



## Case Report

# Photobiomodulator therapy in the glycemic stabilization of diabetes mellitus carrier type 2 patient

Juliano Abreu Pacheco<sup>1\*</sup>, Adriana Schapochnik<sup>2</sup>, Antônio Cesar M Santiago<sup>3</sup> and Andressa Figueiredo<sup>4</sup>

<sup>1</sup>Odontologist; Research Coordinator of Oncology Hospital Ribeirão Preto; Specialist in Hospital Dentistry; Master's Degree in Intensive Care by IMBES, Brazil

<sup>2</sup>Physiotherapist; Specialist in Traditional Chinese Medicine; Master's degree in Biophotonics by Uninove, Brazil

<sup>3</sup>Doctor, Oncologist at Cancer Hospital of Ribeirão Preto, Brazil

<sup>4</sup>Pediatric Endocrinologist at Hospital São Lucas in Ribeirão Preto, Brazil.

\*Corresponding author. E-mail: [japacheco@hcancerderibeirao.org.br](mailto:japacheco@hcancerderibeirao.org.br), [coepacheco@gmail.com](mailto:coepacheco@gmail.com)

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*The purpose of this study was to perform transcutaneous, non-invasive and Intravascular Irradiation of blood (Ilib) photobiomodulation in the radial artery of the wrist, besides the phototherapeutic complementation in the oral cavity aiming at the short-term control of glycemia in the patient with Diabetes mellitus type 2, in the Hospital of the Cancer of Ribeirão Preto (SP).*

**Key words:** Diabetes mellitus, oncology, laser, photobiomodulation, glycemia

## INTRODUCTION

Type 2 diabetes mellitus (DM) is associated with increased insulin resistance and obesity. Concurrent scientific studies have pointed out that certain susceptibility genes are different from the genes associated with type 1 diabetes. It directly binds DM 2 to increased morbidity and mortality from cardiovascular diseases (Ashok Raj et al., 2009). This congruence between DM 2 and cardiovascular diseases leads to the hypothesis that both have the same genetic component and environmental background, and insulin resistance consider both hypotheses one of the main possible antecedents (Ceriello and Motz, 2004). There is a compromised metabolism of all energy substrates, but what will determine the diagnosis of specific alterations will be the plasma glucose test (Wajchenberg et al., 1992). In Type 2 Diabetes mellitus, resistance to it observes insulin stimulated glucose uptake, even with hyperglycemia, and deterioration of this tolerance will depend on the ability of the pancreas to maintain chronic hyperinsulinemia. It associates insulin-stimulated resistance to glucose uptake with several

alterations that increase the risk for cardiovascular disease, glucose intolerance, hyperinsulinemia, hypertriglyceridemia, HDL-c reduction, arterial hypertension and android obesity (Wajchenberg et al., 1992). Both diabetes and cancer are prevalent diseases whose incidence is increasing. For over 50 years, doctors have reported the existence of patients with concurrent diabetes and cancer, a meta-analysis of several studies has showed that some malignancies are more frequent among patients with diabetes (predominantly type 2). The relative risks induced by diabetes are greater (approximately two or more times) for liver, pancreatic and endometrial cancer and minor (approximately 1.2-1.5 times) for colon and rectal, breast, and bladder cancer. As insulin is produced by  $\beta$ -cells in the pancreas and transported through the portal vein to the liver, it exposes both the pancreas and the liver to high concentrations of endogenously produced insulin.

Factors related to diabetes, such as steatosis, non-alcoholic hepatic steatosis and cirrhosis, may also increase susceptibility

Source	Number of subjects	Mean age (years)	Sex(%male)	Intervention	Blood sugar before mg/dl (Mean ± SD)	Blood sugar after mg/dl (Mean ± SD)
Chen, 2000 (Chen, Chen, Xu, Chen, & Peng, 2000)	10	67.3	93.3	He-Ne laser extravascular irradiation therapy instrument, D=40mm, 632.8nm, 60 min	197.1±73.8	106.2±54.0
Kovalyova, 2002 (Kovalyova, 2002)	27	57.3	13	ILIB intravenously 2 mW/±0.63 mm 405-nm 15-30 min	259.74±15.48	255.78±15.3
V. KazemiKhou, 2013 (Kazemi Khou et al., 2013)	9	60.63	55	ILIB intravenously 1.5 mW, continuous, 405-nm 30 min	190±17	165±20
N. KazemiKhou, 2015 (Kazemi Khou & Moini, 2015)	24	37	63.7	ILIB intravenously 1.5 mW, continuous, 405-nm and 630 nm 20-30min-one day blue one day red laser therapy	214.71±78.99	188.53±75.60

