CASES REPORTS APPLYING VASCULAR SYSTEMIC PHOTOBIOMODULATION TREATMENT

ORIGINAL ARTICLE

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ABSTRACT

The systemic effects of lasers have been observed for a long time. Despite a huge amount of evidence, its foundations are still being systematically investigated with several scientific experiments. As the metabolism in animals is systemic by nature, it should come as no surprise that localized excitation of molecules leads to generalized reactions, which can contribute to the rehabilitation of many diseases. As a new area of research, clinical cases presentations generate evidence for more in-depth fundamental studies. In this work, we report some different clinical cases, demonstrating the value of photobiomodulation in systematic situations. A collection of cases where vascular systemic photobiomodulation were employed are presented and inflammatory markers area evaluated. All cases considered are known to have long treatment and difficult results. The results presented with vascular systemic photobiomodulation are relevant in the considered to improve quality of life, stimulus for its use in general and as a motivation for in-depth studies in the area.

Keywords: Intranasal, Laser, Photobiomodulation, Quality of life, Sublingual, Systemic, Transcutaneous, Transmucosal.

1. INTRODUCTION

Systemic effects are well known on human healthy. The circulatory system is an efficiently and technically elaborated way to promote systemic effects. Since 1967, the use of low power laser irradiation or photobiomodulation (PBM) has been well established as a therapeutic tool for localized application, whether to accelerate tissue repair, relieve acute or chronic pain, drain oedema, and improve immune responses. It happens that, even when irradiation is applied at well-defined points (injury, lymph nodes, trigger and tender points, for example) there is always a systemic gain that was not valued enough. Currently, this correlation has been very important, treating prepared patients, improving their chronic inflammation, including as an adjuvant in the treatment of common and more complex disorders, leading to an improvement in the general conditions of quality of life. Extra benefits began to be observed, beyond the main objective, localized treatment many decades ago.

Tallarida *et al.* (1981) carried out a study on wounds of patients with arteriosclerosis, using a 632.8 nm HeNe laser at the edges of the wounds, and observed that, in addition to accelerating their healing, it also improved the hemorheological properties of patients, reducing tissue ischemic. Such observations triggered more localized photobiomodulation, that is, the irradiation of certain regions, but with physiological gain not only in the irradiation site, but also in the body as an all.

At the beginning of 1980s, some Russian and Chinese researchers have started to describe important systemic effects by promoting intravascular laser irradiation of blood therapy (ILIB therapy). The technique consisted of perforating the skin and introducing a fiber optic catheter into large blood vessels, and depositing energies around 9J with red or infrared lasers.

But as early as 1998, Gasparyan (1988) already cited other methods for this therapeutic idea, being either invasive (intravascular, venous, or extracorporeal) or non-invasive (transcutaneous - where there were arteries or caliber veins, or simply as we already know and do on skin or mucosa near the injured regions.

Currently, a few research, ongoing and recently published, have evaluated other ways of irradiating the blood in a non-invasive via, transcutaneous or transmucosal.

Liu *et al.* (2010) presented, for the first time, intranasal photobiomodulation, called ILILT (intranasal low intensity laser therapy). They evaluated whether the use of laser therapy emitting at 650 nm would have an important effect to restore homeostasis in athletes. This rehabilitation was found to be mediated by the ratio of intracellular nicotinamide adenine dinucleotide (NAD+) and its reduced form NADH, NAD+/NADH, and then sirtuin 1 (SIRT1). ILILT can increase NAD+/NADH and SIRT1 activity until functional homeostasis is achieved.

Ailioaie *et al*. (2014) presented sublingual irradiation (SL) as an innovation for idiopathic juvenile arthritis. They used a three-wavelength (635 nm red, 536 nm green and 405 nm violet) equipment with peak power of 5mW each, in continuous mode (CW), daily for 20 minutes for 7 consecutive days, monthly, for 3 months. The 105 patients who received the therapy had reduced pain, reduced number of joints with limited movement, improved quality of life, and avoided the administration of immunosuppressive drugs, very aggressive agents for children in development, and the high cost.

