LED References & Abstract Summary

Pain & Inflammation - Abstract Summary

Effect of light emitting diodes in the photodynamic therapy of rheumatoid arthritis.

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College of Biomedical Engineering and Applied Sciences, Dhana Ganesh, Handigaun Marg, Kathmandu,

Abstract

BACKGROUND: Complex and painful surgical removal of synovium was replaced by arthroscopic synovectomy as an early treatment of rheumatoid arthritis (RA), which being limited to bigger joints, was replaced by laser synovectomy. Having been more time consuming, laser photodynamic therapy (PDT) replaced this method. Due to thermal side effects of laser PDT, an alternative source of light has been sought. Therefore, to make RA treatment cheaper, less hazardous and suitable according to anatomical geometry, light emitting diodes (LEDs) were used in this study as a potential source of light.

METHODS: Red, white, yellow and infra-red (IR) LEDs were tested to measure the optical penetration for soft tissue and their scattering. In vitro study of the cellular response of normal and inflamed lymphocytes from healthy and RA patients was conducted respectively. Methotrexate was injected as photosensitizer to achieve cell-specific precision.

RESULTS: IR LEDs showed the maximum penetration and least scattering of all LEDs used. Specimen with drug administration and with subsequent exposure to IR LEDs exhibited massive suppression of inflamed activated lymphocytes in comparison to other controls.

CONCLUSION: The properly selected wavelength and intensity of light beam were incident with great precision so that they would not affect unwanted cells, but inflamed activated cells were suppressed due to intense light energy following Methotrexate injection. Without invasion, IR LED PDT showed an effective and cheaper treatment solution for RA.

The combined cytotoxic effects of Methotrexate and IR LEDs brought forth the suppression of inflamed activated lymphocytes during rheumatoid arthritis. Since Methotrexate is already approved as anti-inflammatory drug in RA patients, its use as photosensitizer (in this study) need not be justified as non-hazardous for clinical use *in vivo*. LED PDT for RA is non-invasive because it does not require surgery or incision. This method requires variable number of LEDs (depending upon the anatomical geometry) and few basic electrical parameters; so, the treatment is cheaper than other conventional methods. In this study, IR LEDs were arranged in circular fashion in order to illuminate the circular well of 6-well plates. But the arrangement can vary according to anatomical geometry. Hence, this technique is convenient for application in any type of joint, i.e. smaller to bigger ones. Number of lymphocytes before and after LED PDT

decreased significantly, thereby, reducing the risk of inflammation in joints. Thus, PDT using IR LEDs helped to develop a low cost, non-invasive and convenient treatment.

Improvement of pain and disability in elderly patients with degenerative osteoarthritis of the knee treated with narrow-band light therapy.

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Geriatric Medical Center, Shmuel Harofe Hospital, Beer Yaakov, Israel.

Abstract

OBJECTIVE: To evaluate the effects of low-power light therapy on pain and disability in elderly patients with degenerative osteoarthritis of the knee.

DESIGN: Partially double-blinded, fully randomized trial comparing red, infrared, and placebo light emitters.

PATIENTS: Fifty patients with degenerative osteoarthritis of both knees were randomly assigned to three treatment groups: red (15 patients), infrared (18 patients), and placebo (17 patients). Infrared and placebo emitters were double-blinded.
INTERVENTIONS: Self-applied treatment to both sides of the knee for 15 minutes twice a day for 10 days.

MAIN OUTCOME MEASURES: Short-Form McGill Pain Questionnaire, Present Pain Intensity, and Visual Analogue Scale for pain and Disability Index Questionnaire for disability were used. We evaluated pain and disability before and on the tenth day of therapy. The period from the end of the treatment until the patient's request to be retreated was summed up 1 year after the trial.

RESULTS: Pain and disability before treatment did not show statistically significant differences between the three groups. Pain reduction in the red and infrared groups after the treatment was more than 50% in all scoring methods (P less than 0.05). There was no significant pain improvement in the placebo group. We observed significant functional improvement in red- and infrared-treated groups (p less than 0.05), but not in the placebo group. The period from the end of treatment until the patients required treatment was longer for red and infrared groups than for the placebo group (4.2 +/- 3.0, 6.1 +/- 3.2, and 0.53 +/- 0.62 months, for red, infrared, and placebo, respectively).

CONCLUSIONS: Low-power light therapy is effective in relieving pain and disability in degenerative osteoarthritis of the knee.

The effects of LED emissions on sternotomy incision repair after myocardial revascularization: a randomized double-blind study with follow-up

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Abstract

This study aimed to analyze the effects of light emitting diode (LED) therapy on sternotomy pain and healing in patients who underwent coronary artery bypass grafting (CABG). The patients were followed for 6 months after the surgery to determine their dehiscence. This study was conducted with 90 volunteers who electively submitted to CABG. The volunteers were randomly allocated into three different groups of equal size: LED (λ of 640±20 nm and spatial average energy fluency of 1.2 J/cm2 during hospitalization), placebo, or control. The outcomes assessed were pain when coughing by a visual analog scale (VAS) and the McGill questionnaire and sternotomy healing by clinical assessment and photographical register end interpretation. The LED group had better pain reduction, as indicated by both the VAS and the McGill questionnaire (number of words chosen and pain index) ($p \leq 0.05$), on days 6 and 8 after hospital discharge compared to the placebo and control groups. One month after surgery, almost no individual mentioned pain when coughing. Three researchers blindly analyzed the incision photographs to determine hyperemia and wound closure, and they found that the LED group had both less hyperemia and less incision bleeding or dehiscence. The LED therapy (640 nm) had an analgesic effect on the sternotomies of patients who underwent CABG, increasing their incision healing and preventing dehiscence.

Conclusion

LED therapy (λ of 640±20 nm) had an analgesic effect on the sternotomies of patients submitted to CABG observed by a visual analog scale and the McGill pain questionnaire. This therapy also increases the rate of incision healing including hyperemia reduction and incision closure and, in consequence, preventing dehiscence.

Lasers Surg Med. 2007 Aug;39(7):614-21.

The anti-inflammatory mechanism of 635 nm light-emitting-diode irradiation compared with existing COX inhibitors.

Lim W, Lee S, Kim I, Chung M, Kim M, Lim H, Park J, Kim O, Choi H.

Source: Department of Oral Pathology, 2nd Stage of Brain Korea 21 for School of Dentistry, Dental Science Research Institute, Chonnam National University, Bug-Gu, Gwangju, Korea.

Abstract

BACKGROUND AND OBJECTIVES:

Inhibition of cyclooxygenase (COX) and prostaglandin E(2) (PGE(2)) protects cells against cell injury in specific pathophysiological situations: inflammation and oxidative stress. Although the anti-inflammatory effects have been reported in clinical fields for specific wavelength irradiation during wound healing, the physiological mechanism has not been clarified yet. The aim of the present study is to investigate the anti-inflammatory mechanism of 635 nm light-emitting-diode (LED) irradiation compared with existing COX inhibitors.

STUDY DESIGN/MATERIALS AND METHODS:
The present study investigated anti-inflammatory effects of 635 nm irradiation on PGE(2) release, COX and phospholipase A(2) (PLA(2)) expression, and reactive oxygen species (ROS) dissociation in arachidonic acid (AA)-treated human gingival fibroblast (hGF). These results were compared with their existing COX inhibitors: indomethacin and ibuprofen. The PGE(2) release was measured by enzyme immunoassay, the COX expression was measured by western blot and reverse transcriptase polymerase chain reaction (RT-PCR), and ROS level was measured by flow cytometry, laser scanning confocal microscope and RT-PCR.