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**Figure 1.** Data of different light therapies for DM 2

to liver cancer. In relation to pancreatic cancer, it found a positive association between diabetes and the risk of pancreatic cancer in studies limited to diabetes that appeared at least 5 years before cancer. The results of some epidemiological studies suggest that diabetes can increase mortality among cancer patients (Dres. Giovannucci et al., 2010). And in cases related to photobiomodulation in patients with type 2 diabetes mellitus early or even advanced that when submitted to laser therapy could restore the function of the pancreas and normalize the level of glucose in the blood (Ramdawon, 1999). It reached this conclusion since laser irradiation stimulated and regenerated pancreatic tissues, including Langerhans cells, regardless of disease stage (Ramdawon, 1999). They reported it that the transmembrane ATPase protein was significantly reduced in DM 2 patients due to  $\text{Na}^+ / \text{K}^+ \text{-ATPase}$ ,  $\text{Ca}^{2+}$ ,  $\text{Mg}^{2+} \text{-ATPase}$  (Tiedan, 1992) activated laser irradiation. It has to be suggested that these observational junctions (Ramdawon, 1999; Tiedan, 1992) related to the photo-intravascular system could condition a new therapy for the control of cellular glycemic levels. This radiation emitted by the Low Power Lasers (LBP) has demonstrated regenerative, 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 tissues (Barros et al., 2008; Catão, 2004). And this intravascular laser irradiation would cause regulation of the hemodynamic system in the blood as well as a control over the physiological lysis of leukocytes (Heine, 2007). This intravenous irradiation is a therapeutic biological method that seems adequate to intervene in this hematological system, which would condition the functional connection between the capillaries (the “final flow”), extra-cellular matrix (ECM) and cells. This ECM is located between the capillaries and the cells, and represents a type of molecular filter in which the fibers of the vegetative nerve have their final propagation, establishing a

connection with the nervous and endocrine system (hypothalamus). This molecular selective process facilitates the metabolic changes of the capillaries between cells, especially proteoglycans, glucosaminoglycans, structural proteins such as collagen, elastin and network glycoproteins, such as fibronectin.

There are several defensive cells in ECM that control the synthesis and decomposition of ECM components through a network of cytokines, which during aging and chronic oxidative stress increase the production of free radicals, acidosis and ECM obstruction that increases volume due to the filter function (sieve). Approximately 1.2 million leukocytes from all 1-2 billion leukocytes in the body are disintegrated every second. By this mechanism, a large number of mediators such as cytokines, chemokines, prostaglandins, leukotriens and many others are released into our body. These immunomodulators may intervene in the regulation of blood plasma and extra-cellular matrix (ECM) changes. The studies (Heine, 2007) consider that this physiological lysis of leukocytes would be the central problem of all treatments and measures of medicine of regulation, studies materialized by the doctrine “Lehrbuch der biologischen Medizin” (2007). Analogously, pancreatic islets (or islets of Langerhans) are special group of pancreas cells that produce insulin (by beta cells) and glucagon (by alpha cells) that regulate blood glucose in the human body. Recent studies (Darren, 2017) have shown that light irradiation has improved islet function in rats using red light photobiomodulation (630 nm) or infrared light (810 nm) to significantly increase insulin secretion following glycemic testing (Irani et al., 2009; De Meulenaer et al., 2009). These data (Figure 1) suggest a real possibility of light therapy to aid in type 2 diabetes (DM 2). Tests performed with 70% with type 2 diabetic patients submitted to ILIB, with a baseline mean glucose level ranging from 190 mg / dl to 259 mg / dl, showed a significant decrease in glucose level (mean difference

**Table 1.** Clinical conduct.

Cronology	HbA <sub>1c</sub> ** (mg/dl)	Capillary Glycemia <sup>1</sup> (mg/dl)	hyperglycemia	Capillary Glycemia <sup>2</sup> (mg/dl)	Variation* (mg/dl)
30/11/2017	164	178	+	145	19
25/01/2018	149	147	+	123	26
08/03/2018	148	147	+	116	31
29/05/2018	126	141	+	47	94

**Variation\*:** There were always in the quarterly periods a variation of the capillary glycemia measured in the pre and post consultation.

**HbA<sub>1c</sub>\*\*:** The mean measured by glycated hemoglobin presented greater control of plasma glycemic indexes.

**Capillary glycemia<sup>1</sup>:** Measurement performed fasting without the use of medication prior to laser therapy.

**Capillary glycemia<sup>2</sup>:** Measurement performed after laser therapy.

\*During photobiomodulatory therapy the patient did not use metformine.

\*Therapy was performed 15/15 days and final results were collected at the end of 6 months.