Silva *et al.* (2020) have been investigated the effects of photobiomodulation (PBM) on the expression of IL-10 and nitrites in individuals with Relapsing-Remitting multiple sclerosis (MS), as these biomarkers play a fundamental role in the physiopathology of the disease. They have irradiated using two different vias: transcutaneous (radial artery) and transmucosal (sublingual), at the same laser parameters (808 nm, 100 mW, 6 minutes, in contact mode, continuous wave), twice a week, totaling 24 sessions. Both vias were able to promote positively modulation of the expression of IL-10 but had no effect on nitrite levels.

Our researcher group has published a paper considering vascular systemic photobiomodulation via transcutaneous and transmucosal (LIZARELLI *et al.*, 2021), and our results has showed that there is a possible way to control biochemical inflammatory markers, improving metabolic and physiologic responses.

In this work, we will present clinical cases using these vascular systemic photobiomodulation (VSP) to treat different pathologies: type II diabetes, pos-chemical therapy for mama cancer, pos-COVID-19 infection, dengue infection, high performance athlete; and their effects considering inflammatory biomarkers. While the field is still under construction, the evidence with clinical experiences can construct an important background of applications.

2. MATERIALS AND METHODS

2.1. CLINICAL CASES PRESENTATION

We will present, here, some clinical cases using vascular systemic photobiomodulation (VSP) to treat different pathologies. All patients have given us an authorization to receive laser therapy treatment. All safety rules were used during all sessions, and the professional had a academic post-graduation to use this treatment technique. There is no Ethics Committee because yes, this treatment is new in Brazil, but it already has its approval in the scientific and clinical environment.

First, patients present results from blood tests (biochemical tests through blood collection, evaluating inflammatory and metabolic markers) and then, lasers sessions were performed. At the end of the treatment (10 sessions), these blood tests were repeated to allow effects of VSP. A commercially available pen-shaped dual-wavelength low intensity level laser (Laser Duo, MMO, SP, Brazil) presenting 660 nm and 808 nm, 100 mW/ each, continuous wave, spot size = 0.03 cm^2) (Fig. 1a). we have used 660 nm during irradiation time of 30 minutes, as patients presented phototype III, it means that the interaction between low level laser and skin/mucous did not resulted in temperature rise.

We chose the blood biochemical test and some main inflammatory markers that could help us according to the profile of each patient. The tests chosen were: Ferritin, Gamma Glutamyl Transferase (Gamma GT), TGP (pyruvic transaminase), TGO (oxalacetic transaminase), Basal Glucose and Glycated Hemoglobin, C-reactive protein, Fibrinogen, Homocysteine, Magnesium, Platelets, Triglycerides, High density lipoprotein (HDL) and Low-density lipoprotein (LDL).