RESULTS:
Results showed that 635 nm irradiation and existing COX inhibitors inhibit expression of COX and PGE(2) release. Unlike indomethacin and ibuprofen, 635 nm irradiation leads to a decrease of ROS levels and mRNA expression of cytosolic phospholipase A(2) (cPLA(2)) and secretary phospholipase A(2) (sPLA(2)).

CONCLUSION:
Taken together, 635 nm irradiation, unlike indomethacin and ibuprofen, can directly dissociate the ROS. This inhibits cPLA(2), sPLA(2), and COX expression, and results in the inhibition of PGE(2) release. Thus, we suggest that 635 nm irradiation inhibits PGE(2) synthesis like COX inhibitor and appears to be useful as an anti-inflammatory tool.

Support Care Cancer. 2012 Jul;20(7):1405-15. doi: 10.1007/s00520-011-1223-8. Epub 2011 Jul 3.

Amelioration of oral mucositis pain by NASA near-infrared light-emitting diodes in bone marrow transplant patients.

Hodgson BD[1], Margolis DM, Salzman DE, Eastwood D, Tarima S, Williams LD, Sande JE, Vaughan WP, Whelan HT.

Abstract
PURPOSE: This study seeks to investigate the use of extra-orally applied near-infrared phototherapy for the reduction of oral pain secondary to chemotherapy- and radiation therapy-induced mucositis in adult and pediatric hematopoietic stem cell transplant (HSCT) patients.

METHODS:
Eighty HSCT patients were divided into regular (R) and low (L) risk groups, then to experimental (E) and placebo (P) groups, resulting in four groups (ER, EL, PR, PL). Experimental subjects received 670 (± 10) nm gallium-aluminum-arsinidelight-emitting diode device for 80 s at ~50 mW/cm(2) energy density and power exposure of 4 J/cm(2). Placebo

patients received the same procedures, but with a placebo phototherapy (identical device but <5 mW/cm(2) energy density). Patients received their respective light therapy once per day starting on the day of the HSCT (day 0) and continued through day +14. Blinded evaluators examined the patients three times per week and scored their oral tissues and patient-reported pain assessments at each evaluation utilizing the WHO, NCI-CTCAE, and OMAS scales.

RESULTS:
Analysis of the mean scores at each observation demonstrate that the extra-oral application of phototherapy resulted in a significant reduction in patient-reported pain between the ER and PR patients ($p < 0.05$) at day +14 when graded via the WHO criteria. The ER and EL patients were improved in almost all other categories and assessment scales, but the differences were not statistically significant.

CONCLUSION:
Phototherapy demonstrated a significant reduction in patient-reported pain as measured by the WHO criteria in this patient population included in this study. Improvement trends were noted in most other assessment measurements.

J Cosmet Dermatol. 2008 Mar;7(1):30-4. doi: 10.1111/j.1473-2165.2008.00358.x.

Use of light-emitting diode photomodulation to reduce erythema and discomfort after intense pulsed light treatment of photodamage.

Khoury JG[1], Goldman MP.

Abstract
OBJECTIVES:
This study evaluates the use of light-emitting diode (LED) photomodulation therapy to accelerate resolution of post-intense pulsed light(IPL) erythema.

METHODS:
In this split-face study, 15 subjects were randomized to receive LED treatment to one side of the face as determined by computer-generated randomization numbers. All 15 subjects received a single IPL treatment for facial photodamage. Immediately after IPL treatment, one side of the face was treated for 35 s with the LED device. The other side was not treated. Subjects returned 24 h later for a second LED treatment on the same side of the face. Posttreatment erythema was rated on both sides of the face by the blinded investigator and by subjects immediately after IPL treatment, 24 h later, and 1 week later on a scale of 0% (no erythema) to 100% (severe erythema). Patients commented on post treatment discomfort immediately after IPL treatment.

RESULTS:
Mean erythema scores on the first visit were significantly higher ($P = 0.0054$) on the side not treated with LED (52.7 +/- 24.6) than on the LED-treated side (43.3 +/- 21.9). Visit 2 data showed a similar trend ($P = 0.0281$). The subjects reported similar findings with mean erythema scores on the first visit on the LED-treated side (46.7 +/- 25.3) compared with the untreated side (60.0 +/- 23.3); the difference was significant ($P = 0.0382$). On the second visit, the mean

erythema scores trended lower on the LED-treated side (24.3 +/- 22.1) than on the untreated side (27.9 +/- 25.8), but the difference did not reach statistical significance (P = 0.1365). Erythema scores on both facial sides were 0 for all subjects 1 week after IPL treatment. Four patients commented that post treatment discomfort was considerably less on the LED-treated side immediately after treatment.

CONCLUSION:
LED photomodulation treatment may accelerate the resolution of erythema and reduce post treatment discomfort in IPL-treated patients with photo damage.

The effect of two phototherapy protocols on pain control in orthodontic procedure—a preliminary clinical study -
Maria Ângela Lacerda Rangel Esper & Renata Amadei Nicolau & Emília Ângela Lo Schiavo Arisawa
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Conclusions

The results obtained in the present study suggest that:
- The LLLT (LASER) with the parameters used, did not promote significant lowering in the pain reported by patients with tooth movement as compared to the other groups.
- The LED therapy, with the dosimetry used, promotes a marked pain decrease after orthodontic movement when compared to control (during the entire experimental time) and placebo groups (pain peak)
– The LED group was superior to the LLLT (LASER) group regarding the pain decrease in post-orthodontic movement.

Wound Healing Abstracts

(Celluma original research) Comparison of laser and diode sources for acceleration of in vitro wound healing by low-level light therapy
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Abstract.
Low-level light therapy has been shown to improve in vitro wound healing. However, well-defined parameters of different light sources for this therapy are lacking. The goal of this study was (1) to determine if the wavelengths tested are effective for in vitro wound healing and (2) to

compare a laser and a light-emitting diode (LED) source at similar wavelengths. We show four wavelengths, delivered by either a laser or LED array, improved in vitro wound healing in A549, U2OS, and PtK2 cells. Improved wound healing occurred through increased cell migration demonstrated through scratch wound and transwell assays. Cell proliferation was tested by the (3-(4,5-dimethylthiazol-2-yl)-5-(3-car-boxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium) (MTS) assay and was found generally not to be involved in the wound healing process. The laser and LED sources were found to be comparable when equal doses of light were applied. The biological response measured was similar in most cases. We conclude that the laser at 652 (5.57 mW⁄cm2, 10.02 J⁄cm2) and 806 nm (1.30 mW⁄cm2, 2.334 J⁄cm2) (full bandwidth 5 nm), and LED at 637 (5.57 mW⁄cm2, 10.02 J⁄cm2) and 901 nm (1.30 mW⁄cm2, 2.334 J⁄cm2) (full bandwidth 17 and 69 nm respectively) induce comparable levels of cell migration and wound closure.

DARPA Soldier Self Care: Rapid Healing of Laser Eye Injuries with Light Emitting Diode Technology –

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5Walter Reed Army Institute of Research, Washington D.C.

The results of this study and others suggest that photobiomodulation with red to near infrared light augments recovery pathways promoting neuronal viability and restoring neuronal function following injury. Importantly, there was no evidence of damage to the normal retina following 670 nm LED treatment. Based on these findings, we suggest that photobiomodulation may represent an innovative and novel therapeutic approach for the treatment of retinal injury as well as the treatment of retinal diseases, including age-related macular degeneration, glaucoma, diabetic retinopathy, and Leber's hereditary optic neuropathy.

