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Photo-kinesiotherapy - Photobiomodulation associated with some kinesiotherapies for orofacial rehabilitation

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ABSTRACT

Physiological aging leads to dysfunction of the stomatognathic system. Photo-kinesiotherapy (PKT) is a program using photobiomodulation (PBM) in combination with different kinesiotherapies. PBM can slow down and manage aging process resulting in orofacial dermal-neuro-muscle rehabilitating. We are searching for a new more efficient therapy to decrease and manage velocity of senescence and dysfunction of stomatognathic system. Under Ethical Comittee approval (CAAE no. 45390715.2.0000.5419), fifteen female patients were selected and divided into 5 groups: G1 - Control group (cosmetics); G2 - Light group (cosmetics + PBM); G3 - Exercises Group (Cosmetics+ PBM + orofacial exercises); G4 - Electrotherapy Group (Cosmetics+ PBM + Electrotherapy - Aussie current); and, G5 - Taping Group (Cosmetics+ PBM + kinesiotherapy). Muscle evaluation was performed using electromyography, ultrasonography and bite force. Skin evaluation was performed in terms of skin hydration and viscoelasticity, skin echogenicity using ultrasonography and standardized high resolution photographs. Measures were done before (baseline values) and after 7 days and 30 days of treatment. The pilot phase (fifteen patients) was concluded using Kruskal-Wallis statistical tests that showed non-significant differences between groups. However, all treatments affected muscle tone, cutaneous elasticity and dermis echogenicity resulting in interesting individual clinical observations. We suggest that the combination of cosmetics, mechanical and optical stimulus to all kind of different tissues from stomatognathic system can be an efficient choice to orofacial functional and aesthetic rehabilitation. (CNPq - 114735/2015-8)

1. INTRODUCTION

Photobiomodulation employing lasers and LEDs, operating at low and medium intensity, have been established as an efficient and well-successful therapeutic modality¹⁻⁵. Recently, some publications have shown a very interesting association: PBM and kinesiotherapies. This combination seems able to shorter the time of nerve and muscle rehabilitation; besides it is capable to improve muscle performance and to keep the biological systems less intoxicated with free radicals⁶⁻¹³.

Different wavelengths and spectral bands have contributed to the cellular, tissue and physiological return to homeostasis situation. The spectral range of the near infrared laser, red light and the amber LED is very well absorbed by the cytochrome C-oxidase, promoting efficient photo-discharging of nitric oxide, which will result in a significant improvement of the cellular, tissue and local metabolism¹⁴⁻¹⁶. Lasers that emit in the infrared band (980nm) and in low intensity, have their absorption in the biomembranes, promoting a photophysical reaction of change in the polarity of these structures and changing its permeability. Besides of that, infrared band is able to promote a localized control of inflammation drainage of metabolites¹⁷ and to induce a decrease of inflammation and an increase of new lymphatic

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pathways¹⁸. And, the blue LED light can promote disinfection, hydration of the integumentary system (skin), and also improve the immune response to external environment aggressions¹⁹⁻²¹.

Indeed, red and amber light are able to promote inhibition of melanogenesis²² and induces autophagy in melanocytes²³, it means that using red laser or LED, it is possible to improve neuro-muscle metabolism and also lighten the skin.

The superficial orofacial tissues (skin, mucosa, gingiva) are strongly connected with the deep tissues (hypodermis, muscles, connective tissue, nerves and bones). In addition, the thickness of these tissues, which make up the stomatognathic system, differs from the rest of the body due to its delicacy, but highly reactive and functionally required. The guarantee of the good functioning of the stomatognathic system is in the maintenance of homeostasis between superficial and deep orofacial tissues. This homeostasis will be able to prevent orofacial dysfunctions and manage physiological senescence.

The purpose of this study was to evaluate some aspects of orofacial muscle and skin tonification, when using photobiomodulation, lasers and LEDs, associated or not with three kinesiotherapies: orofacial exercises, functional elastic bandages and the Australian current, in women. We are proposing Photokinesio-Therapy (PKT).

2. MATERIALS AND METHOD

Fifteen women were divided into 5 groups: Control = cosmetics, light = cosmetics + photobiomodulation, Aussie = cosmetics + photobiomodulation + aussie current, exercises = cosmetics + photobiomodulation + facial exercises, and, bandages = cosmetics + photobiomodulation + elastic bandages. In the first phase of the project, each group had 3 participants, respecting the age range (35-55) and skin phototype (II or III). Muscle evaluation was performed using electromyography, ultrasonography and bite force in terms of skin hydration and viscoelasticity, skin echogenicity using ultrasonography and standardized high resolution photographs. Measures were done before (baseline values) and after 7 days and 30 days of treatment. However, here, we will present evaluation under these tests chosen:

- Electromyography activity of the frontal (R and L), masseter (R and L) and temporal (R and L) muscles, orbicularis oculi and orbicularis oris, at the following postural conditions of the mandible: rest, lateral (right and left) with dental contact, maximum protrusion with dental contact and dental tightening in maximum voluntary contraction with inert material placed in the occlusal plane and the orbicularis muscles of the eyes and mouth;
- Echogenicity of the dermis;
- High Resolution Digital photography.

