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Photobiomodulator Effect on Fibromyalgia Stabilization in the Oncoterapeutic Process

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Abstract- In this case study, Photobiomodulation was used in the craniofacial and systemic region for the symptomatic control in patients with Fibromyalgia (fibrositis syndrome or fibromyositis), simultaneously with oncoterapeutic therapy through the specific hormone (Tamoxifen-TMX). This non-invasive and low-cost planning emerges as an alternative in the systemic recovery of patients with this syndrome at Hospital of Câncer de Ribeirão Preto.

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1. INTRODUCTION

Fibromyalgia is a syndrome characterized by the presence of a wide range of symptoms that directly influence multiple systems in the body promoting a difficulty to designate it into a specific systemic category. It is usually manifested by generalized and persistent pain, abnormal sensitivity to pain, and additional symptoms such as fatigue, sleep disturbances, and mood symptoms (1-2). However the pathogenesis is controversial, but can be attributed or suggested by stress or idiopathic psychological factors. It was initially known as fibrositis, from which it evolved to the current specification of the term Fibromyalgia (FM), due to the symptoms of continuous or intermittent pain observed in patients with these generalized pain charts (3), and greater susceptibilities to comorbid psychiatric disorders (1-2). Research has come over the years that changes in the production of the hormones serotonin and epinephrine have fostered a possible etiology for triggering Fibromyalgia since the tricyclic antidepressants and selective serotonin antidepressants used in treatment therapy alter the balance that would provide the etiology of the disease. It is possible that the abnormalities promoted in the hormonal pathways favor the damping of the afferent pain signals, causing an increase in the perception of pain (4). This syndrome affects 2% of the population

with a high incidence of middle-aged women. And it usually overlaps with other functional somatic syndromes, such as chronic fatigue syndrome and temporomandibular joint dysfunction. But even associated with mood and anxiety disorders, research suggests that although functional somatic disorders are related and potentially interact with psychological conditions, they are independent (5). This generalized, deep tissue-sensitive somatic pain results from sensitization of neural pain pathways, without departing from variable combinations of fatigue, sleep disturbances, cognitive dysfunction, and psychological distress (6). However, it should be noted that musculoskeletal conditions such as temporomandibular dysfunction (TMD) (7) have a direct relation in mandibular compression during daily activities and rest in patients with Fibromyalgia (7-8), in whom the coexistence of these pathologies generates a clinical outcome of high complexity (9). Aerobic, strength and mixed training programs (combination of aerobics, strength and flexibility) have been shown to reduce pain, number of sensitive points, fatigue, depression and anxiety, and improved health-related quality of life as well as functional capacity (10-11). Dental activities directed to the facial skull region are indicated for the treatment of Temporomandibular Dysfunction (TMD) as a procedure combined with other therapies such as electrotherapy, physiotherapy, temporomandibular joint mobilization and facial massage to reduce pain (12-13). TMD is a dysfunction that is difficult to control and treat due to external factors that act as a complicating psychosomatic signal that contributes to the chronicity of the (systemic) fibromyalgia picture. In the new nuances of treatments, the use of a non-invasive therapy (photobiomodulation = laser therapy) emerges as a noble auxiliary resource, since it has the capacity to interact with biological tissues, and can trigger bioenergetic and cellular and molecular proliferative effects, whose primary photoreceptors are located in the mitochondrial respiratory chain (14-15) contributing with punctual analgesic and anti-inflammatory responses, reaching satisfactory muscle relaxation (16). Phototherapy using the low-intensity laser (LIB) and light-emitting diode (LED) therapy are being performed in patients with painful syndromes, including Fibromyalgia and Temporomandibular Dysfunction TMD (17). LIB contributes to the modulation of various

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signaling pathways and physiological mechanisms involved in analgesia (18-19). Research suggests that photobiomodulation increases the levels of β -endorphin, lymphatic flow and blood supply, as well as reducing bradykinin, releasing histamine, swelling, molecules associated with pain and inflammation, which leads to muscle relaxation (20-21). And it also corroborates with the therapeutic foundation, elucidated in the research that treated a group of patients with the low power laser protocol, of which the group exposed to the laser showed a greater decrease of pain than the group that did not undergo this phototherapy, supported by the image examination, through the monopotonic emission computed tomography (SPECT) of the involved ATMs (16). Already in this case study of Ribeirão Preto Cancer Hospital, we will address a patient who is a carrier of FM, but also uses adjuvant hormone (TMX-Tamoxifen) for breast cancer in the post-cycle of chemotherapy. This hormone has a significant reduction of 47% in the risk of recurrence and 26% in the risk of death (22). However, among the side effects of this drug, one of them is joint stiffness and / or pain similar to the feeling of recurrence of arthritis in several joints at the same time. This situation is most worrying, since joint pain can lead to the interruption of this therapy, which is so effective in controlling the disease (23). In a comparative study of therapies with patients receiving tamoxifen, most had joint symptoms, which were mild to moderate in severity, eliminating the need for treatment withdrawal. They observed that the most appropriate intervention for pain management in TMX-associated arthralgia may be a combination of changes in lifestyle, such as weight training, smoking cessation, moderation in alcohol consumption, dietary supplement intake of calcium and vitamin D for bone protection, and pharmacological options (24) (Table 1).