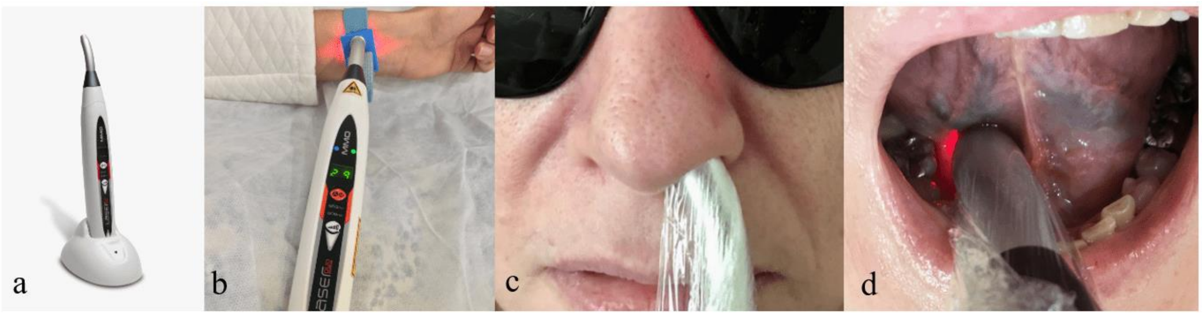
To evaluated liver health: Gamma GT, TGO and TGP, also known as transaminases, are enzymes that are normally measured to assess liver health. When there is any change in this organ, there is an increase in the amount circulating in the blood. Changes in these enzymes' levels are usually indicative of liver damage, which can happen due to hepatitis, cirrhosis, or the presence of fatty liver, and it is possible to evolute to damage in the heart. C-reactive protein or ultrasensitive CRP is a protein synthesized in the liver, whose levels increase in value when there is some inflammation happening in the body. CRP is considered an acute phase reactant, having its rates increased in response to some type of inflammation and being hardly detected in healthy people. CRP responds to inflammatory proteins known as cytokines, which are produced by white blood cells during the inflammatory process. The CRP test is also used to detect exacerbated manifestations of inflammatory diseases.

Concern hemorheological function, we have chosen: a) Fibrinogen is a clotting factor (factor I), a protein necessary for clot formation. It is produced in the liver and released into the circulation along with other factors. It is triggered when there is damage to a blood vessel, a process called hemostasis, which stops bleeding. High fibrinogen levels are related to thrombosis, whether arterial or venous; b) Homocysteine is an amino acid. It is in blood plasma, related to the emergence of cardiovascular diseases such as stroke, coronary heart disease or heart attack, as its levels on a large scale can alter blood vessels; c) Triglycerides and High-density lipoprotein (HDL) is responsible for removing excess fat from our tissues. It guides the particles to the liver, where they will be eliminated. All this contributes to an antioxidant and anti-inflammatory action; d) Low-density lipoprotein (LDL) works the opposite way – transporting cholesterol from the liver and intestine to the membranes, cells, and veins. The accumulation of particles in these places, without proper elimination, ends up harming the proper functioning of the body and can cause cardiovascular problems, for example, e) Glycated hemoglobin test is done with the aim of evaluating glucose levels in the last few months, being useful in the diagnosis of diabetes. In addition, this test is useful to check if the treatment is being effective or is being done correctly, because if it is not, a change in the result can be verified; and, f) Basal glucose is a blood test is widely used to investigate the diagnosis of diabetes, and to monitor blood sugar levels in people with diabetes or at risk for this disease.

Finally, Ferritin and Magnesium. Ferritin is a protein produced by the liver, responsible for storing iron in the body. It may be elevated in conditions such as liver disease, alcoholism, malignancies, infectious and inflammatory diseases. Magnesium is necessary for energy production and for the development of bone structure. In addition, this element is related to the transport of calcium and potassium ions across cell membranes, an essential process for the conduction of nerve impulses, control of heart rate and muscle contraction. Magnesium can improve metabolism and indeed, photobiomodulation action (ANJU *et al*., 2019).

During all sessions, patients were questioned about the sensations and quality of life, on the day of the VSP session and on the following days, and very positive reports were reported. Blood exams were done before and after irradiations. The cases were selected according to the need to control the patients' systemic inflammation, without opting for systemic medication.

Figure 1 - A commercially available pen-shaped dual-wavelength low intensity level laser (Laser Duo, MMO, SP, Brazil; 660 nm and 808 nm, 100 mW/each, continuous wave, spot size = 0.03 cm^2) (a); the VSP routes used in the clinical cases presented here: transcutaneous (radial artery, left arm) (b), intranasal transmucosal (c) and sublingual transmucosal (d)



Source: Lizarelli, 2020.