The following sequence was observed in all 8 treatment sessions with light therapy (light + kinesiotherapy), 2 sessions per week for 4 weeks: orofacial skin hygiene, irradiation with purple light (blue LED + red laser, 30 seconds per point or area); kinesiotherapy; irradiation with yellow light (amber LED + infrared laser); and, finish with dermocosmetic moisturizing and sunscreen. The Light group followed the same sequence without kinesiotherapy; and, the control group did not receive treatment sessions. Prior care in all sessions performed in the office: always clean the skin before - suggested dermocosmetic sequence: pure facial cleansing soap (10% glycolic acid soap - Neofarma, SP, Brazil), spread on all sides with circular movement; without removing the soap, add the physical exfoliant (apricot seeds - Neofarma, SP, Brazil) exfoliation of the skin, leave to act for 2 minutes; and then remove everything with mineral water on the gauze. Cleansing followed by exfoliation results in a mild "controlled trauma" located in the integumentary and muscular system, this will facilitate the coupling (absorption) of the lasers and LEDs and also the other therapies.



Figure 1 – A piece pf equipment for photobiomodulation with lasers and LEDs, with acrylic tip (diode cluster) Venus (MMOptics, São Carlos, Brazil). In "b", a detail of one of the handles where it is possible to observe the presence of 3 LEDs interspersed by 2 laser diodes: in one handle the device has 3 blue LEDs with 2 red LEDs, and in the other one it has 3 LEDs infrared lasers with 2 infrared lasers (personal archive).

In order to carry out the Photobiomodulation sessions, a piece of equipment was used, with sources based on diode lasers and the base of light emitting diodes (LEDs), both operating in low intensity (Venus - model Omega, MMO, São Carlos, São Paulo, Brazil) (Fig. 1). It is a tabletop device that has 2 handles: one with 3 light emitting diodes in the blue spectral band (460 + -20 nm) and 2 red lasers (660 + -20 nm); and another handle with 3 light emitting diodes

in the amber spectral band ($590 \pm 20\text{nm}$) and 2 infrared lasers ($808 \pm 20\text{nm}$). Each red laser diode presents 75mW of optical power each, and each infrared laser diode, 90mW. The blue LED diodes presents 400mW of optical power each while each amber LED diode, 187mW. Both handles feature an acrylic tip for application in contact. This tip has an area of $889\text{mm}^2 \pm 10\%$, that is, around 8.9cm^2 . This acrylic tip works as a diffuser and homogenizer of the light delivered, ensuring that the energy deposited in the entire area in contact with the acrylic tip is the same, resulting in the irradiance of: $134.83\text{mW}/\text{cm}^2$ of Blue LED, $63\text{mW}/\text{cm}^2$ of Amber LED, $16.85\text{mW}/\text{cm}^2$ red laser and $20.22\text{mW}/\text{cm}^2$ infrared laser. While the handle with the blue LEDs and the red lasers operate in the CW emission mode, the handle with amber LEDs and infrared lasers operate in the CW hybrid mode, 1 minute of irradiation, and switched on, 4 minutes of irradiation, each minute, the number of pulses per minute increases (60, 138, 168 and 198ppm), always maintaining the same "light" and "dark" time, thus, the percentage of use of energy delivered will always be 100% in the CW and 50% in switched mode, regardless of the repetition rate. In order to illuminate the entire facial area, with the same irradiance, and depositing the same amount of energy, the blue LED and the red laser were deposited simultaneously in contact and fixed (or stopped) in 22 regions (face), 30 seconds each, resulting in a total deposited energy of 40.5J (36J of blue LED + 4.5J of red laser) per region. The amber LED and the infrared laser were also deposited simultaneously in sweep and contact mode (spot scanning), dividing the face into 3 portions (upper third, middle third and lower right side and middle third and lower left side) for 5 minutes each, totaling 120J (90J of amber and 30J of Infrared) of Total deposited Energy in each of these three regions (Fig. 2).



Figure 2 – Schematic drawing showing how the light was applied to the face: purple light (blue LED + red laser), punctual (a); and yellow light (amber LED + infrared laser), punctual scanning (b). In both pictures, the delineated areas represent the surface covered with applications.

The equipment used was a compact unit with the Australian/Aussie current (Neurodyn - Sport model, Ibramed, Amparo, São Paulo, Brazil). The equipment provides four output channels with independent intensity controls, allowing the simultaneous stimulation or not of four different regions during a treatment session. The pre-programmed protocol that will be used in this project will be the motor re-education. This program should be used for the purpose of motor facilitation and motor re-learning. For stimulation Aussie current is used with carrier frequency of 4 kHz with burst duration equal to 4ms. The frequency of the Bursts must be equal to 50Hz. A ramp is used with 2 seconds of rise time, 4 seconds of contraction, 2 seconds of descent and 1 second of rest time or off time. The muscle groups that received this therapy will be: orbicular oculis muscles, right and left, and orbicular oris (for 20 minutes) and then major zygomatic muscles and masseters, right and left (for another 20 minutes). Totalizing 40 minutes of stimulation with the Australian current for motor reeducation. Then the finish with moisturizing and skin protection, and guidance for daily home care. For the group of orofacial exercises and light, the total of ten (10) orofacial exercises were taught so that the participant performs them daily, in their home, in a moment of tranquility, performing 10 repetitions of each exercise. In the service sessions, all ten exercises were also performed, but with 3 repetitions each, in order to stimulate the tissues and better absorb the applied lights.