Effect of Light-emitting Diode Irradiation on Wound Healing –

Harry T. Whelan, Medical College of Wisconsin, Robert L. Smits, Medical College of Wisconsin, Ellen V. Buchman, Medical College of Wisconsin, Noel T. Whelan, Medical College of Wisconsin, Scott G. Turner, Medical College of Wisconsin. *Journal of Clinical Laser Medicine and Surgery, Volume 19, No. 6 (December 2001), DOI: 10.1089/104454701753342758*

Conclusion:

We believe that the use of NASA LED for light therapy alone, and in conjunction with hyperbaric oxygen, will greatly enhance the natural wound healing process, and more quickly return the patient to a preinjury/illness level of activity. This work is supported and managed through the NASA Marshall Space Flight Center–SBIR Program.

Mitochondrial signal transduction in accelerated wound and retinal healing by near-infrared light therapy

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Abstract

Photobiomodulation by light in the red to near infrared range (630–1000 nm) using low energy lasers or light-emitting diode (LED) arrays has been shown to accelerate wound healing, improve recovery from ischemic injury in the heart and attenuatedegeneration in the injured optic nerve. Recent evidence indicates that the therapeutic effects of red to near infrared light result, in part, from intracellular signaling mechanisms triggered by the interaction of NIR light with the mitochondrial photoacceptor molecule cytochrome c oxidase. We have demonstrated that NIR-LED photo-irradiation increases the production of cytochrome oxidase in cultured primary neurons and reverses the reduction of cytochrome oxidase activity produced by metabolic inhibitors. We have also shown that NIR-LED treatment prevents the development of oral mucositis in pediatric bone marrow transplant patients. Photobiomodulation improves wound healing in genetically diabetic mice by upregulating genes important in the promotion of wound healing. More recent studies have provided evidence for the therapeutic benefit of NIR LED treatment in the survival and functional recovery of the retina and optic nerve in vivo after acute injury by the mitochondrial toxin, formic acid generated in the course of methanol intoxication. Gene discovery studies conducted using microarray technology documented a significant upregulation of gene expression in pathways involved in mitochondrial energy production and antioxidant cellular protection. These findings provide a link between the actions of red to near infrared light on mitochondrial oxidative metabolism in vitro and cell injury in vivo. Based on these findings and the strong evidence that mitochondrial dysfunction is involved in the pathogenesis of numerous diseases processes, we propose that NIR-LED

photobiomodulation represents an innovative and non-invasive therapeutic approach for the treatment of tissue injury and disease processes in which mitochondrial dysfunction is postulated to play a role including diabetic retinopathy, age-related macular degeneration, Leber's hereditary optic neuropathy and Parkinson's disease.

Journal of Clinical Laser Medicine & Surgery, Volume 19, Number 6, 2001, Mary Ann Liebert, Inc. Pp. 305–314

Effect of NASA Light-Emitting Diode Irradiation on Wound Healing

HARRY T. WHELAN, M.D.,1,6,8 ROBERT L. SMITS, JR., M.D.,1 ELLEN V. BUCHMAN, B.S.,1 NOEL T. WHELAN, B.S.,1,8 SCOTT G. TURNER, M.S.,1 DAVID A. MARGOLIS, M.D.,4 VITA CEVENINI, 8 HELEN STINSON, B.S.,8 RON IGNATIUS,3 TODD MARTIN, B.S.,3 JOAN CWIKLINSKI, M.S.,1ALAN F. PHILIPPI, M.D.,6 WILLIAM R. GRAF, Ph.D.,6 BRIAN HODGSON, D.D.S.,4,5LISA GOULD, M.D., Ph.D.,2 MARY KANE, B.S.,2 GINA CHEN, B.S.,2 and JAMES CAVINESS, M.D.7

ABSTRACT

Objective: The purpose of this study was to assess the effects of hyperbaric oxygen (HBO) and near-infrared light therapy on wound healing. *Background Data*: Light-emitting diodes (LED), originally developed for NASA plant growth experiments in space show promise for delivering light deep into tissues of the body to promote wound healing and human tissue growth. In this paper, we review and present our new data of LED treatment on cells grown in culture, on ischemic and diabetic wounds in rat models, and on acute and chronic wounds in humans. *Materials and Methods*: *In vitro* and in vivo (animal and human) studies utilized a variety of LED wavelength, power intensity, and energy density parameters to begin to identify conditions for each biological tissue that are optimal for biostimulation. *Results*: LED produced in vitro increases of cell growth of 140–200% in mouse-derived fibroblasts, rat-derived osteoblasts, and rat-derived skeletal muscle cells, and increases in growth of 155–171% of normal human epithelial cells. Wound size decreased up to 36% in conjunction with HBO in ischemic rat models. LED produced improvement of greater than 40% in musculoskeletal training injuries in Navy SEAL team members, and decreased wound healing time in crew members aboard a U.S. Naval submarine. LED produced a 47% reduction in pain of children suffering from oral mucositis. **Conclusion:** We believe that the use of NASA LED for light therapy alone, and in conjunction with hyperbaric oxygen, will greatly enhance the natural wound healing process, and more quickly return the patient to a preinjury/illness level of activity. This work is supported and managed through the NASA Marshall Space Flight Center–SBIR Program.

Anti-Aging Abstracts

The utilization of nonthermal blue (405-425 nm) and near infrared (850-890 nm) light in aesthetic dermatology and surgery-a multicenter study.

Lask G, Fournier N, Trelles M, Elman M, Scheflan M, Slatkine M, Naimark J, Harth Y.

UCLA Medical School, Los Angeles, CA.

Abstract
BACKGROUND: A major cause of skin aging is a chronic micro-inflammation triggered by UV radiation and external pollutants. It has been demonstrated that blue light diminishes inflammatory conditions and near infrared light enhances circulation.

OBJECTIVES: To assess the effectiveness of a non thermal dual wavelength -- blue (405 - 420 nm) and near infrared (850 - 900 nm) -- light source in skin rejuvenation, in the reduction of the duration of post skin resurfacing erythema and in the acceleration of healing of post surgical conditions (face lift and breast augmentation).

METHODS: We have utilized a non contact, hand free dual wavelength light source (iClearXL and Clear100XL, Curelight Ltd) to treat over 60 patients and perform three controlled studies in four centers. Follow up duration was three months. Control group for photo-rejuvenation consisted of patients treated with Glycolic peeling and daily appliance of vitamin C Control group for post skin resurfacing erythema duration consisted of patients untreated by the light source and control group for post surgical healing consisted of patients untreated by the light source or treated by the light source on one side only.

RESULTS: Post skin resurfacing erythema duration is reduced by 90%. The healing of post surgical conditions is substantially accelerated and discomfort is reduced. The anti aging effect of the light source includes: reduction of pore size in 90% of patients with stable results at three months follow up, enhanced skin radiance in 90% of patients with stable results at three months follow up and smoothing of fine wrinkles in 45% of patients with stable results at three months follow up. The control group showed poor results which were stable for a duration of less than one month.

CONCLUSIONS: A non thermal, non contact / hand free light source emitting at 405-420 nm and 850-900 nm considerably enhances aesthetic and surgical aesthetic procedures without consuming user time.

Clinical experience with light-emitting diode (LED) photomodulation.
Weiss RA, McDaniel DH, Geronemus RG, Weiss MA, Beasley KL, Munavalli GM, Bellew SG.
Maryland Laser, Skin and Vein Institute, Hunt Valley, MD 21030, USA.

Abstract
BACKGROUND: Light-emitting diode (LED) photomodulation is a novel nonthermal technology used to modulate cellular activity with light.

OBJECTIVE: We describe our experience over the last 2 years using 590 nm LED photomodulation within a dermatologic surgery environment.