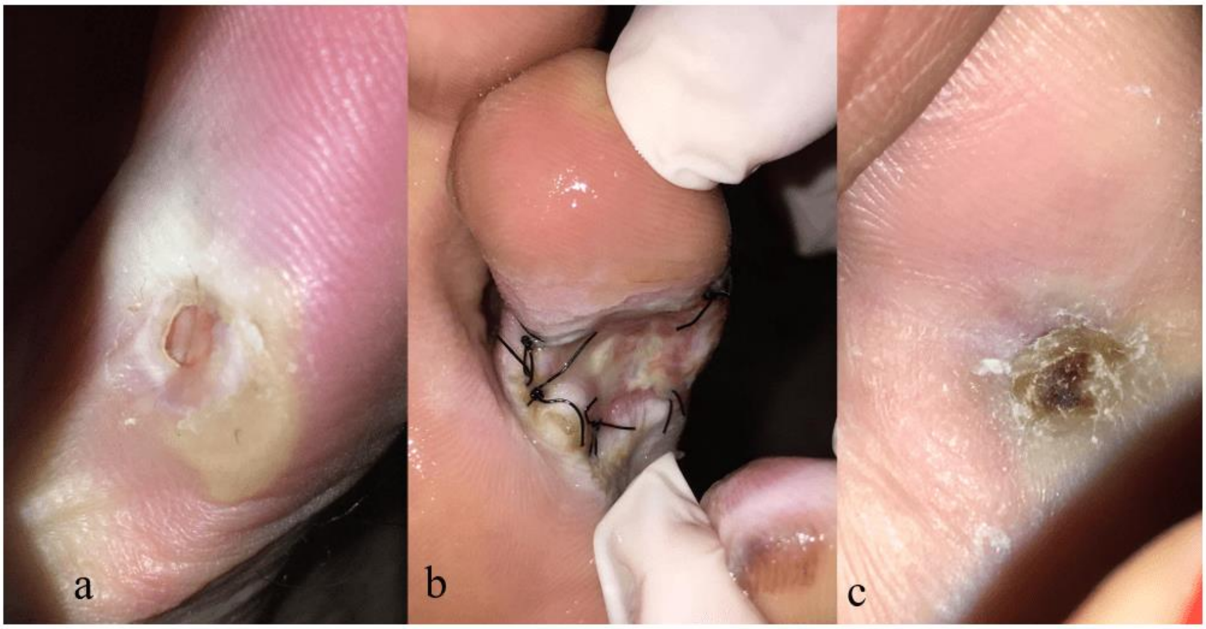
2.2. CLINICAL CASES PRESENTATION

The proposal of irradiating circulating blood with laser operating at low intensity began using the intravascular route, but here, we will describe clinical cases where we have used different routes: transcutaneous route (radial artery, left arm - the active tip of the laser pen was positioned, in contact with the skin, where the radial artery is more superficial, in the distal part of the forearm, laterally to the tendon of the flexor carpi radialis muscle, and where it is possible to take the arterial pulse) (Fig. 1b), intranasal transmucosal route (both nostrils - the active tip of the laser pen was positioned facing the midline of the nose, at the level of the middle turbinate) (Fig. 1c) and transmucosal sublingual route (the active tip of the laser pen was positioned perpendicularly to the mucosa of the floor of the mouth, in the sublingual region, between the sublingual fold over the sublingual gland and the sublingual caruncle on the right side) (Fig. 1d). Both transmucosal routes are regions with a high concentration of blood vessels, while the transcutaneous route chosen coincides with the point where the radial artery is more superficial towards the epidermal layer.

