Review Article

iMedPub Journals
http://www.imedpub.com

Medical & Clinical Reviews
ISSN 2471-299X

2015
Vol. 1 No. 1:7

The Hypoglycemic Effect of Intravenous Laser Therapy in Diabetic Mellitus Type 2 Patients; A Systematic Review and Meta-analyses

Kazemikhoo N[1, 2], Ansari F[2] and Nilforoushzadeh[2]

1 1Skin Diseases and Leshmaniasis Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
2 Skin and Stem Cell Research Center, Tehran University of Medical Sciences, Tehran, Iran

Corresponding author:
Ansari F

Skin and Stem Cell Research Center, Tehran University of Medical Sciences, Tehran, Iran.

fereshtehansari66@gmail.com

Tel: +98-21-61117000

Abstract

Objectives: Intravenous Laser Blood Irradiaton (ILBI) is applied in some countries for the treatment of diferent diseases including diabetes mellitus. But there is not any systematc review available in this feld. The aim of this study is to review the artcles on the efects of ILIB in diabetc type 2 patents systematcally.

Material and Methods: PubMed, SciELO, Science Direct and Google Scholar databases were searched for primary artcles: The literature search was restricted to studies published in English and from the unrestricted past tll April 2015. The keywords used were "Intravascular laser", "Intravenous laser", "low level laser", "low intensity laser", "phototherapy", "cold laser" combined with "fastng blood glucose", "blood sugar" and "blood glucose".

Results: Seven potentally suitable artcles were found and among them four artcles met all inclusion criteria. All these 4 artcles were included in the fnal meta-analysis. Comparing before and afer laser therapy, showed a signifcant decrease in glucose level (mean diference =14.445, 95% CI: −1.12 to 30.031 P=0.007). There was not any signifcant heterogeneity between trials (P=0.158, I2=42.3%).

Conclusion: ILIB is a safe and efectve therapeutc modality for decreasing blood sugar level in diabetc type 2 patent.

Keywords: Intravenous laser; FBG; Systematc review

Received: September 28, 2015, **Accepted:** November 10, 2015, **Published:** November 13, 2015

Introduction

During past 40 years, Low-level Laser Therapy (LLLT) has been broadly used in medical felds. Recently, there has been an increase in the clinical applicatons of low-level laser irradiaton in various therapeutc felds. One of the most important functonal aspects of laser therapy is photobiostmulatory efects of low-level lasers on various biological systems that is based on the efects of low intensity lasers, ofen described as lasers with less than 500 mW average power [1-4]. One of the Methods for irradiaton of laser is Intravenous or (ILBI) with red, UV, and blue light, which is widely applied in the treatment of diferent pathologies. Blood irradiaton therapy can be administered through a catheter in a vein, usually a vein in the forearm [5]. The medical efects are mainly systemic healing mechanisms including analgesic, biostmulatve, immunocorrectve, antbacterial, ant-allergic, anttoxic, vasodilatve, antarrhythmic, anthy-poxic, spasmolytc, ant-infammatory, and other propertes [6]. It expands the arterio-venous oxygen diference that afrms the liquidaton of a tssue hypoxia and enrichment of oxygenaton which is a sign of tssue metabolism normalizaton and improves oxidaton of energy-carrying molecules like glucose, pyruvate, and other substances. Laser irradiaton actvates ATP synthesis and energy formaton in cells [5]. ILIB reduces glucose, cholesterol, low-density, and very low density lipoproteins (VLDL) and alleviates immune and hormonal system status. As ILBI has systematc efects, it can be a proper therapeutc modality in complex diseases like diabetes mellitus. Diabetes is a pathological metabolic state caused by

insufficient transport and breakdown of glucose. It reveals low serum insulin to glucagon ratio and high levels of fatty acids. The liver produces glucose while other tissues use ketones and fatty acids instead of glucose [7].

As there is not any systematic review available in the field of the effects of ILIB in diabetic type 2 patients, we designed this study to review these articles systematically.

Materials and Methods

The following databases were searched for primary articles: PubMed, SciELO, Science Direct and Google Scholar. The literature search was restricted to studies published in English and from the unrestricted past till April 2015. The keywords used were "Intravascular laser", "Intravenous laser", "low level laser", "low intensity laser", "phototherapy", "cold laser" combined with "fasting blood glucose", "blood sugar" and "blood glucose".

Studies were eligible for inclusion if they fulfilled the following criteria: (i) enrolled participants diagnosed with type 2 diabetes; (ii) Intra venous laser irradiation was applied; (iii) The blood sugar of patients before and after laser irradiation has been measured.