Figure 3 – Orofacial exercises sequence using isometric movements addressing the three parts of face: superior (forehead, eyes and nose root) – the first 5 exercises - on top; medium third (cheeks, face lift muscles, buccinator muscles and masseters) - the first 4 exercises below; and, lower third of the face - contour of the face, supra-hyoid muscles and responsible for the protrusion of the mandible - the last 2 exercises - below.

Using the Therapy Taping Method, developed by Prof. Nelson Morini Jr., the functional elastic bandages (taping) will be applied in the session immediately before the application of the sunscreen, and the patient should stay with them for at least 8 hours and then remove them. The muscles selected were: frontal and masseter, receiving inhibitory stimulus (stretching); and, zygomatic major, nose lift, orbicularis oculi and orbicularis of the mouth receiving excitatory stimulus (contraction). (Fig. 4) However, you should return them every day, at home, when you return from work, sleep with them to total 8 hours, again. This procedure should be performed for 4 weeks, daily. The participant was properly instructed how to apply the bandage or taping, for each specific muscle, and was monitored in all sessions. The chosen bandage was Therapy Tex (Korea). Therapy Tex is an elastic band made up of elastane yarns covered with woven cotton yarns for easy attachment thanks to its adhesion adhesive acrylic polymers that last on average 7 days. It is not contain medicine in its composition.



Figure 4 – Woman from Light Taping Group using the functional elastic bandages (Therapy Tex, Korea) treating some orofacial muscles: frontal and masseter, receiving inhibitory stimulus (stretching); and, zygomatic major, nose lift, orbicularis oculi and orbicularis of the mouth receiving excitatory stimulus (contraction) – front side (a) and lateral side (b).

There were 3 evaluation periods: Initial, 1 week and 30 days, to perform all measurement methods (electromyography activity and thickness of the dermis).

Statistical analysis was performed with analysis of variance (ANOVA) and differences considered significant when $p \leq 0.05$.

3. RESULTS AND DISCUSSION

Measures are evaluated under statistical test: ANOVA One-way. The results showed non-statistical difference between groups, however it is possible realize particular behavior concern skin ultrasonography and electromyography from some muscle under some postural contraction.

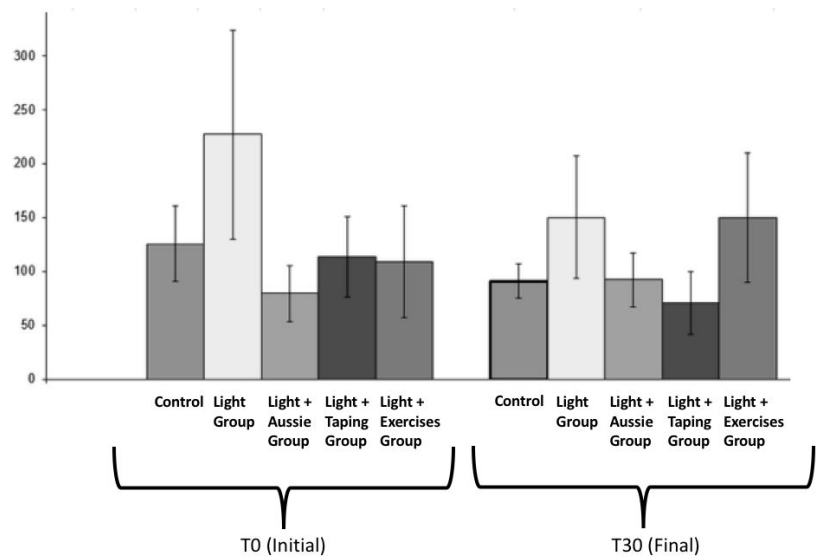


Figure 5 – Graph represents EMG (vertical axis) of right masseter muscles considering Maximal Intercuspation (MI) and Control/Experimental Groups (horizontal axis): Light Group and Light Taping Group showed a decrease of muscle activity, by the other way, Light Exercises Group showed an increasing of muscle activity.

Figure 5 shows EMG of right masseter muscles during isometric situation of MI. Light Group and Light Taping Group showed a decrease of muscle activity, while, Light Exercises Group showed an increasing of muscle activity. Light Group and Light Taping Group have decreased EMG signal, this fact associated to values from temporalis muscles, denoting that this, specific treatment, could promote a balance between force vectors of temporalis and masseter muscles. By the other side, Light Exercises Group had promoted a better masseter muscles tonus, improving physiological responses during chewing.

Figure 6 shows EMG of orbicularis oculis muscles when patients have closed eyes forcibly. Light Group, Light Taping Group and Light Exercises Group have increased muscle activity at this isometric situation, that result in improvement of tissue tonus. Light Aussie Group has decreased EMG signal, this fact associated to values from frontalis muscles, denoting that this, specific treatment, could promote a balance between force vectors of frontalis and orbicularis oculis muscles.