METHODS: Practical use of nonthermal light energy and emerging applications in 3,500 treatments delivered to 900 patients is detailed.

RESULTS: LED photomodulation has been used alone for skin rejuvenation in over 300 patients but has been effective in augmentation of results in 600 patients receiving concomitant nonablative thermal and vascular treatments such as intense pulsed light, pulsed dye laser, KTP and infrared lasers, radiofrequency energy, and ablative lasers.

CONCLUSION:
LED photomodulation reverses signs of photoaging using a new nonthermal mechanism. The anti-inflammatory component of LED in combination with the cell regulatory component helps improve the outcome of other thermal-based rejuvenation treatments.

A prospective, randomized, placebo-controlled, double-blinded, and split-face clinical study on LED phototherapy for skin rejuvenation: clinical, profilometric, histologic, ultrastructural, and biochemical evaluations and comparison of three different treatment settings.

Lee SY, Park KH, Choi JW, Kwon JK, Lee DR, Shin MS, Lee JS, You CE, Park MY.
Department of Dermatology, National Medical Center, 18-79, Euljiro 6-ga, Jung-ku, Seoul, Republic of Korea.

Abstract

Light-emitting diodes (LEDs) are considered to be effective in skin rejuvenation. We investigated the clinical efficacy of LED phototherapy for skin rejuvenation through the comparison with three different treatment parameters and a control, and also examined the LED-induced histological, ultrastructural, and biochemical changes. Seventy-six patients with facial wrinkles were treated with quasimonochromatic LED devices on the right half of their faces. All subjects were randomly divided into four groups treated with either 830nm alone, 633nm alone, a combination of 830 and 633nm, or a sham treatment light, twice a week for four weeks. Serial photography, profilometry, and objective measurements of the skin elasticity and melanin were performed during the treatment period with a three-month follow-up period. The subject's and investigator's assessments were double-blinded. Skin specimens were evaluated for the histologic and ultrastructural changes, alteration in the status of matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs), and the changes in the mRNA levels of IL-1ss, TNF-alpha, ICAM-1, IL-6 and connexin 43 (Cx43), by utilizing specific stains, TEM, immunohistochemistry, and real-time RT-PCR, respectively. In the results, objectively measured data showed significant reductions of wrinkles (maximum: 36%) and increases of skin elasticity (maximum: 19%) compared to baseline on the treated face in the three treatment groups. Histologically, a marked increase in the amount of collagen and elastic fibers in all treatment groups was observed. Ultrastructural examination demonstrated highly activated fibroblasts, surrounded by abundant elastic and collagen fibers. Immunohistochemistry showed an increase

of TIMP-1 and 2. RT-PCR results showed the mRNA levels of IL-1ss, TNF-alpha, ICAM-1, and Cx43 increased after LED phototherapy whereas that of IL-6 decreased. This therapy was well-tolerated by all patients with no adverse effects. We concluded that 830 and 633nm LED phototherapy is an effective approach for skin rejuvenation.

Varying ratios of wavelengths in dual wavelength LED photomodulation alters gene expression profiles in human skin fibroblasts.

McDaniel DH, *Weiss RA*, *Geronemus RG*, *Mazur C*, *Wilson S*, *Weiss MA*.

Source

Laser Skin & Vein Center of Virginia, Institute of Anti-Aging Research; Virginia Beach, Virginia 23462, USA.

Abstract

BACKGROUND AND OBJECTIVE:

LED photomodulation has been shown to profoundly influence cellular behavior. A variety of parameters with LED photomodulation can alter cellular response in vitro. The effects of one visible and one infrared wavelength were evaluated to determine the optimal ratio to produce a net increase in dermal collagen by altering the ratio of total energy output of each wavelength. The ratio between the two wavelengths (590 and 870 nm) was shifted in 25% increments.

STUDY DESIGN/MATERIALS AND METHODS: Human skin fibroblasts in culture were exposed to a 590/870 nm LED array with total combined energy density fixed at 4.0 mW/cm.. The ratio of 590/870 nm tested parameters were: 100/0%, 75/25%, 50/50%, 25/75%, and 0/100%. These ratios were delivered using pulsed duty cycle of exposure (250 milliseconds "on" time/100 milliseconds "off" time/100 pulses) for a total energy fluence of 0.1 J/cm.. Gene expression was examined using commercially available extra cellular matrix and adhesion molecule RT PCR Arrays (SA Biosciences, Frederick, MD) at 24 hours post-exposure.

RESULTS: Different expression profiles were noticed for each of the ratios studied. Overall, there was an average (in an 80 gene array) of 6% expression difference in up or downregulation between the arrays. The greatest increase in collagen I and decrease in collagenase (MMP-1) was observed with 75/25% ratio of 590/870 nm. The addition of increasing proportions of IR wavelengths causes alteration in gene expression profile. The ratios of the wavelengths caused variation in magnitude of expression.

CONCLUSIONS: Cell metabolism and gene expression can be altered by simultaneous exposure to multiple wavelengths of low energy light. Varying the ratios of specific wavelength intensity in both visible and near infrared light therapy can strongly influence resulting fibroblast gene expression patterns

A Controlled Trial to Determine the Efficacy of Red and Near-Infrared Light Treatment in Patient Satisfaction, Reduction of Fine Lines, Wrinkles, Skin Roughness, and Intradermal Collagen Density Increase

Alexander Wunsch1 and Karsten Matuschka2

Abstract
Objective: The purpose of this study was to investigate the safety and efficacy of two novel light sources for large area and full body application, providing polychromatic, non-thermal photobiomodulation (PBM) for improving skin feeling and appearance. Background data: For non-thermal photorejuvenation, laser and LED light sources have been demonstrated to be safe and effective. However, lasers and LEDs may offer some disadvantages because of dot-shaped (punctiform) emission characteristics and their narrow spectral bandwidths. Because the action spectra for tissue regeneration and repair consist of more than one wavelength, we investigated if it is favorable to apply a polychromatic spectrum covering a broader spectral region for skin rejuvenation and repair. Materials and methods: A total of 136 volunteers participated in this prospective, randomized, and controlled study. Of these volunteers, 113 subjects randomly assigned into four treatment groups were treated twice a week with either 611–650 or 570–850nm polychromatic light (normalized to *9 J/cm2 in the range of 611–650 nm) and were compared with controls (n = 23). Irradiances and treatment durations varied in all treatment groups. The data collected at baseline and after 30 sessions included blinded evaluations of clinical photography, ultrasonographic collagen density measurements, computerized digital profilometry, and an assessment of patient satisfaction. Results: The treated subjects experienced significantly improved skin complexion and skin feeling, profilometrically assessed skin roughness, and ultrasonographically measured collagen density. The blinded clinical evaluation of photographs confirmed significant improvement in the intervention groups compared with the control. Conclusions: Broadband polychromatic PBM showed no advantage over the red-light-only spectrum. However, both novel light sources that have not been previously used for PBM have demonstrated efficacy and safety for skin rejuvenation and intradermal collagen increase when compared with controls.