Studies were excluded if they (i) included participants diagnosed with pre-diabetes, gestational diabetes, or type 1 diabetes; (ii) reported only categorical data of outcomes; or were posters or just abstracts. Studies that gave insufficient information regarding the laser interventions were also excluded if the related information could not be obtained from the corresponding authors.

Initial screen was based on titles or abstracts of retrieved publications; if they provided inadequate information with regard to inclusion or exclusion criteria, full-text articles were retrieved and evaluated. For each study, data regarding study sources (including author and publication year), characteristics of study population (including sample size, baseline mean age, sex [proportion of females] and duration of diabetes), characteristics of laser therapy (including frequency, intensity and wave length of laser applied), mean and standard deviation or standard error of mean of fasting blood sugar (FBS) before and after laser therapy and adherence and dropout rates, were extracted.

Two authors performed the literature selection, data collection, and quality assessment of studies.

In Kazemikhoo's [8] study, 2015 the results of blue and red laser irradiation and all the repettons have been combined. The Change from baseline after laser irradiation was entered in the meta-analysis and SD of mean difference was calculated using SD of glucose level before and after laser therapy and r equals 0.93.

$$r = \frac{SD_B^2 + SD_A^2 - SD_C^2}{2 \times SD_B \times SD_A}$$

r=Pearson correlation coefficient.

SD_B=Standard deviation of glucose level before laser therapy.

SD_B= Standard deviation of glucose level after laser therapy.

SD_C= Standard deviation of glucose level changes.

The heterogeneity among studies was assessed using Q test, with a P value of <10 being considered of statistical significance.

Publication bias in the meta-analyses was detected and assessed by the Begg's test and Egger's test. Statistical analyses were performed using STATA Software (Version 12.0, College Station, Texas, USA).

Results

The initial search identified 7 potentially suitable articles and among them 4 articles met all inclusion criteria. All these 4 articles were included in the final meta-analysis.

The detailed characteristics of these trials are summarized in **Table 1**. Of these 4 trials, a total of 70 participants were included, with sample sizes ranging from 9 to 27 in individual trials.

All the participants were diabetic type 2 with the base line mean glucose level ranging from 190 mg/dl to 259 mg/dl.

Table 1 Characteristics of included trials.

Source	Number of subjects	Mean age (Years)	Sex(%male)	Intervention	Blood sugar before mg/dl (Mean ± SD)	Blood sugar after mg/dl (Mean ± SD)
R. Chen, 2000 (Chen, Chen, Xie, Chen, & Zhang, 2000)	10	67.3	93.3	He-Ne laser extravacular irradiation therapy instrument, , O—4Omw, 632.8nm, 60 min	197.1±73.8	106.2±540
T.V. Kovalyova, 2002 (Kovalyava, 2002)	27	57.3	13	ILBI intravenously 2 mW,I =0,63 mm 405-nm 15-30 min	259.74±15.48	255.78±15.3
N. KazemiKhoo, 2013 (N Kazemi Khoo et al., 2013)	9	60.63	55	ILBI intravenously 1.5 mW, continuous, 405-nm 30 min	190±17	165±20
N. KazemiKhoo, 2015 (KazemiKhoo & Ansari, 2015)	24	37	63.7	ILBI 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

Compared with the before laser therapy, the pooled estmate showed a signifcant decrease in glucose level (Mean difference =14.445, 95% CI: −1.12 to 30.03, p=0.007; **Figure 1**). There was not any signifcant heterogeneity between trials (P=0.158, I2=42.3%).

There was no signifcant publicaton bias as evidenced by the Begg's test and Egger's test (all P>05).

Discussion

The result of this meta-analysis suggests that Intravenous laser therapy decreases blood glucose level in diabetc type 2 patents signifcantly. Immediately afer ILIB blood glucose decreases 14 mgr/dlit. It seems that laser irradiaton may have an efect on arginine and increase nitric oxide (NO) producton. Arginine afects on the release of hormone like glucagon, insulin, prolactn, adrenal catecholamins and growth hormone [9]. It decreases tssue hypoxia, stmulates oxygenation and normalizes tissue metabolism [10]. Ramadawon concluded that even in advanced cases of diabetes mellitus, laser therapy could restore the pancreas functon and normalize the blood glucose level. They concluded that laser irradiaton could stmulate and regenerate pancreatc tssues, including the Langerhans β-cells, even in advanced disease states [11].Tiedan et al reported that ATPase was signifcantly lower in diabetc patents than that in control subjects, and laser irradiaton signifcantly actvated Na^+/K^+-ATPase, Ca^{2+},Mg^{2+}-ATPase. They suggested that intravascular laser might be a new complex therapeutcs for diabetes [12].