= 14,445, 95% CI: -1.12 to 30.03,  $p = 0.007$ ; Table below). Comparing previous laser therapy, the aggregate estimate showed a significant decrease in glucose level.

## CASE REPORT

A 66-year-old female patient, MSMSB, diagnosed with invasive right breast carcinoma in the year 2003, underwent tumorectomy and axillary emptying in the same year, followed up with therapy, followed by chemotherapy (CT) - 2 CMF cycles (cyclophosphamide, methotrexate and 5-fluoracil), radio and anastrozole. In 2014, another primary CA in the left breast and submitted to the same protocol with the exception of CTX; but maintained at HT with Letrozole, Calcium and Vit D. Patient with type 2 diabetes and regular use of metformine 500 mg twice daily. In November, 2017, already during the period of hormone therapy was submitted to the Dentistry Service of the Hospital de Cancer for diagnosis and presenting residual symptoms from oncological therapies. In the initial consultation, the use of a superior removable prosthesis and lower teeth under normal conditions, halitosis, hypogeusia related to salt/sweet flavors, PA 13: 8, reported nonspecific discomfort in daily tasks, capillary glycemia 165mg / dl, glycated Hb 167mg / dl and psoriasis. A protocol was promoted by commercial EC laser, DMC brand, useful red / infrared laser emitter power: 100 mW  $\pm$  20%, red laser wavelength 660 nm  $\pm$  10 nm, photobiomodulator effect, and use of the I / Ilib phototherapy function (Intravascular Laser Irradiation of Blood) in the radial artery of the wrist (Makela, 2005).

## Clinical conduct

- i) Before each session, the patient's initial blood pressure was evaluated;
- ii) Hygiene of the oral cavity with chlorhexidine 0.12% by digital friction, using the sterile gauze;
- iii) Measurement of initial capillary glycemia;
- (iv) Application of the Low-Density Laser (LDL) EC laser, DMC brand, useful red emitter laser power: 100 mW  $\pm$  20%, red laser wavelength 660 nm  $\pm$  10 nm, 1joule (10 seconds) -

- red 10 seconds at (parotid, sublingual and submandibular) salivary glands, and in the lingual region (lateral border 9 points 1 joule / point and 2 joules on the back);
- v) 15-minute complementary photoenteral therapy (Ilib) in the radial artery of the wrist;
- vi) Final blood pressure measurement;
- vii) Measurement of final capillary glycemia.

See Table 1 for details

## DISCUSSION

The result of this meta-analysis suggests that the therapy used influenced the decrease of blood glucose level in type 2 diabetic patients on time. It is suggested that laser irradiation could have an effect on arginine and increase the production of nitric oxide (Makela, 2005). Arginine affects the release of hormones such as glucagon, insulin, prolactin, adrenal catecholamines and growth hormone. This decreases tissue hypoxia, stimulates oxygenation and normalizes tissue metabolism (Brill et al., 2003). This study indicate that in advanced stages phototherapy could restore pancreatic function and normalize blood glucose levels, as a consequence, stimulate and regenerate pancreatic tissues, including Langerhans beta cells (Ramdawn, 1999). That is, the importance of Low Intensity Laser (LBI) for the patient's global recovery in several health specialties is a pleasing methodological reality; and the organic responses are considered beneficial (Pacheco and Bezinelli, 2018) in a variety of different modalities, due to its photobiomodulatory effect, besides emphasizing that it has preponderant connections to neuronal repair and in neurogenesis, not excepting in the formation of new brain cells, but also in the synaptogenesis, which is the formation of new connections between existing brain cells. 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 (Posten et al., 2005; Kreisler et al., 2003). In addition to the Intravascular Laser Irradiation of Blood function, it triggers an antioxidant system composed of enzymes, the main metallo-enzyme

superoxide dismutase, or SOD ZnCu, is the major antioxidant agent in the human body (Bellou et al., 2016). However, evidence confirms that the enzymes catalase, peroxidase and ceruloplasmin also absorb the red laser which potentiates other enzymes, which obviously further maximizes the antioxidant property of these enzymes when irradiated in the ILIB process (Bellou et al., 2016).

## Conclusion

Throughout the process of this case study, multidisciplinary parameters were established so that the physical responses could correspond to the recovery of the general well-being of the patient. Parallel to the glycemic measurements there was also a significant reduction of the signs and symptoms initially reported that allowed an organic balance of great relevance in the recovery of self-esteem. It is necessary to maintain the lucidity about this study, even though it is known that in this period the bioelectrical and bioenergetic functions favored the mitochondrial respiratory chain with positive responses to the capillary and plasma glycemic indices. However, a new perspective of non-invasive therapy and longevity to be explored opens.

## Conflict of interest

The author has not declared any conflict of interest

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