2.2.1. DIABETIC ULCER PATIENT

Male, NAB, 52 years-old, type II diabetic and with a medical history of Hepatitis A and C. Due to its comorbidities, a systemic treatment with photobiomodulation was suggested to balance its inflammatory markers. Then, with two weeks on VSP, the patient developed an ulcer on his left foot.Patient had, over the last six months, an average basal glucose value of 127.2. Medication was maintained and the only therapy added was transcutaneous systemic vascular photobiomodulation. Due to the possibility of amputation of the fourth toe of the left foot, which presented a rapid evolution of a wound to osteomyelitis, VSP was associated to conventional medical treatment for healing after surgical scaling and hydro-alginate with silver dressings (Silvercel, Systagenix, UK).Figure 2 shows the evolution of the wound on the fourth toe of the left foot, from its initial diagnosis until its healing was practically completed. The patient underwent a blood test for his inflammatory markers to be evaluated (Table 1), on 08/02/2018. Then, we started the vascular systemic photobiomodulation was treated using 660 nm laser 100 mW power, 30 minutes of irradiation time, transcutaneous at radial artery, twice a week, for three months in August to October 2018) and after that, then twice a week for more three months (Nov-Jan/2019), and, finally, once a week from Jan to May/2019.

Figure 2 – Evolution of the wound on the lateral face of the fourth toe of the left foot: appearance on 09/29/2018 (a) the ulcer had a halo around necrotic tissue that needed to be debrided and removed; on 10/23/2018 (b) the ulcer no longer had an infection, which was very extensive, as a debridement with surgical curettage had been performed; and, finally on 01/18/2019 (c) the ulcer already showing deep healing, well retracted edges and practically closed



Source: Lizarelli, 2018.

Table 1 – Table with dates and tests performed to assess the systemic biochemical behavior in the face of systemic photobiomodulation

Periods\ Tests	Basal Glucose [< 100 mg/dL]	Glycated Hemoglobin [4 to 6.3 %]	Gamma GT [< 50.0 U/L]	TGP [3 to 50 U/L]	TGO [12 to 46 U/L]	Ferritin [21 to 334 ng/mL]
08/02/2018	177.6	8.4	53.9	27.2	22.4	719.0
09/27/2018	166.9	7.2	33.4	26.8	17.6	463.3
05/06/2019	89.9	5.3	16.0	21.2	16.0	324.3

Source: Lizarelli, 2018.

Inflammatory markers referring to the liver were collected: Ferritin, Gamma Glutamyl Transferase (Gamma GT), TGP (pyruvic transaminase), TGO (oxalacetic transaminase), Basal Glucose and Glycated Hemoglobin. The patient showed improvement for all inflammatory markers evaluated, regardless of the frequency of vascular systemic photobiomodulation (3, 2 or 1 session per week). The improvement, denoted by the decrease in the concentration of markers in the blood, happened steadily.

Despite all efforts with well-placed procedures (dressings and surgical curettages), irrigation, which is essential for the healing of an ulcer, has systemic activity, so activities that can facilitate this blood nutrition will certainly contribute to the well-obtained result. VSP, probably, allowed a faster and more successful recovery in this patient, who, systemically, would have altered inflammatory markers that would impair the healing of this ulcer.

2.2.2. POS-CHEMOTHERAPY CANCER PATIENT

Female, SABM, 66 years old, with a medical history of breast cancer with successful treatment for 6 months after. She was treated using 808 nm laser 100 mW power, 30 minutes of irradiation time, transmucosal under tongue, twice a week, for two months. Proservation was performed 1 year after vascular systemic photobiomodulation was proposed.

During the two months of transmucosal systemic photobiomodulation, the patient was supplemented with vitamin D3 orally, starting 30 days with 50,000 iu/ day and the 20,000 iu/ day for another 30 days.

Table 2 – Table with dates and tests performed to assess the systemic biochemical behavior in the face of vascular systemic photobiomodulation

Periods\Tests	Ultrasensitive CRP [< 3.0 mmg/ L]	Glycated Hemoglobin [4 to 6.3 %]	Ferritin [21 to 334 ng/ mL]	Glucose [< 100 mg/ dL]
04/25/2018	12.4	5.3	262.7	109.5
06/25/2018	0.98	5.2	188.9	86.7
03/11/2019	2.33	5.6	220.0	102.8

Source: Lizarelli, 2019.