Regulation of Skin Collagen Metabolism In Vitro Using a Pulsed 660nm LED Light Source: Clinical Correlation with a Single-Blinded Study
Daniel Barolet1,2, Charles J. Roberge3, Francois A. Auger3,4, Annie Boucher1 and Lucie Germain3,4

It has been reported that skin aging is associated with a down regulation in collagen synthesis and an elevation in matrix metalloproteinase (MMP) expression. This study investigated the potential of light-emitting diode (LED) treatments with a 660nm sequentially pulsed illumination formula in the photobiomodulation of these molecules. Histological and biochemical changes were first evaluated in a tissue-engineered Human Reconstructed Skin (HRS) model after 11 sham or LED light treatments. LED effects were then assessed in Aged/photoaged individuals in a split-face single-blinded study. Results yielded a mean percent difference between LED-treated and non-LED-treated HRS of 31% in levels of type-1 procollagen and of _18% in MMP-1. No histological changes were observed. Furthermore, profilometry quantification revealed that more than 90% of individuals showed a reduction in rhytid depth and surface roughness, and, via a blinded clinical assessment, that 87% experienced a reduction in the Fitzpatrick wrinkling

severity score after 12 LED treatments. No adverse events or downtime were reported. Our study showed that LED therapy reversed collagen down regulation and
MMP-1 upregulation. This could explain the improvements in skin appearance observed in LED-treated individuals. These findings suggest that LED at 660nm is a safe and effective collagen-enhancement strategy.

Acne - Abstract Summary

Clinical Efficacy of Self-applied Blue Light Therapy for Mild-to-Moderate Facial Acne.
Gold MH, *Andriessen A*, *Biron J*, *Andriessen H*.

Abstract
This study was an evaluation of the performance of self-applied, blue light, light-emitting diode therapy in the treatment of mild-to-moderate inflammatory acne on the face, concerning: 1) time to improvement and/or resolution of the number of blemishes and lesions on the face; 2) quality of skin condition; 3) occurrence and count of the number of new blemishes and lesions; and 4) ease of product use; patient comfort, wellbeing, and satisfaction during the treatment period; and safety of treatment. Subjects (N=21) were included according to the inclusion/exclusion criteria and after they had given informed consent. The blue light treatment was conducted over an eight-week period. For study data management and analysis, SPSS 16.0 statistical software was used. Data management and analysis was performed independently using, where appropriate, ANOVA, student t-test, and Mann-Whitney test for N=20. Tests were carried out at the five-percent significance level. The confidence interval was 95 percent. Twenty-one subjects concluded the study (18/21 were female and 3/21 were male). Upon the first outbreak of acne, subjects had a mean age of 15 years (range 8-28 years), and 19 subjects had mild-to-moderate acne for a mean duration of 13.1 years. During the study period with self-applied blue light treatment, the total number of comedones on the face had significantly reduced for the assessment at Day 7 ($p<0.019$) and at Day 28 ($p<0.001$). The total number of open comedones (blackheads) on the face during the treatment period was reduced significantly ($p<0.02$) for assessment at treatment Day 7 ($p<0.005$) and for the assessment at Day 28. The total number of closed comedones (whiteheads) on the face during the treatment period, was reduced significantly ($p<0.007$) for the assessment at Day 28. The total number of papules during treatment had reduced significantly for assessment at Day 7 ($p<0.048$) and Day 28 ($p<0.005$). The total number of pustules during treatment had reduced, but this difference was not statistically significant. This was similar for nodules present. Subjects expressed confidence in using the self-applied blue light without the supervision of a doctor. Regarding previous treatments, subjects expressed dissatisfaction and considered self-applied blue light treatment to be better for their condition. Self-applied blue light treatment was reported to be easy and safe to use.

Combination blue (415 nm) and red (633 nm) LED phototherapy in the treatment of mild to severe acne vulgaris.

Goldberg DJ, *Russell BA*.

Source

Skin Laser & Surgery Specialists of New York/New Jersey, and Department of Dermatology, Mount Sinai School of Medicine, New York, NY 10022, USA.

Abstract

BACKGROUND AND OBJECTIVE: Acne vulgaris represents both a challenge to the treating dermatologist and a major concern for the patient. Conventional treatments have proved inconsistent with often unacceptable side effects and high rates of recurrence. Non-thermal, non-laser, phototherapy for acne with a combination of blue and red light has recently attracted attention. The present study was designed to assess the efficacy of this combination phototherapy.

METHODS: Twenty-four subjects, Fitzpatrick skin types II-V, with mild to severe symmetric facial acne vulgaris were recruited for the study. Subjects were well matched at baseline in terms of both age and duration of acne. Subjects were treated over eight sessions, two per week 3 days apart, alternating between 415 nm blue light (20 minutes/session, 48 J/cm2) and 633 nm red light (20 minutes/session, 96 J/cm2) from a light-emitting diode (LED)-based therapy system. Patients received a mild microdermabrasion before each session. Acne was assessed at baseline and at weeks 2, 4, 8 and 12.

RESULTS: Twenty-two patients completed the trial. A mean reduction in lesion count was observed at all follow-up points. At the 4-week follow-up, the mean lesion count reduction was significant at 46% (p=0.001). At the 12-week follow-up, the mean lesion count reduction was also significant at 81% (p=0.001). Patient and dermatologist assessments were similar. Severe acne showed a marginally better response than mild acne. Side effects were minimal and transitory. Comedones did not respond as well as inflammatory lesions.

CONCLUSIONS: Combination blue and red LED therapy appears to have excellent potential in the treatment of mild to severe acne. Treatment appears to be both pain- and side effect-free.

Light-emitting diode 415 nm in the treatment of inflammatory acne: an open-label, multicentric, pilot investigation.

Tremblay JF, *Sire DJ*, *Lowe NJ*, *Moy RL*. UCLA School of Medicine, Los Angeles, CA, USA.

Abstract

BACKGROUND: The management of acne remains a challenge, with current therapies linked to significant side effects and patient non-compliance. Phototherapy using blue light has been proven in the treatment of acne vulgaris and offers the clinician an effective alternative.

OBJECTIVE: To determine the effect of narrowband light-emitting diode (LED) blue light in the reduction of inflammatory and non-inflammatory lesions in patients with mild to moderate acne and to evaluate patient tolerance of the therapy.

METHODS: Forty-five patients were treated with high-intensity pure blue light, 415 nm and 48 J/cm2, receiving two treatments of 20 minutes per week for a period of 4-8 weeks. Clinical

assessment was performed at baseline, and 2, 4 and 8 weeks after treatment. A patient's therapeutic response was measured using a global improvement scoring system.
RESULTS: The mean improvement score was 3.14 at 4 weeks and 2.90 at 8 weeks. Nine patients experienced complete clearing at 8 weeks. The treatment was well tolerated, with 50% of patients highly satisfied with the treatment.
CONCLUSION: This open-label study suggests the therapeutic efficacy of high-intensity LED pure blue light in the treatment of acne vulgaris with no reported side effects.

An open study to determine the efficacy of blue light in the treatment of mild to moderate acne.

Morton CA, Scholefield RD, Whitehurst C, Birch J.
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Abstract
BACKGROUND: The effective management of acne remains a challenge; achieving an optimal response whilst minimizing adverse events is often difficult. The rise in antibiotic resistance threatens to reduce the future usefulness of the current mainstay of therapy. The need for alternative therapies remains important. Phototherapy has previously been shown to be effective in acne, with renewed interest as both endogenous and exogenous photodynamic therapies are demonstrated for this condition.
OBJECTIVES: To determine the effect of narrowband blue light in the reduction of inflammatory and non-inflammatory lesions in patients with mild to moderate acne and to evaluate patient tolerance of the therapy.
METHODS: We performed an open study utilizing a blue LED light source in 30 subjects with mild to moderate facial acne. Two weeks after screening, lesions were counted and recorded by lesion type. Over 4 weeks, patients received eight 10- or 20-minute light treatments, peak wavelength 409-419 nm at 40 mW/cm2. Assessments were taken at weeks 5, 8 and 12 and lesion counts were recorded. Repeated measures-ANOVA and Dunnett's tests, respectively, allowed assessment of the different scores over time and permitted comparison of mean counts.
RESULTS: An overall effect on inflammatory counts was observed at week 5, and a statistically significant decrease in inflamed counts was detected at the week 8 assessments, which continued to week 12. There was little effect on non-inflamed lesions. The treatment was well tolerated with adverse events experienced generally rated as being mild and usually self-limiting.
CONCLUSIONS: Eight 10- or 20-minute treatments over 4 weeks with a narrowband blue light was found to be effective in reducing the number of inflamed lesions in subjects with mild to moderate acne. The treatment had little effect on the number of comedones. The onset of the effect was observable at the first assessment, at week 5, and maximal between weeks 8 and 12. Blue light phototherapy using a narrowband LED light source appears to be a safe and effective additional therapy for mild to moderate acne.

