infrared diode operating at wavelength 875 nm and another red at 660 nm. The parameters used were: Wavelength 660 nm, Power 67.5 mW, energy density 0.03J / cm^2, energy 3 Joules, beam area 4 cm, pulsed mode, time 240 seconds. The PBM was applied to the popliteal cavus and throughout the popliteal vein.

3. Results

The PBM resulted in vasodilation vein medial gastrocnemius ($p<0.01$, ANOVA), although this effect was not observed in other veins analyzed. Messenger RNA expression (mRNA) of iNOS was found to be increased significantly ($p<0.01$, ANOVA) in the blood collected after the laser irradiation.

4. Conclusion

Thus, we suggested that photobiomodulation caused venous vasodilation and increased iNOS gene expression in patients with deep vein thrombosis.

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