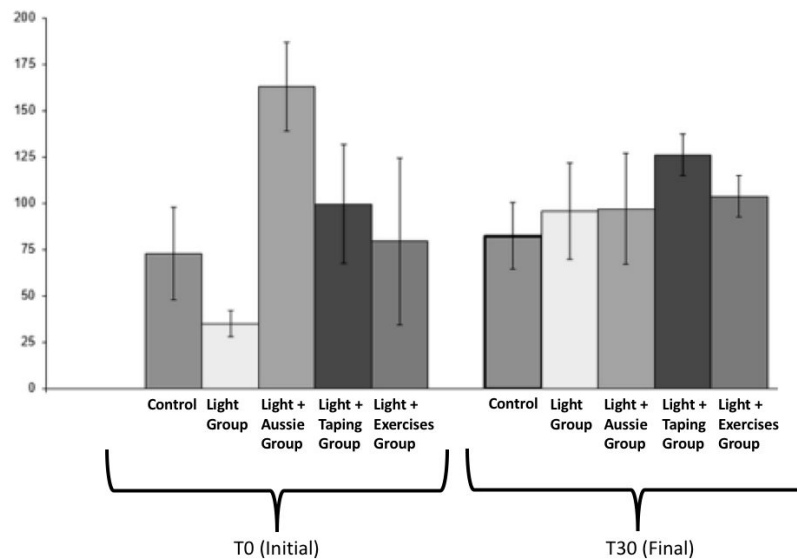


Figure 6 – Graphs represents EMG (vertical axis) of orbicularis oculis muscles considering Forced Closure of the eyes and Control/Experimental Groups (horizontal axis): Light Group, Light Taping Group and Light Exercises Group have increased muscle activity at this isometric situation; and, Light Aussie Group has decreased EMG signal.

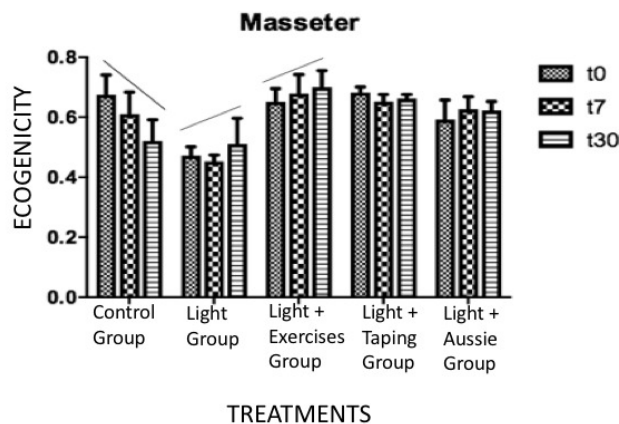


Figure 7 – Ultrasonography with Dermascan (Cortex Technology, Denmark) to evaluate echogenicity of the skin, considering all treatment/control groups and evaluation time (t0, t7 and t30).

Figure 7 shows ultrasonography of the skin through evaluation of echogenicity. Echogenicity is a term used in ultrasonography that describes how much a tissue, organ or fluid lets pass or reflects ultrasound sound waves (US), compared to nearby tissues and organ. By analyzing the skin layers, through the measured echogenicity, it was possible to verify the organization and quantification of the collagen fibers present in the dermis, these values are represented in figure 7.

Although it did not present a statistically significant difference between the groups, it was possible to observe the behavior, over time of 30 days, that, from t0, all measures for the control group, independent of the evaluated region (here represented by the muscle masseter), there was a decrease in skin echogenicity, and for the experimental groups the behavior was the opposite, from t0 to t30 there was a growth of this echogenicity or it was maintained. This can be interpreted as a degradation of these collagen fibers and their organization, a fact that occurs even with the passage of time and with the aging of the skin and other facial tissues, as long as there is no intervention with some therapy, as observed in the group control. On the other hand, the experimental groups, where the Light (Photobiomodulation) or Light associated with some of the kinesiotherapies (Orofacial Exercises, Functional Elastic Bandages/Taping or Aussie Current) intervened, although many free radicals were generated during these passive or it seems clear that the photobiomodulation with lasers and LEDs was able to control the dermal degradation action, preserving the situation, initially presented at t0, or improving the echogenicity, that is, preventing degradation and even stimulating the production and organization of these collagen fibers present in these assessed facial regions.

These findings on the increase in water retention in the dermis and quantification of collagen fibers, agree with Weiss et al.²⁴ when affirming the combination of the amber LED with the infrared laser, improving the gene expression for the synthesis of collagen fibers.

We can observe from each group, interesting results:

3.1 Light Group

Photobiomodulation without any kinesiotherapy seems promote a balance between all orofacial muscles and more elongated orofacial muscles, may be related to the ability of amber and red lights, with low doses, to promote such a physiological response. At the end of 8 sessions, patients had shown a calm and relaxing aspect, besides, some lifting is presented, giving the patients a joviality. Skin are more the skin of the face appears to be lighter, brighter and homogeneously textured, it could be related to drainage and detoxification of the tissues promoted by red and infrared light, and also due to the disinfection and hydration promoted by the blue LED, agreeing with Lizarelli et al.²⁵ (Fig. 8).



Figure 8 – Digital photographs of face at the initial time (a) and after 8 sessions of photobiomodulation (b).

3.2 Light and Aussie Group

The association between photobiomodulation and Aussie current seems giving to patients, a balance between orofacial muscles, as Light Group. However, Aussie current allows the direct electrical stimulation of the muscle fibers, facilitating the ionic exchanges necessary to amplify the contractions. Therefore, this type of phototherapy seems to be very well indicated for rehabilitation in cases of PNI (peripheral nerve injury), but it has also been shown to be very efficient to harmonize faces already in the process of aging. Figure 9 shows a case that It presents a realignment of the facial lines, raising and straightening the nose, as well as the upper lip, besides softening the eyelid-malar grooves (rupture of the buccomaxilar ligaments), and raising the left eyebrow, finally the left side of the face appears to have received a facelift.