Table 1: Pharmacological Options, Source (24)

Opções farmacológicas para melhoria da dor em pacientes com câncer de mama inicial com sintomas de artralgia	
Medicação	Dosagem
Acetaminofeno ^a	≤daily (considere 33)
NSAID ^a	Naproxeno: 500-750 mg por dia (analgesia) 1000-1500 mg por dia (inflamação)
Inibidores da ciclooxigenase ^a	Celecoxib: 100-200 mg por dia ^b
Tramadol	≤400 mg por dia (considere 33)
Narcóticos	Codeína versusoxicodona
Modificadores de dor	TCA : nortriptilina 10-100 mg por dia gabapentina, pregabalina
Esteróides intra-articulares	Acetato de metilprednisolona, suspensão de triancinolona: 40 mg / cm ³

^a Mínimo 2 semanas a dose tolerada.
^b Máximo 400 mg por dia.
 NSAID = medicamento anti-inflamatório não esteróide, 33 = liberação prolongada, TCA = antidepressivo tricíclico.

Phototherapy (systemic) through the Intravascular Irradiation off blood (Ilib), triggers an antioxidant system composed of enzymes, the main one, SOD ZnCu, is the largest antioxidant agent (25) that we have and fifth enzyme in volume in the human organism. However, according to a recent review,

evidence suggests that the enzymes catalase peroxidase and ceruloplasmin also absorb the red laser which potentiates other enzymes, which obviously further increases the antioxidant property of these enzymes when irradiated in the Ilibprocess. And these therapeutic effects of light may minimize the side effects caused by chemotherapeutic, hormone therapy and radiation therapy sessions as an important reduction in inflammation and pain.

II. CASE REPORT

A 53-year-old white female EMGH diagnosed with multifocal invasive right breast carcinoma in 2013. Tumorectomy and lymphadenectomy of axillary lymph nodes were performed in the same year, followed by chemotherapy (QT) - 4 cycles (Taxol), Radiotherapy that ended in October 2013. Patient made use of Gabapentin 300mg oral and Tamoxifen with clinical symptoms of hot flushes, moderate hepatic steatosis and Fibromyalgia (FM). In October 2017, he presented to the Dentistry Service of the Hospital do Câncer to diagnose and monitor the reflexes arising from oncological therapies. The initial consultation revealed deficiency in oral hygiene, incipient xerostomia, dysgeusia and muscular fatigue in the bilateral face region. The patient underwent physical therapy at the same hospital once a week. The central object of this study was to perform the controlled phototherapy in the region in the external region of the face by noting the Temporal, Masseter and articular capsule (TMJ) muscles in a noninvasive way at the Cancer Hospital of Ribeirão Preto (SP), through the XT laser, DMC brand, useful red emitter laser power: 100 mW \pm 20%, red laser wavelength 660 nm \pm 10 nm, photobiomodulator effect, with specific protocol, and use of the Intravascular Laser Irradiation of Blood (IR) function in the radial artery of the wrist as complementary action. This radiation emitted by Low Power Lasers (LBP) has shown analgesic, anti-inflammatory and healing effects and is therefore widely used in the tissue repair process due to the low energy densities used and wavelengths capable of penetrating in tissues (26-27). Currently, this Low Intensity Laser (LBI) is being used for the overall recovery of the patient in several specialties of the health area; and their responses are considered to be beneficial (28-29) in a variety of different modalities due to their photobiomodulatory effect (30). Specifically, this mechanism when triggered in the craniofacial region is related to "neuronal repair and in neurogenesis, "not only in the formation of new brain cells, but also in" synaptogenesis, "which is the formation of new connections between existing brain cells (31). Therefore, it should be noted that the systemic and localized conditions during cancer treatment therapy contribute to the symptomatology of arthralgias, and in this niche of patients who use chemotherapy drugs and hormone