Phototherapy with blue (415 nm) and red (660 nm) light in the treatment of acne vulgaris.

Papageorgiou P, Katsambas A, Chu A.
Unit of Dermatology, Imperial College of Science, Technology and Medicine, Hammersmith Hospital, DuCane Road, London W12 0NN, U.K.

Abstract
In this study we have evaluated the use of blue light (peak at 415 nm) and a mixed blue and red light (peaks at 415 and 660 nm) in the treatment of acne vulgaris. One hundred and seven patients with mild to moderate acne vulgaris were randomized into four treatment groups: blue light, mixed blue and red light, cool white light and 5% benzoyl peroxide cream. Subjects in the phototherapy groups used portable light sources and irradiation was carried out daily for 15 min. Comparative assessment between the three light sources was made in an observer-blinded fashion, but this could not be achieved for the use of benzoyl peroxide. Assessments were performed every 4 weeks. After 12 weeks of active treatment a mean improvement of 76% (95% confidence interval 66-87) in inflammatory lesions was achieved by the combined blue-red light phototherapy; this was significantly superior to that achieved by blue light (at weeks 4 and 8 but not week 12), benzoyl peroxide (at weeks 8 and 12) or white light (at each assessment). The final mean improvement in comedones by using blue-red light was 58% (95% confidence interval 45-71), again better than that achieved by the other active treatments used, although the differences did not reach significant levels. We have found that phototherapy with mixed blue-red light, probably by combining antibacterial and anti-inflammatory action, is an effective means of treating acne vulgaris of mild to moderate severity, with no significant short-term adverse effects.

Evaluation of self-treatment of mild-to-moderate facial acne with a blue light treatment system.
Abstract

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INTRODUCTION: This study evaluated the efficacy and tolerability of treating mild-to-moderate facial acne using a new, hand-held, light-emitting diode blue light device in conjunction with a foam cleanser containing 5% glycolic acid and 2% salicylic acid plus a skin rebuilding serum containing 1.25% salicylic acid, 0.5% niacinamide, 0.08% liposomal-based azelaic acid and superoxide dismutase.
METHODS: Volunteers with mild-to-moderate facial inflammatory acne used the blue light device twice daily for eight weeks, plus the cleanser before treatments and the serum after each evening treatment.
RESULTS: Among 33 subjects aged 25-45 years old, 28 completed. In a 3 cm x 5 cm target area receiving a daily dose of ~29 J/cm2, treatment was associated with significant reductions from baseline in the inflammatory lesion count from week 1 onward ($P \leq .01$) and in the non-inflammatory lesion count from week 4 onward ($P \leq .05$). The number of flares was significantly reduced from baseline from week 2 onward ($P \leq .05$), and flare severity and flare redness were significantly reduced from baseline from week 4 onward ($P \leq .01$ and $P \leq .05$, respectively). At week 8, more than 90 percent of subjects reported improvements in their skin's overall

appearance, clarity, radiance, tone, texture and smoothness. In addition, 82 percent were satisfied, very satisfied, or extremely satisfied with the blue light treatment system and 86 percent agreed the treatment system was much gentler than traditional acne treatments. **CONCLUSION:** The blue light treatment system offers effective, rapid, convenient and well tolerated treatment of inflammatory and non-inflammatory acne lesions. The majority of subjects consider it much gentler than traditional acne treatments and it facilitates effective treatment without the need for antibiotic exposure. The blue light treatment system and blue light therapy alone are attractive treatment options for acne vulgaris, both as alternatives to traditional acne treatments and as adjunctive treatments to complement existing therapies

Misc Abstracts

DARPA Soldier Self Care: Rapid Healing of Laser Eye Injuries with Light Emitting Diode Technology –

Harry T. Whelan, M.D1, Margaret T. T. Wong-Riley, Ph.D2 , Janis T. Eells, Ph.D3, James N. VerHoeve, Ph.D4, Rina Das, Ph.D. 5, Marti Jett, Ph.D5
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The results of this study and others suggest that photobiomodulation with red to near infrared light augments recovery pathways promoting neuronal viability and restoring neuronal function following injury. Importantly, there was no evidence of damage to the normal retina following 670 nm LED treatment. Based on these findings, we suggest that photobiomodulation may represent an innovative and novel therapeutic approach for the treatment of retinal injury as well as the treatment of retinal diseases, including age-related macular degeneration, glaucoma, diabetic retinopathy, and Leber's hereditary optic neuropathy.

The NASA Light-Emitting Diode Medical Program – Progress in Space Flight and Terrestrial Applications -

Harry T. Whelan, M.D.1a,2,3, John M Houle, B.S.1a, Noel T. Whelan1a,3, Deborah L. Donohoe, A.S., L.A.T.G.1a,

Joan Cwiklinski, M.S.N., C.P.N.P.1a, Meic H. Schmidt, M.D.1c, Lisa Gould, M.D., PhD.1b, David Larson, M.D.1b,
Glenn A. Meyer, M.D.1a, Vita Cevenini3, Helen Stinson, B.S.3 1a, Departments of Neurology, 1bPlastic Surgery and1c Neurosurgery,Medical College of Wisconsin, Milwaukee, WI 53226, (414) 456-40902Naval Special Warfare Group TWO, Norfolk, VA 23521, (757) 462-77593, NASA-Marshall Space Flight Center, AL 35812, (256) 544-2121

Abstract. This work is supported and managed through the NASA Marshall Space Flight Center – SBIR Program.
Studies on cells exposed to microgravity and hypergravity indicate that human cells need gravity to stimulate cell growth. As the gravitational force increases or decreases, the cell function responds in a linear fashion. This poses significant health risks for astronauts in long term space flight. LED-technology developed for NASA plant grown experiments in space shows promise for delivering light deep into tissues of the body to promote wound healing and human tissue growth. This LED-technology is also biologically optimal for photodynamic therapy of cancer.

NEAR-INFRARED LIGHT VIA LIGHT-EMITTING DIODE TREATMENT IS THERAPEUTIC AGAINST ROTENONE- AND MPP+-INDUCED NEUROTOXICITY

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Abstract
Parkinson's disease is a common progressive neurodegenerative disorder characterized by the degeneration of dopaminergic neurons in the substantia nigra pars compacta. Mitochondrial dysfunction has been strongly implicated in the pathogenesis of Parkinson’s disease. Thus, therapeutic approaches that improve mitochondrial function may prove to be beneficial. Previously, we have documented that near-infrared light via light-emitting diode (LED) treatment was therapeutic to neurons functionally inactivated by tetrodotoxin, potassium cyanide (KCN), or methanol intoxication, and LED pretreatment rescued neurons from KCN-induced apoptotic cell death. The current study tested our hypothesis that LED treatment can protect neurons from both rotenone- and MPP+-induced neurotoxicity. Primary cultures of postnatal rat striatal and cortical neurons served as models, and the optimal frequency of LED treatment per day was also determined. Results indicated that LED treatments twice a day significantly increased cellular ATP content, decreased the number of neurons undergoing cell death, and significantly reduced the expressions of reactive oxygen species and reactive nitrogen species in rotenone- or MPP+-exposed neurons as compared to untreated ones. These results strongly suggest that LED treatment may be therapeutic to neurons damaged by neurotoxins linked to Parkinson’s disease by energizing the cells and increasing their viability.