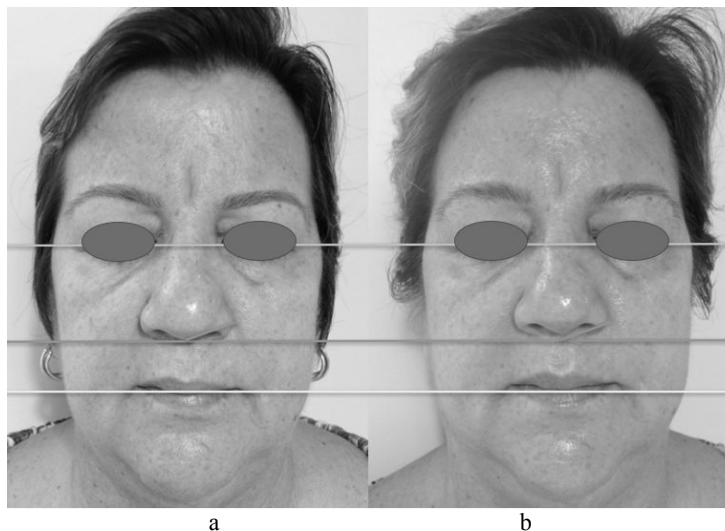


Figure 9 - Digital photographs of face at the initial time (a) and after 8 sessions of photobiomodulation in association with Aussie current (b).

3.3 Light and Exercise Group

This group presented the best result of photokinesiotherapy. As there is a perfect synergism between the orofacial muscles and the photobiomodulation, this experimental group was able to optimize the physiological responses; when the patient is disciplined and performs all the isometry exercises daily, in the taught sequence (orofacial exercises that work the 3 thirds of the face, including the muscles), both muscular and tissue toning (skin) occurs, ensuring better orofacial neuro-muscular functioning. In addition, our results agree with Patrocínio's et al.²⁶ findings when the association of infrared laser with resistance exercises modified the gene expression for muscular hypertrophy and improved performance of the whole system.

With regard to echogenicity (Fig. 10e), it is possible to understand that there was a sum of mechanical and photonic stimuli that were constructive and stimulated the increase of the echogenicity of the dermis, that is, a greater retention of liquids understood as an improvement in the quantity and organization of the dermal collagen fibers.