therapy these functions are altered with a certain frequency influencing negatively well-being organic and emotional. When it acts at the cellular level, the low power laser causes biochemical, bioelectric and bioenergetic modifications, influencing the increase of metabolism, cell proliferation and maturation, the amount of granulation tissue and the decrease of the inflammatory mediators, inducing the healing process (32-33). And when the molecule is absorbed by light, it allows an increase in cellular metabolism, characterized by stimulation of photoreceptors in the mitochondrial respiratory chain, changes in cellular ATP levels, release of growth factors and collagen synthesis (34-35). This complementary function, Ilib, has triggered an antioxidant system composed of enzymes, and the main Zn Cu SOD is the largest antioxidant agent (36) that we have and fifth volume enzyme in the human body and is more resistant to variations in temperature and to denaturation by substances like guanidine chloride, sodium duodecil sulfate, or urea. That is, several enzymes in our body absorb the red laser which potentiates other enzymes, improving the antioxidant function of these enzymes when irradiated in the ILIB process. And these therapeutic effects of light can minimize the side effects caused by the chemotherapeutic, hormone-therapeutical and radiotherapeutic sessions.

a) *Clinical Conduct (Therapy¹)*

- i. Hygiene of the oral cavity with clorexidine 0.12 % by digital friction, using the sterile gauze.
- ii. Measurement of pain² (Table 2).
- iii. Application of the Low Intensity Laser² (LIB) laser XT, DMC brand, useful red emitter laser power: 100 mW ± 20%, red laser wavelength 660 nm ± 10 nm, 1joule (10 seconds) - red / infrared 10 seconds in bilateral marked muscles) - figure a, e.
- iv. Complementary 15-minute photoentheral therapy (Ilib) in the radial artery of the wrist.

²The measurement of pain was permeated by the Behavioral Pain Scale (EC):

Table 2: Pain Measurement¹: Behavioral Pain Scale (EC) / Source (37)

Nota zero	Dor ausente ou sem dor
Nota três	Dor presente, havendo períodos em que é esquecida
Nota seis	A dor não é esquecida, mas não impede exercer atividades da vida diária
Nota oito	A dor não é esquecida, e atrapalha todas as atividades da vida diária, exceto alimentação e higiene
Nota dez	A dor persiste mesmo em repouso, está presente e não pode ser ignorada, sendo o repouso imperativo

The patient was monitored periodically for 4 months according to the table below (Table 3), through the proposed localized Lib protocol (Figure a), and simultaneously with Ilib therapy (Figure (b)) permeating the indoctrination proposed by the student Dr. Adriana shaposhink on "patient management" that require a greater regulatory control to maintain the state of general health.

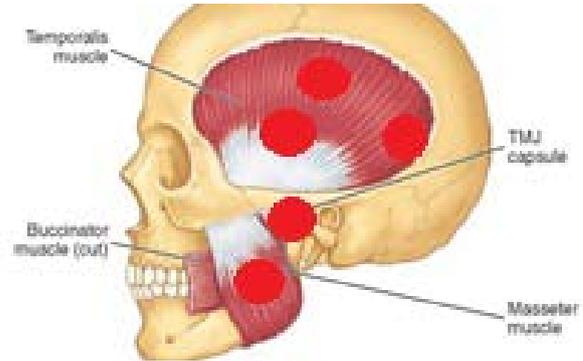


Fig1: Points of Application of the Lib



Fig. 2: Ilib in the Radial Artery of the Right Wrist / Fonte Hospital Câncer Ribeirão Preto

The results obtained were increasing until they reached the normalization of the sensory function previous to the proposed period initially, according to the table (Table 3) below:

Table 3: Cronologia dos Protocolos Propostos Para Utilização do Lib e Ilib.