The patient showed a significant improvement in the inflammatory markers evaluated, however, after the end of vascular systemic photobiomodulation, most of them returned to their high values (inflammation), except for Ultrassentive CRP. In an equivalent situation, without the application of systemic vascular PBM, the improvement would be much more slow or absent.

2.2.3. POS-COVID-19 INFECTION PATIENT

Female IBA, 24 years-old, single, undergraduate student, she tested positive for COVID-19 along with her entire family. She was isolated and did not need to be hospitalized. Her symptoms were mild: headache, malaise, anosmia and ageusia, coryza, tiredness, for 8 days. In the post-COVID-19 period: tiredness, indisposition, still have partial loss of smell, recurring headaches, hair loss and shortness of breath.

Even though she was younger than the previous patient and did not present comorbidities or systemic dysfunctions already diagnosed, and the symptoms were not as severe, the biochemical examination showed a picture of great systemic alteration.

VSP was performed in two sessions per week, being transcutaneous in the region of the radial artery with a pen laser emitting in the red wavelength (660 nm) for 16 minutes in each session. No exogenous supplementation with vitamins or hormones was performed, only irradiation.

Table 3 – Comparative table of inflammatory markers before the first session (04/17/2021); immediately after the tenth session (05/25/2021); and, after the twentieth session (07/12/2021)

Period\ Tests	Ultrasensitive CRP [< 3.0 mg/ L]	Fibrinogen 180 to 400 mg/ dL	Homocysteine 5.0 to 12.0 mmol/ L	Magnesium 1.3 to 2.7 mg/ L
Initial	3.60	289.0	10.4	2.2
After 10 sessions	2.87	262.2	12.9	2.0
After 20 sessions	1.02	115.0	14.6	1.7

Source: Lizarelli, 2021.

The combination of DMB (vitamin D3 orally 1000 IU OD, magnesium 150 mg OD, and vitamin B12 500 mcg OD - DMB) in older patients with COVID-19 was associated with a significant reduction in the proportion of patients with clinical deterioration who required supportive care. oxygen and/or intensive care support (TAN *et al*., 2020). In this patient, during treatment with VSP, exogenous supplementation with Magnesium was not instituted.

Exception of Homocysteine, clinically, the patient showed an improvement in her mood to work, she started to wake up more willing and her headache eased and continues. Her Anosmia condition resolved without specific treatment, but her Ageusia condition continues. The next step was to supplement if with Magnesium and treat the headache and ageusia with PBM, then this last treatment solved these sequelae in 6 sessions over 3 weeks.

2.2.4. DENGUE INFECTION PATIENT

Female, GCR, 25 years-old, nutritionist, single, started irradiation on 06/17/20, when she was diagnosed with dengue. He developed acute hepatitis, but irradiation helped to recover very quickly, in 1 week, which would normally happen without photobiomodulation, in 3 months.

The patient presented a serious clinical case conditions of dengue progressing to hepatitis and meningitis. This case is being reported because the hepatic enzymes restoration was within just one week, very fast, which would normally take about three months.

There is much evidence that thrombocytopenia is due to the autoimmune action caused by antibodies induced by dengue virus infection. Clinical evidence: petechiae and ecchymoses. Laboratory Evidence: Moderate to marked decrease in platelets. And one of the most aggressive types (DEN-3), being very aggressive to the liver, can cause marked changes in clotting factors and causes severe bleeding (DAS *et al.*, 2022). She has been used transcutaneous photobiomodulation for 30 minutes in the radial artery alternating 660nm and 808nm daily for 15 consecutive days.

Table 4 shows some blood serum inflammatory markers: number of platelets, hepatic transaminases oxalacetic (TGO) and pyruvic (TGP) enzymes, in addition to the patient's clinical conditions. The increase in TGO describes extensive liver damage, while the increase in TGP describes a functional change in the same organ.