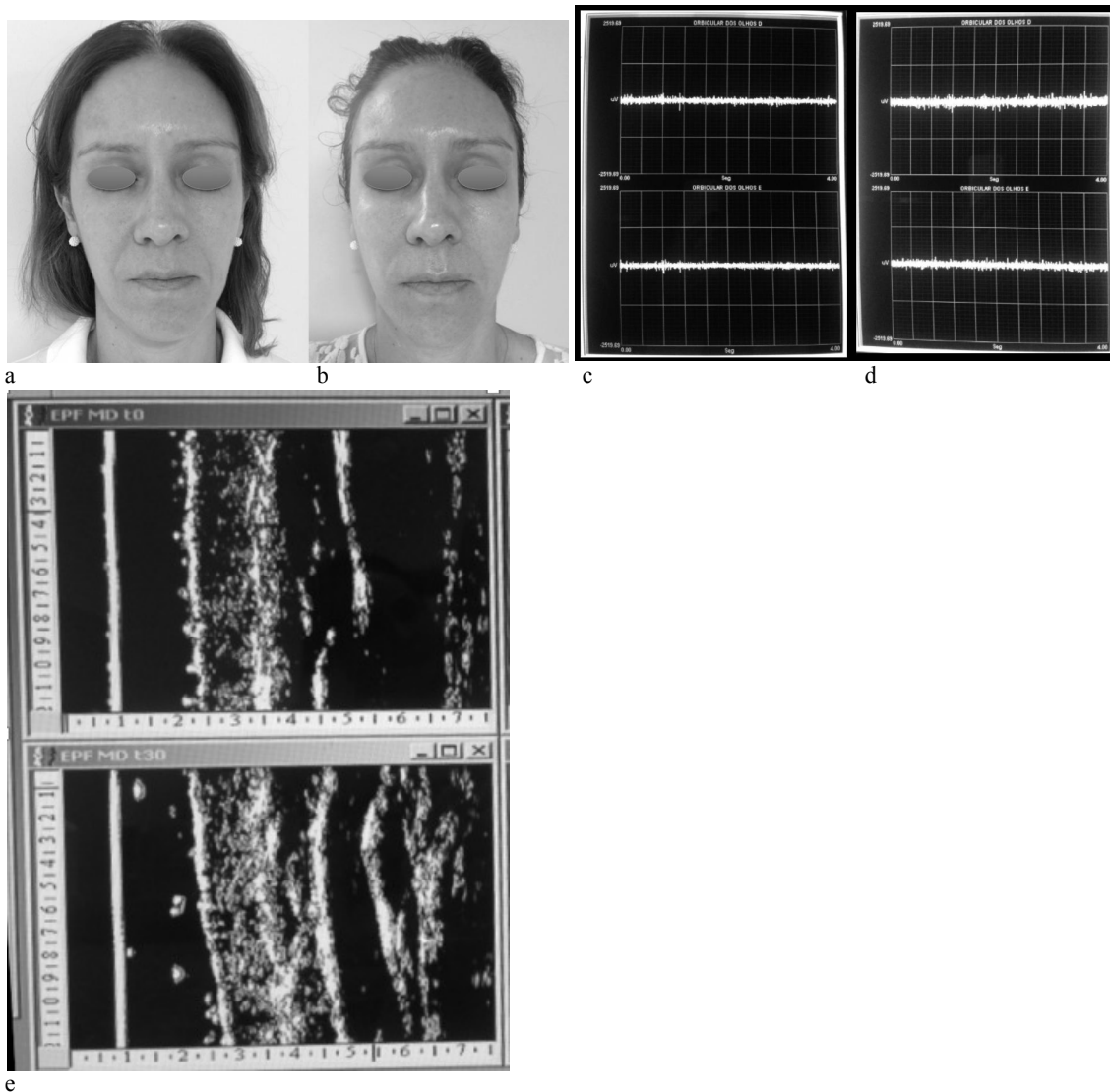


Figure 10 - Digital photographs of face at the initial time (a) and after 8 sessions of photobiomodulation in association with Orofacial Exercises (b); EMG of orbicular oculi (c – above – right side, and, c – below – left side); and echogenicity (skin ultrasonography) of right masseter before (e – above) and after treatment (c – below).

3.4 Light and Taping Group

Functional elastic bandages or taping bonded to the skin may stimulate different muscle responses, and may stabilize more complex systems, such as the knee joint. In our study, we used, in association with photobiomodulation, for excitatory and inhibitory stimuli, depending on the treated orofacial muscle. As it is a functional device, to all muscular

movement performed, these bandages, again, come into play, in this way, end up acting very similar to a functional orthopedic device for jaws. It is a great option of treatment concern neural-muscle orofacial rehabilitation in cases of paralysis²³, however, if we consider the physiological, nutritional and metabolic losses that aging provides to the stomatognathic system, to ensure an efficient response of the neuro-muscular system, as required here, it is essential that the mitochondrial muscles of these muscle cells are not damaged, which could lead to sarcopenia. Therefore, photobiomodulation has the essential function of maintaining functional cellular respiration. Photobiomodulation can prevent the installation of a chronic oxidizing situation that could degrade many mitochondria of these muscle cells, dis-functioning the orofacial neuro-muscular system.

Figure 11 shows Echogenicity of superior orbicularis oris and EMG of temporalis and masseter muscle, before and after the use of taping, every night, and 2 sessions of phototaping (initial period of treatment – 7 days). Thus, it seems simple and clear that the synergism between the mechanical (taping) and photonic (light) stimuli, must be added in a constructive way to the physiological orofacial metabolism, tonifying the superficial and deep tissues, in addition to restoring the balance between the facial cutaneous muscles.