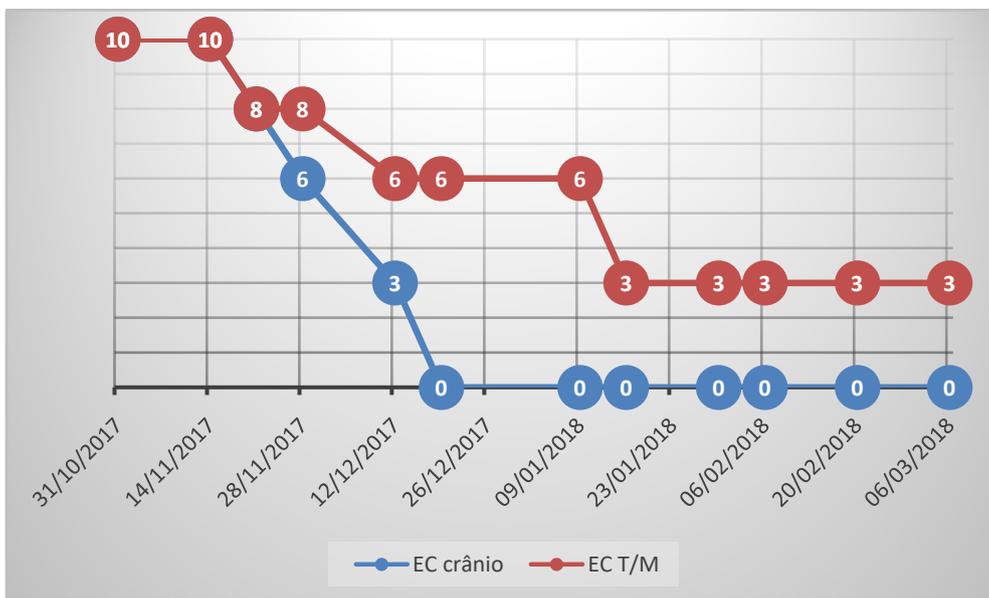
Date	Therapy ¹	Craniofacial Pain	EC ¹	Trunk Pain / Limbs	EC ²
31/10/2017	Lib / Ilib	Sim	10	Sim	10
14/11/2017	Lib / Ilib	Sim	10	Sim	10
21/11/2017	Lib / Ilib	Sim	8	Sim	8
28/11/2017	Lib / Ilib	Sim	6	Sim	8
12/12/2017	Lib / Ilib	Sim	3	Sim	6
19/12/2017	Lib / Ilib	Não	0	Sim	6
09/01/2018	Lib / Ilib	Não	0	Sim	6
16/01/2018	Lib / Ilib	Não	0	Sim	3
30/01/2018	Lib / Ilib	Não	0	Sim	3
06/02/2018	Lib / Ilib	Não	0	Sim	3
20/02/2018	Lib / Ilib	Não	0	Sim	3
06/03/2018	Lib / Ilib	Não	0	Sim	3

EC¹ / EC²: Measurements performed before the phototherapy intervention.
 Therapy¹: Suggested clinical conduct.

III. DISCUSSION

In this study, the initial proposal was to promote a noninvasive dosing through local and systemic photobiomodulation aiming at an improvement of the pain picture in the facial and general region caused by fibromyalgia. The results obtained after the first and second applications of the laser (lib and ilib) did not change the condition, but from the 3rd application there was a decrease in pain in both the facial and trunk / limb regions, even with simultaneous hormone therapy. This evolution produced a greater balance in the habitual activities of the patient and a fundamental impact on the self-esteem which allowed an improvement in the resumption of the quality of life. The positive sequence in EC¹ compared to EC², a trend that became increasing

in the 10 subsequent consultations until reaching an acceptable level in the Level 3 Behavioral Scale (EC), which made it relevant for a fibromyalgia syndrome in association with TMX. In addition to this, the support that phototherapy demonstrates in exercising healthy cellular activity, an increase in cellular metabolism, improves cellular regeneration, invokes an anti-inflammatory response, promotes the reduction of edema, reduces the formation of fibrous tissue, stimulates the function reduces the production of substance P, stimulates the long-term production of nitric oxide, decreases the formation of bradykinin, histamine and acetylcholine, and stimulates the production of endorphins (38). And the following graphic elucidates the treatment of pain until the neutralization in the facial skull region (EC skull) and acceptable stage in the trunk and limb regions (EC T/M or P/L):



Source: Hospital Câncer Ribeirão Preto

Chart 1: Initial and Final Stage

IV. CONCLUSION

The clinical evolution of this specific case is undeniable through photobiomodulation, and it is important the multidisciplinary involvement of all the staff in their various specialties that contributed in an assertive way to stabilize the picture. Although the clinical results look very promising, and the low-power laser fits perfectly into the realm of "high-tech" therapy, care must be taken not to regard it as a new panacea. The ideal that this technology continues to perpetuate advances in this topic of pain control related to fibromyalgia, from which the systemic repercussions potentiate benefits irradiated to other sites fundamental to the maintenance of health. The biomedical effects of low power laser irradiation were investigated in several health areas. Beneficial effects such as immunosuppression, immunostimulation, autoimmune disease and nerve regeneration have been described and gain strength as a new therapeutic modality, due to the recognition as a viable treatment option for a diverse range of diseases and conditions characterized by injury, degeneration, inflammation and pain (39). But it is important to emphasize that the goals of containment of the disease have been reached and reiterate the need to permanently manage these patients affected by fibromyalgia and who are still undergoing oncoterapias. to control the disease. And I stress that "Laser was not able to replace many of today's techniques and physical modalities, however, it can be used together to improve the health of patients (40)."

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