NASA Light Emitting Diode Medical Applications From Deep Space to Deep Sea

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Abstract. This work is supported and managed through the NASA Marshall Space Flight Center - SBIR Program. LED-technology developed for NASA plant growth experiments in space shows promise for delivering light deep into tissues of the body to promote wound healing and human tissue growth. We present the results of LED-treatment of cells grown in culture and the effects of LEDs on patients' chronic and acute wounds. LED-technology is also biologically optimal for photodynamic therapy of cancer and we discuss our successes using LEDs in conjunction with light-activated chemotherapeutic drugs.

Effects of 635nm Light-Emitting Diode Irradiation on Angiogenesis in CoCl2-Exposed HUVECs

Won Bong Lim,1 Ji Sun Kim,1 Young Jong Ko,1 HyukIl Kwon,1 Sang Woo Kim,1 Heung Kee Min,1 Oksu Kim,2 Hong Ran Choi,1 and Ok Joon Kim1_ 1Department of Oral Pathology, 2nd Stage of Brain Korea 21 for School of Dentistry, Dental Science Research Institute, Chonnam National University, Bug-Gu, Gwangju, Korea 2 Department of Periodontology, 2nd Stage of Brain Korea 21 for School of Dentistry, Dental Science Research Institute, Chonnam National University, Bug-Gu, Gwangju, Korea

The results of the present study show that overproduction of ROS in a hypoxia model of CoCl2 treatment leads to up-regulation of HIF-1 and VEGF, but down-regulation of VEGFR-1 and VEGFR-2. Irradiation with 635 nm was shown to reduce intracellular ROS production. This leads to alleviation of the suppressed VEGFR-1 levels, enhanced VEGF expression ndERKMAPK activation, and that this ultimately results in increased angiogenesis under hypoxic/ischemic conditions.

J Photochem Photobiol B. 2011 Mar 2;102(3):182-91. Epub 2010 Dec 25.

Low intensity light stimulates nitrite-dependent nitric oxide synthesis but not oxygen consumption by cytochrome c oxidase: Implications for phototherapy.

Ball KA, Castello PR, Poyton RO.

Source : Department of Molecular, Cellular, and Developmental Biology, University of Colorado, Boulder, CO 80309-0347, USA.

Abstract : Cytochrome c oxidase (Cco) has been reported to be a receptor for some of the beneficial effects of low intensity visible and near-infrared light on cells and tissues. Here, we have explored the role of low intensity light in affecting a newly described function of Cco, its ability to catalyze nitrite-dependent nitric oxide (NO) synthesis (Cco/NO). Using a new assay for Cco/NO we have found that both yeast and mouse brain mitochondrial Cco produce NO over a wide range of oxygen concentrations and that the rate of NO synthesis increases as the oxygen concentration decreases, becoming optimal under hypoxic conditions. Low intensity broad-spectrum light increases Cco/NO activity in an intensity-dependent fashion but has no effect on oxygen consumption by Cco. By using a series of bandpass filters and light emitting devices (LEDs) we have determined that maximal stimulation of Cco/NO activity is achieved by exposure to light whose central wavelength is 590 ± 14 nm. This wavelength of light stimulates Cco/NO synthesis at physiological nitrite concentrations. These findings raise the interesting possibility that low intensity light exerts a beneficial effect on cells and tissues by increasing NO synthesis catalyzed by Cco and offer a new explanation for the increase in NO bioavailability experienced by tissue exposed to light.

Therapeutic effect of near infrared (NIR) light on Parkinson's disease models.

Quirk BJ, Desmet KD, Henry M, Buchmann E, Wong-Riley M, Eells JT, Whelan HT.

Source: Department of Neurology, Medical College of Wisconsin, 8701 W. Watertown Plank Rd, Milwaukee, WI 53226, USA.

Abstract: Parkinson's disease (PD) is a neurodegenerative disorder that affects large numbers of people, particularly those of a more advanced age. Mitochondrial dysfunction plays a central role in PD, especially in the electron transport chain. This mitochondrial role allows the use of inhibitors of complex I and IV in PD models, and enhancers of complex IV activity, such as NIR light, to be used as possible therapy. PD models fall into two main categories; cell cultures and animal models. In cell cultures, primary neurons, mutant neuroblastoma cells, and cell cybrids have been studied in conjunction with NIR light. Primary neurons show protection or recovery of function and morphology by NIR light after toxic insult. Neuroblastoma cells, with a gene for mutant alpha-synuclein, show similar results. Cell cybrids, containing mtDNA from PD patients, show restoration of mitochondrial transport and complex I and IV assembly. Animal models include toxin-insulted mice, and alpha-synuclein transgenic mice. Functional recovery of the animals, chemical and histological evidence, and delayed disease progression show the potential of NIR light in treating Parkinson's disease.

The Nuts and Bolts of Low-level Laser (Light) Therapy

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(Received 26 July 2011; accepted 20 October 2011; published online 2 November 2011)

Abstract—Soon after the discovery of lasers in the 1960s it was realized that laser therapy had the potential to improve wound healing and reduce pain, inflammation and swelling. In recent years the field sometimes known as photobiomodulation has broadened to include light-emitting diodes and other light sources, and the range of wavelengths used now includes many in the red and near infrared. The term ''low level laser herapy'' or LLLT has become widely recognized and implies the existence of the biphasic dose response or the Arndt-Schulz curve. This review will cover the mechanisms of action of LLLT at a cellular and at a tissular level and will summarize the various light sources and principles of dosimetry that are employed in clinical practice. The range of diseases, injuries, and conditions that can be benefited by LLLT will be summarized with an emphasis on those that have reported randomized controlled clinical trials. Serious life-threatening diseases such as stroke, heart attack, spinal cord injury, and traumatic brain injury may soon be amenable to LLLT therapy.

Conclusion - Advances in design and manufacturing of LLLT devices in the years to come will continue to widen the acceptability and increase adoption of the therapy among the medical profession, physical therapists and the general public. While the body of evidence for LLLT and its mechanisms is still weighted in favor of lasers and directly comparative studies are scarce, ongoing work using non-laser irradiation sources is encouraging and provides support for growth in the manufacture and marketing of affordable home-use LED devices. The almost complete lack of reports of side effects or adverse events associated with LLLT gives security for issues of safety that will be required.

We believe that LLLT will steadily progress to be better accepted by both the medical profession and the general public at large. The number of published negative reports will continue to decline as the optimum LLLT parameters become better understood, and as reviewers and editors of journals become aware of LLLT as a scientifically based therapy. On the clinical side, the public's distrust of big pharmaceutical companies and their products is also likely to continue to grow. This may be a powerful force for adoption of therapies that once were considered as ''alternative and complementary,'' but now are becoming more scientifically accepted. LLLT is not the only example of this type of therapy, but needle acupuncture, transcranialmagnetic stimulation and microcurrent therapy also fall into this class. **The day may not be far off when most homes will have a light source (most likely a LED device) to be used for aches, pains, cuts, bruises, joints, and which can also be applied to the hair and even transcranially to the brain.**

J Orthop Sci. 2010 Mar;15(2):233-9. doi: 10.1007/s00776-009-1438-4. Epub 2010 Apr 1.