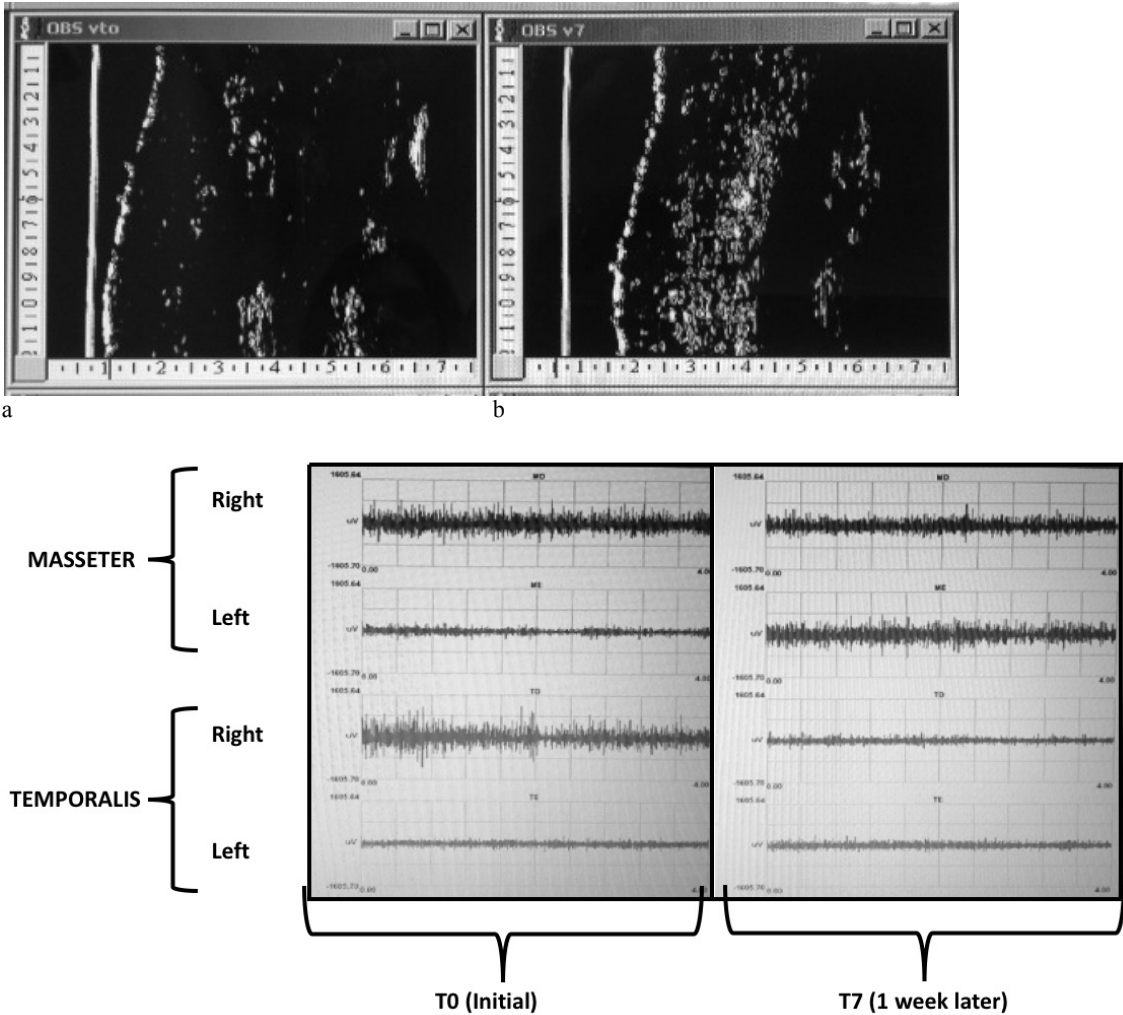


Figure 11 – Echogenicity of superior orbicularis oris at the beginning (a) and after 1 week of treatments (2 sessions and 7 nights using taping (b); and EMG of temporalis and masseter muscles at the beginning (T0) and after 1 week of treatments (2 sessions and 7 nights using taping (T7) (c).

Photobiomodulation has allow different clinical results at clinical Dentistry. However, all situations search for homeostasis condition of systems. There is a gap to be filled with legitimate dental actions that can abbreviate discomforts of our patients from trauma, dysfunctions and orofacial aging. The association of therapies that promote different orofunctional, optical (lasers and LEDs), mechanical (functional elastic bandages and facial exercises) and electrical physiological stimuli (Australian current), presented very fast results for orofacial neuromuscular rebalancing, as well as nutritional stimulation and of

the facial integumentary system, a fact that decelerates natural senescence. Concluding this phase of this research, it was possible to understand that there is a strong potential of photobiomodulation by associating integumentary and muscular tissues, not only to tone these more superficial tissues (integumentary system - skin) but also the deeper ones (muscular and neural), promoting an equilibrium relation of the force vectors between the facial muscles studied. In addition, both the digital photographs and the comments of the participants, the general appearance of the skin of the face was clearer and brighter, which can be interpreted as drainage of the toxins from the physiological metabolism and hydration of the treated tissues.

4. CONCLUSION

We have concluded that since all considered groups, with the exception of the control group, here had photobiomodulation in their protocols, it was clear that the use of lasers and LEDs at the chosen doses (low) was able to manage the physiological degradation that occurs with aging, although there was the mechanical or electrical stimulation induced to promote isometric contractions or not of the facial muscles studied. Photo-kinesiotherapy seems an interesting modality into photobiomodulation to be used searching for orofacial rehabilitation or harmonization.

5. ACKNOWLEDGEMENTS

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6. REFERENCES

- 1 - Argenta PA, Ballman KV, Geller MA, Carson LF, Ghebre R, Mullany SA et al. The effect of photobiomodulation on chemotherapy-induced peripheral neuropathy: A randomized, sham-controlled clinical trial. *Gynecol Oncol*. 2017 Jan;144(1):159-166.
- 2 - da Silva Neves FL, Silveira CA, Dias SB, Santamaria Júnior M, de Marco AC, Kerbaux WD et al. Comparison of two power densities on the healing of palatal wounds after connective tissue graft removal: randomized clinical trial. *Lasers Med Sci*. 2016 Sep;31(7):1371-8.
- 3 - Larkin-Kaiser KA, Borsa PA, Baweja HS, Moore MA, Tillman MD, George SZ et al. Photobiomodulation delays the onset of skeletal muscle fatigue in a dose-dependent manner. *Lasers Med Sci*. 2016 Sep;31(7):1325-32.
- 4 - Douglas De Oliveira DW, Lages FS, Guimarães RC, Pereira TS, Botelho AM, Glória JC et al. Do TMJ symptoms improve and last across time after treatment with red (660 nm) and infrared (790 nm) low level laser treatment (LLLT)? A survival analysis. *Cranio*. 2017 Feb 20:1-7.
- 5 - Tian F, Hase SN, Gonzalez-Lima F, Liu H Transcranial laser stimulation improves human cerebral oxygenation. *Lasers Surg Med*. 2016 Apr;48(4):343-9.
- 6 - Paolillo FR, Milan JC, Aniceto IV, Barreto SG, Rebelatto JR et al. Effects of infrared-LED illumination applied during high-intensity treadmill training in postmenopausal women. *Photomed Laser Surg*. 2011 Sep; 29(9):639-45.
- 7 - Assis L, Moretti AI, Abrahão TB, Cury V, Souza HP, Hamblin MR et al. Low-level laser therapy (808 nm) reduces inflammatory response and oxidative stress in rat tibialis anterior muscle after cryolesion. *Lasers Surg Med*. 2012 Nov;44(9):726-35.
- 8 - Higashi RH, Toma RL, Tucci HT, Pedroni CR, Ferreira PD, Baldini G et al. Effects of low-level laser therapy on biceps brachialis muscle fatigue in young women. *Photomed Laser Surg*. 2013 Dec;31(12):586-94.
- 9 - Dos Reis FA, da Silva BA, Laraia EM, de Melo RM, Silva PH, Leal-Junior EC et al. Effects of pre- or post-exercise low-level laser therapy (830 nm) on skeletal muscle fatigue and biochemical markers of recovery in humans: double-blind placebo-controlled trial. *Photomed Laser Surg*. 2014 Feb;32(2):106-12.
- 10 - de Brito Vieira WH, Bezerra RM, Queiroz RA, Maciel NF, Parizotto NA, Ferraresi C. Use of low-level laser therapy (808 nm) to muscle fatigue resistance: a randomized double-blind crossover trial. *Photomed Laser Surg*. 2014 Dec;32(12):678-85.
- 11 - Assis L, Yamashita F, Magri AM, Fernandes KR, Yamauchi L, Renno AC. Effect of low-level laser therapy (808 nm) on skeletal muscle after endurance exercise training in rats. *Braz J Phys Ther*. 2015 Nov-Dec;19(6):457-65.
- 12 - Guaraldo SA, Serra AJ, Amadio EM, Antônio EL, Silva F, Portes LA et al. The effect of low-level laser therapy on oxidative stress and functional fitness in aged rats subjected to swimming: an aerobic exercise. *Lasers Med Sci*. 2016 Jul;31(5):833-40.
- 13 - de Paiva PR, Tomazoni SS, Johnson DS, Vanin AA, Albuquerque-Pontes GM, Machado CD et al. Photobiomodulation therapy (PBMT) and/or cryotherapy in skeletal muscle restitution, what is better? A randomized, double-blinded, placebo-controlled clinical trial. *Lasers Med Sci*. 2016 Dec;31(9):1925-1933.
- 14 - McDaniel DH, Weiss RA, Geronemus RG, Mazur C, Wilson S, Weiss MA. Varying ratios of wavelengths in dual wavelength LED photomodulation alters gene expression profiles in human skin fibroblasts. *Lasers Surg Med*. 2010 Aug;42(6):540-5.