Table 4 – Table with dates and tests performed to assess the systemic biochemical behavior in the face of systemic photobiomodulation

Periods\Tests	Platelets [125.000 to 450.000/ mm³]	TGP [14 to 59 U/ L]	TGO [15 to 37 U/ L]	Patient Condition
06/04/2020	236.000	12	19	Healthfully
06/10/2020	166.000	----	----	Dengue +
06/17/2020	202.000	251	160	Acute Hepatitis
06/29/2020	238.000	81	34	Almost Healthfully

Source: Lizarelli, 2020.

From the data in Table 4, it seems quite clear that, once systemic vascular FBM started on 17/06/2020, the TGP and TGO values tended to the healthy levels of 04/06/2020, as well as the number of platelets. Then, again, the irradiation of the circulating blood denoted an important systemic improvement, resulting in the healthy integrative condition of the patient.

2.2.5. HIGH-PERFORMANCE ATHLETE

Female, EPP, 40 years old, high-performance runner. She was irradiated twice a week, totaling 16 sessions (for two months), 660 nm low level laser therapy, intranasal, 100 mW, irradiation time of 30 minutes.

Table 5 – Table with dates and tests performed to assess the systemic biochemical behavior in the face of systemic photobiomodulation

Periods\Tests	Glucose [< 100 mg/ dL]	Triglicerides [< 150 mg/ dL]	HDL [> 40 mg/ dL]	LDL [< 130 mg/ dL]
Initial	90	70	57	95
30 days	87	67	59	70
60 days	81	62	60	87

Source: Lizarelli, 2018.

To monitor cholesterol levels, it is necessary to perform the test called lipidogram. With the laboratory test, the doctor responsible for the order will check your lipid profile according to the amount of LDL and HDL. The result will also present values of total cholesterol and triglycerides. Upon reaching the answers, the professional identifies the risk of developing diseases and guides the next steps, whether prevention or treatment.

An athlete who is demanding beyond her physical and physiological capacity, under high stress, with intense training of 4 hours/ day, still showed control of inflammatory markers in the biochemical serum test. This level of physical demand probably results in a high concentration of oxidative and nitrative free radicals, acidifying the tissues, so this could be the cause of a better absorption of the 660 nm laser irradiation.

Although the patient presented an excellent profile, due to her antioxidant attitudes and daily care with food, hydration, rest, and training, vascular systemic photobiomodulation was able to control the inflammation that was probably the result of intense physical training.

3. GENERAL DISCUSSION OF THE CASES

All the clinical cases presented here received the well-established conventional treatment plus systemic photobiomodulation through irradiation directed to the circulating blood, even though it was not by the intravascular route. Here, we used the transcutaneous and transmucosal routes, both of which have already been well described in the literature with similar results to the intravascular route. In fact, photobiomodulation needs photoacceptors to have its effect, and in this case, it is hemoglobin, which is the functional protein of erythrocytes. Since the circulating blood acts as an integrative and systemic vehicle, vascular systemic photobiomodulation will result in a very useful instrument so that we can modulate the patient in an integral way and thus, different dysfunctions and diseases can be treated, at least in the sense of improving the physiological baseline conditions.

Zhao *et al.* (2008), in a meta-analysis on the use of intravascular laser therapy that patients with diabetes can be improved with intravascular laser irradiation of blood, which can be mediated by the improvement of blood parameters. Our Patient #1 has presented a great response to Vascular Systemic Photobiomodulation (VSP) as an adjuvant treatment.

The VSP seems to be interesting for both acute and chronic cases, that is, it seems to be possible to work with the VSP daily in acute cases, and 2 to 3 sessions per week for chronic cases, very similar to the different protocols for pain acute and chronic. In the latter case, lower doses are indicated for acute cases, while higher doses are indicated for chronic cases. It remains to be seen whether this would also apply to systemic PBM. This was possible to observe both in the patient with a history of hepatitis and diabetes, and in the patient who had just been diagnosed with dengue.