Effect of near-infrared light-emitting diodes on nerve regeneration.

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Source: Department of Orthopaedic Surgery, Graduate School of Medicine, Kanazawa University, 13-1 Takara-machi, Kanazawa, Ishikawa, 920-8641, Japan.

Abstract

BACKGROUND: Photobiomodulation by red to near-infrared light-emitting diodes (LEDs) has been reported to accelerate wound healing, attenuate degeneration of an injured optic nerve, and promote tissue growth. The purpose of this study was to investigate the effect of LEDs on nerve regeneration. A histological study as well as a measurement of antioxidation levels in the nerve regeneration chamber fluid was performed.

METHODS: For the histological study, the bilateral sciatic nerves were transected, and the left proximal stump and the right distal stump were inserted into the opposite ends of a silicone chamber, leaving a 10-mm gap. Light from an LED device (660 nm, 7.5 mW/cm(2)) was irradiated for 1 h per day. At 3 weeks after surgery, regenerated tissue was fixed and examined by light microscopy. For the antioxidation assay of chamber fluid, the left sciatic nerve and a 2-mm piece of nerve from the proximal stump were transected and inserted into opposite sides of a silicone chamber leaving a 10-mm gap. LEDs were irradiated using the same parameters as those described in the histological study. At 1, 3, and 7 days after surgery, antioxidation of the chamber fluid was measured using an OXY absorbent test.

RESULTS: Nerve regeneration was promoted in the LED group. Antioxidation of the chamber fluid significantly decreased from 3 days to 7 days in the control group. In the LED group, antioxidation levels did not decrease until 7 days.

CONCLUSIONS: Chamber fluid is produced from nerve stumps after nerve injury. This fluid contains neurotrophic factors that may accelerate axonal growth. Red to near-infrared LEDs have been shown to promote mitochondrial oxidative metabolism. In this study, LED irradiation improved nerve regeneration and increased antioxidation levels in the chamber fluid. Therefore, we propose that antioxidation induced by LEDs may be conducive to nerve regeneration.

Near-Infrared Photobiomodulation in an Animal Model of Traumatic Brain Injury: Improvements at the Behavioral and Biochemical Levels

Brendan J. Quirk, Ph.D.,1 Michel Torbey, M.D.,2 Ellen Buchmann, B.S.,1 Sumit Verma, M.D.,1 and Harry T. Whelan, M.D.1

Abstract

Objective: The purpose of this was to evaluate the neuroprotective effects of near-infrared (NIR) light using an in-vivo rodent model of traumatic brain injury (TBI), controlled cortical impact (CCI), and to characterize changes at the behavioral and biochemical levels. Background data: NIR upregulates mitochondrial function, and decreases oxidative stress. Mitochondrial oxidative stress and apoptosis are important in TBI. NIR enhanced cell viability and mitochondrial function in previous in-vitro TBI models, supporting potential NIR in-vivo benefits. Methods: Sprague–Dawley rats were divided into three groups: severe TBI, sham surgery, and anesthetization only (behavioral response only). Cohorts in each group were administered either no NIR or NIR. They received two 670nm LED treatments (5 min, 50 mW/cm2, 15 J/cm2) per day for 72 h (chemical analysis) or 10 days (behavioral). During the recovery period, animals were tested for locomotor and behavioral activities using a TruScan device. Frozen brain tissue was obtained at 72 h and evaluated for apoptotic markers and reduced glutathione (GSH) levels. Results: Significant differences were seen in the TBI plus and minus NIR (TBI + / -) and sham plus and minus NIR (S + / -) comparisons for some of the TruScan nose poke parameters. A statistically significant decrease was found in the Bax pro-apoptotic marker attributable to NIR exposure, along with lesser increases in Bcl-2 anti-apoptotic marker and GSH levels. Conclusions: These results show statistically significant, preclinical outcomes that support the use of NIR treatment after TBI in effecting changes at the behavioral, cellular, and chemical levels.

NEAR-INFRARED LIGHT VIA LIGHT-EMITTING DIODE TREATMENT IS THERAPEUTIC AGAINST ROTENONE- AND MPP+-INDUCED NEUROTOXICITY

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Abstract
Parkinson's disease is a common progressive neurodegenerative disorder characterized by the degeneration of dopaminergic neurons in the substantia nigra pars compacta. Mitochondrial dysfunction has been strongly implicated in the pathogenesis of Parkinson’s disease. Thus, therapeutic approaches that improve mitochondrial function may prove to be beneficial. Previously, we have documented that near-infrared light via light-emitting diode (LED) treatment was therapeutic to neurons functionally inactivated by tetrodotoxin, potassium cyanide (KCN), or methanol intoxication, and LED pretreatment rescued neurons from KCN-induced apoptotic cell death. The current study tested our hypothesis that LED treatment can protect neurons from both rotenone- and MPP+-induced neurotoxicity. Primary cultures of postnatal rat striatal and cortical neurons served as models, and the optimal frequency of LED treatment per day was also determined. Results indicated that LED treatments twice a day significantly increased cellular ATP content, decreased the number of neurons undergoing cell death, and significantly reduced the expressions of reactive oxygen species and reactive nitrogen species in rotenone- or MPP+-exposed neurons as compared to untreated ones. These results strongly suggest that LED treatment may be therapeutic to neurons damaged by neurotoxins linked to Parkinson’s disease by energizing the cells and increasing their viability.

J Neurotrauma. 2014 May 8. [Epub ahead of print]

Significant Improvements in Cognitive Performance Post-Transcranial, Red/Near-Infrared Light-Emitting Diode Treatments in Chronic, Mild Traumatic Brain Injury: Open-Protocol Study.

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Abstract

This pilot, open-protocol study examined whether scalp application of red and near-infrared (NIR) light-emitting diodes (LED) could improve cognition in patients with chronic, mild traumatic brain injury (mTBI). Application of red/NIR light improves mitochondrial function (especially in hypoxic/compromised cells) promoting increased adenosine triphosphate (ATP) important for cellular metabolism. Nitric oxide is released locally, increasing regional cerebral blood flow. LED therapy is noninvasive, painless, and non-thermal (cleared by the United States Food and Drug Administration [FDA], an insignificant risk device). Eleven chronic, mTBI participants (26-62 years of age, 6 males) with nonpenetrating brain injury and persistent cognitive dysfunction were treated for 18 outpatient sessions (Monday, Wednesday, Friday, for 6 weeks), starting at 10 months to 8 years post- mTBI (motor vehicle accident [MVA] or sports-related; and one participant, improvised explosive device [IED] blast injury). Four had a history of multiple concussions. Each LED cluster head (5.35 cm diameter, 500 mW, 22.2 mW/cm^2) was applied for 10 min to each of 11 scalp placements (13 J/cm^2). LEDs were placed on the midline from front-to-back hairline; and bilaterally on frontal, parietal, and temporal areas. Neuropsychological testing was performed pre-LED, and at 1 week, and 1 and 2 months after the 18th treatment. A significant linear trend was observed for the effect of LED treatment over time for the Stroop test for Executive Function, Trial 3 inhibition (p=0.004); Stroop, Trial 4 inhibition switching (p=0.003); California Verbal Learning Test (CVLT)-II, Total Trials 1-5 (p=0.003); and CVLT-II, Long Delay Free Recall (p=0.006). Participants reported improved sleep, and fewer post-traumatic stress disorder (PTSD) symptoms, if present. Participants and family reported better ability to perform social, interpersonal, and occupational functions. These open-protocol data suggest that placebo-controlled studies are warranted.