However, it shows inadequate evidence regarding the efects of other factors related to health of diabetc people. Numerous studies showed the positve efect of laser therapy on diabetc complicatons [13-17]. Our previous studies showed that laser irradiaton may be efectve in neuropathy and wound healing in these patents [18-20].It could be recommended to include these factors for future systematc reviews.

Since results from this meta-regression fnd intravenous laser therapy as an efectve way to decrease blood sugar level in diabetc patents it could be suggested to prescribe this kind of therapy for patents with type 2 diabetes along with other classic methods such as diet, weight control, medicatons and exercise to gain benefts on glycemic control [21,22].

To the tme being, this is the frst analysis that systematcally assesses the hypoglycemic efect of intravenous laser therapy, in patents with type 2 diabetes. This study analyses the quantty of therapeutc efects of this method including Mean, SD and SE. We included trials with before-afer study designs. Even though it is difcult to assess causal associaton in this kind of trials, they are the most feasible way to measure medical interventon efects. Due to small numbers of trials in this feld it was the only way to include more trials and to improve external validity of the meta-analysis.

It is recommended that future RCTs with proper control groups and appropriate descripton of adequate informaton should be conducted. Despite no signifcant publicaton bias was detected by the Begg's test and Egger's test, the risk of publicaton bias stll cannot be fully ruled out due to the language restricton to English, the selecton of only published papers, as well as the potentally underpowered statstcal tests.

In conclusion, the meta-analysis shows that Intravenous laser therapy is associated with a decreased blood sugar level among

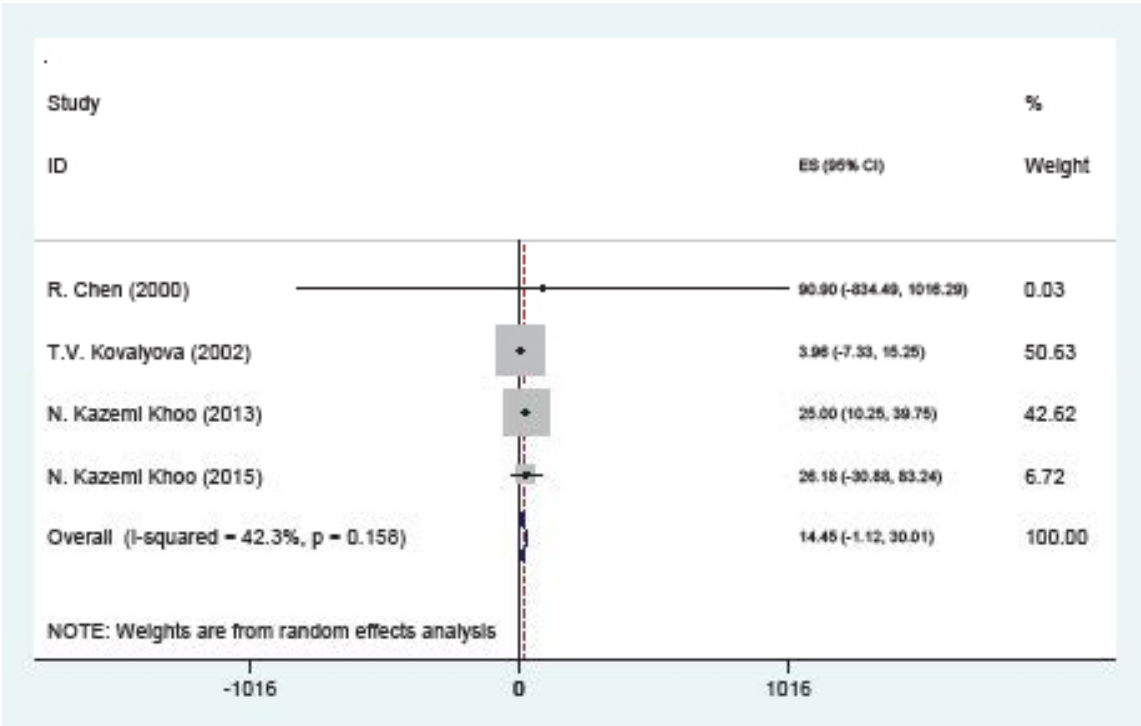

Figure 1 Forest plot of trials examining LLLT efects on glucose level in type 2 diabetes patents. ES, mean difference; CI, confdence interval Summary estmates were analyzed with a random-efects model.

patents with type 2 diabetes. As the selected studies evaluate the effects of intravenous laser for a short period of time, it seems more studies are needed to assess the long term effects. Future RCTs with head-to-head designs comparing intravenous laser therapy versus hyperglycemia control drugs, and with extended length of interventions (6 months) and with assessing more health related outcomes, are required to strengthen the findings in this meta-analysis.

Acknowledgements

We dedicate here our acknowledgments to Dr.Mohammadreza Rahbar for English Editon of the manuscript.