The two patients who went through intensely stressful clinical situations, breast cancer and COVID-19, also showed an excellent response to vascular systemic photobiomodulation, denoting that it is a therapeutic approach that should always be instituted as an adjunct, regardless of the degree of severity of the installed disease.

Even for the high-performance athlete patient, whose diet was strict and who already had good values of inflammatory biomarkers, systemic vascular photobiomodulation was able to effectively modulate to better levels.

Although Yamaikina *et al*. (2008) suggested that intravascular irradiation with 633 nm red laser should not be used for a weakened organism in the period of disease worsening, because they believe that, initially, intravascular laser irradiation of blood

(ILIB) promotes, at cellular level, an important disturb like heating of blood, then the organism must replenish the store of blood cells, which leads to the strengthening of immunity and improvement of the deformability of erythrocytes; we observed, here, in the descriptions of these cases, an important coadjuvant effect for the recovery of homeostasis, clinically.

Photobiomodulation acts at the molecular level with consequences at the tissue and systemic level. In the case of direct illumination of the blood the oxy and redox peaks in the hemoglobin are known at specific wavelengths. Of course, the excitation of these molecules may have interesting systemic reactions. There are still no laboratory experiments that indicate the change in blood characteristics due to such excitation. However, the action of light in this case can promote a wide variety of reactions that culminate in a favorable set of effects. Judging by the well-being reported by the patients who received this therapy, there is no reason not to apply it.

Siposan and Lukacs (2001) presented a very important result after 632,8 nm laser irradiation of fresh blood, the effect of low-level laser therapy (photobiomodulation). Concern red blood cells, they confirm the nonresonant mechanism of this biostimulating effect, probably because of the changes occurring in the cell membrane, by revitalizing of these red blood cell functional capacities, indeed by several biochemical effects at the membrane's level. The physical-biochemical and biological effects promoted by photobiomodulation on blood can influence the physical-chemical parameters needed for the long-term storage of blood products. These effects can also lead to a quicker revitalization of the erythrocyte membrane to perform its oxyphoric function in transfusion procedures.

Mi *et al*. (2004) have been used 632,8 nm HeNe ILIB and the results showed that decreasing of the erythrocyte sedimentation rate of blood samples, which had a hyper-sedimentation rate originally; and the deformability of erythrocytes from pathological samples and Calcio ions treated samples was improved after laser irradiation. In a second paper, Mi *et al.* (2006) have been confirmed the improvement of erythrocyte deformability after 632,8 nm and 532 nm laser irradiation.

Oxiforic functions is the capability of erythrocytes to deliver oxygen to the tissues in your body. This condition added to improved erythrocyte deformability can promote some fundamentals circumstance to facilitate homeostasis recovery: better blood circulation into nanocapillaries and better oxygen delivery. Nanocapillaries are present in noble organs, being the structures responsible for oxygenation and its efficient functioning. Thus, it seems clear to say that vascular systemic photobiomodulation seems to guarantee the best metabolism of several important organs throughout the organism.

4. CONCLUSIONS

In all the clinical cases presented here, there is a common clinical condition: disturbance of the immune system, due to an acute or chronic inflammation. The clinical option of irradiating, through the blood circulation, the whole organism, obtaining an abscopal effect, provides the professional with a facilitation to normalize patients towards systemic homeostasis.

At the same time, the scientific basis for this action must be built, observing improvement parameters to achieve positive results and return to having the best possible condition to maintain quality of life. Then, we will be able to suggest when, how and how many sessions each patient at the singular situation must receive this great light treatment.

If the patient does not have any medical restrictions for the use of photobiomodulation, we strongly recommend the vascular systemic approach as a treatment or adjuvant to restore their integrative health.

There are a few propositions to explain mechanisms associated with systemic effect: better blood oxygenation, deformation of blood red cell and other possibilities. That is a topic that should be deeply investigated based on the growing reported evidence.

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