- 15 - Ball KA, Castello PR, Poyton RO. Low intensity light stimulates nitrite-dependent nitric oxide synthesis but not oxygen consumption by cytochrome c oxidase: Implications for phototherapy. *J Photochem Photobiol B*. 2011 Mar 2;102(3):182-91.
- 16 - de Freitas LF, Hamblin MR. Proposed Mechanisms of Photobiomodulation or Low-Level Light Therapy. *IEEE J Sel Top Quantum Electron*. 2016 May-Jun;22(3). pii: 7000417.
- 17 - Wang Y, Huang YY, Wang Y, Lyu P, Hamblin MR. Photobiomodulation of human adipose-derived stem cells using 810nm and 980nm lasers operates via different mechanisms of action. *Biochim Biophys Acta*. 2017 Feb;1861(2):441-449.
- 18 - Jang DH, Song DH, Chang EJ, Jeon JY. Anti-inflammatory and lymphangiogenetic effects of low-level laser therapy on lymphedema in an experimental mouse tail model. *Lasers Med Sci*. 2016 Feb;31(2):289-96.
- 19 - Wheeland RG, Koreck A. Safety and effectiveness of a new blue light device for the self-treatment of mild-to-moderate acne. *J Clin Aesthetic Dermatol*. 2012; 5(5):25-31.
- 20 - Lizarelli RFZ, Grandi NDP, Florez FLE, Grecco C, Almeida-Lopes L. Clinical study on orofacial photonic hydration using phototherapy and biomaterials. *Biophotonics South America, Proc. of SPIE, Rio de Janeiro, Vol. 9531, 95311W*, 2015. doi: 10.1117/12.2181132
- 21 - Carvalho-Costa TM, Mendes MT, Silva MC, Rodrigues V. et al. Light emitting diode at 460+-20nm increases the production of IL-12 and IL-6 in murine dendritic cells. *Photomedicine and Laser Surgery*, 2017. DOI: 10.1089/pho.2016.4244
- 22 - Oh CT, Kwon TR, Choi EJ. et al. Inhibitory effect of 660nm LED on melanin synthesis in in vitro and in vivo. *Photodermatology, Photoimmunology and Photomedicine* 2017; 33:49-57.
- 23 - Chen L., Xu Z., Jiang M. et al. Light-emitting diode 585nm photomodulation inhibiting melanin synthesis and induces autophagy in human melanocytes. *J Dermatol Sci* 2018; 89:11-18.
- 24 - Weiss RA, McDaniel DH, Geronemus RG, Weiss MA. Clinical trial of a novel non-thermal LED array for reversal of photoaging: clinical, histologic and surface profilometric results. *Lasers in Surgery and Medicine* 2005; 36:85-91.
- 25 - Lizarelli RFZ. Photokinesio Therapy for Orofacial Paralysis. *JSM Oro Facial Surg*. 2017; 2 (1): 1007-1012.
- 26 - Patrocínio T, Sardim AC, Assis L, Fernandes KR, Rodrigues N, Renno AC. Effect of low-level laser therapy (808 nm) in skeletal muscle after resistance exercise training in rats. *Photomed Laser Surg*. 2013 Oct;31(10):492-8.