References

1 Grossman N, Schneid N, Reuveni H, Halevy S, Lubart R (1998) 780 nm low power diode laser irradiaton stmulates proliferaton of keratnocyte cultures: involvement of reactve oxygen species, Lasers in surgery and medicine 22: 212-218.

2 Lubart R, Wollman Y, Friedmann H, Rochkind S, Laulicht I (1992) Efects of visible and near-infrared lasers on cell cultures. J Photochem Photobiol B 12: 305-310.

3 Passarella S, Casamassima E, Molinari S, Pastore D, Quagliariello E, et al. (1984) Increase of proton electrochemical potental and ATP synthesis in rat liver mitochondria irradiated in vitro by helium-neon laser. FEBS leters 175: 95-99.

4 Yu W, Naim J, Lanzafame R (1994) The efects of photo-irradiaton on the secreton of TGF and PDGF from fbroblasts in vitro. Lasers Surg Med Suppl 6.

5 Gasparyan L (2003) Laser Irradiaton of the blood. Laser Partner-Clinixperience 1-4.

6 Moshkovska T, Mayberry J (2005) It is tme to test low level laser therapy in Great Britain. Postgrad Med J 81: 436-441.

7 Makela A (2004) Theoretcal backgrounds for light applicaton in diabetes, Laser, Florence.

8 KazemiKhoo N, Ansari F (2015) Blue or red: which intravascular laser light has more efects in diabetc patents? Lasers Med Sci 30: 363-366.

9 Makela A (2005) Role of L-arginine in the biological efects of blue light [5968-06]. Proceedings-Spie The Internatonal Society For Optcal Engineering.

10 Brill G, Gasparyan L, Makela A (2003) Modifcaton in relatonships in the system endothelial cell-blood platelet by low level laser radiaton. Laser Florence meetng.

11 Ramdawon P (1999) Bioresonance informaton laser therapy of diabetes mellituse a frst clinical experience of the hypoglycemic efect of low level laser terapy and its perspectves, Paper presented at the North American Laser Therapy Associaton Conference.

12 Tiedan W (1992) Efects of low-energy He-Ne laser irradiaton of extracorporeally circulatory blood on ATPase actvites of erythrocyte membrane in patents with IDDM [J]. Laser Journal 6: 011.

13 Chung H, Dai T, Sharma SK, Huang YY, Carroll JD, et al. (2012) The nuts and bolts of low-level laser (light) therapy. Ann Biomed Eng 40: 516-533.

14 Hawkins D, Houreld N, Abrahamse H (2005) Low level laser therapy (LLLT) as an efectve therapeutc modality for delayed wound healing. Ann N Y Acad Sci 1056: 486-493.

15 Maiya GA, Kumar P, Rao L (2005) Efect of low intensity helium-neon (He-Ne) laser irradiaton on diabetc wound healing dynamics. Photomed Laser Surg 23: 187-190.

16 Schindl A, Schindl M, Schön H, Knobler R, Havelec L, et al. (1998) Low-intensity laser irradiaton improves skin circulaton in patents with diabetc microangiopathy. Diabetes Care 21: 580-584.

17 Zinman LH, Ngo M, Ng ET, Nwe KT, Gogov S, et al. (2004) Low-intensity laser therapy for painful symptoms of diabetc sensorimotor polyneuropathy: a controlled trial. Diabetes Care 27: 921-924.

18 Kazemi-Khoo N (2006) Successful treatment of diabetc foot ulcers with low-level laser therapy. The Foot 16: 184-187.

19 Khamseh ME, Kazemikho N, Aghili R, Forough B, Lajevardi M, et al. (2011) Diabetc distal symmetric polyneuropathy: efect of low-intensity laser therapy. Lasers Med Sci 26: 831-835.

20 Kazemi-Khoo N, Shokrgozar MA, Kashani IR, Amanzadeh A, Mostafavi E, et al. (2014) In vitro therapeutc efects of low level laser at mRNA level on the release of skin growth factors from fbroblasts in diabetc mice. Avicenna journal of medical biotechnology 6: 113.

21 DeFronzo RA, Ratner RE, Han J, Kim DD, Fineman MS, et al. (2005) Efects of exenatde (exendin-4) on glycemic control and weight over 30 weeks in metformin-treated patents with type 2 diabetes. Diabetes Care 28: 1092-1100.

22 Turner RC, Cull CA, Frighi V, Holman RR (1999) Glycemic control with diet, sulfonylurea, metformin, or insulin in patents with type 2 diabetes mellitus: progressive requirement for multple therapies (UKPDS 49). UK Prospectve Diabetes Study (UKPDS) Group. JAMA 281: 2005-2012.