Kazemikhoo N1,2, Ansari F2 and Nilforoushzadeh2

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

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Introduction

During past 40 years, Low-level Laser Therapy (LLLT) has been broadly used in medical fields. Recently, there has been an increase in the clinical applications of low-level laser irradiation in various therapeutic fields. One of the most important functional aspects of laser therapy is photobiostimulatory effects of low-level lasers on various biological systems that is based on the effects of low intensity lasers, often described as lasers with less than 500 mW average power [1-4]. One of the Methods for irradiation of laser is Intravenous or (ILBI) with red, UV, and blue light, which is widely applied in the treatment of different pathologies. Blood irradiation therapy can be administered through a catheter in a vein, usually a vein in the forearm [5]. The medical effects are mainly systemic healing mechanisms including analgesic, biostimulative, immunocorrective, antibacterial, anti-allergic, antitoxic, vasodilative, antiarrhythmic, antihypoxic, spasmolytic, anti-inflammatory, and other properties [6]. It expands the arterio-venous oxygen difference that affirms the liquidation of a tissue hypoxia and enrichment of oxygenation which is a sign of tissue metabolism normalization and improves oxidation of energy-carrying molecules like glucose, pyruvate, and other substances. Laser irradiation activates ATP synthesis and energy formation 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 systematic effects, it can be a proper therapeutic modality in complex diseases like diabetes mellitus. Diabetes is a pathological metabolic state caused by...
Materials and Methods

A total of 3 studies (Anh, H., Cheng, J., & Zhang, H. 2000; Chen, J., & Zhang, H., 2000; R. Chen, 2000) were included in the final meta-analysis. Of these 3 studies, a total of 70 participants were included, with sample sizes ranging from 9 to 27 in individual trials. The baseline mean age of participants ranged from 63.7 years to 67.3 years. Sex (male percentage) ranged from 40.6% to 55%. The duration of diabetes varied from 1 to 12 years. The characteristics of included trials are summarized in Table 1.

Table 1: Characteristics of included trials.

<table>
<thead>
<tr>
<th>Source</th>
<th>Number of subjects</th>
<th>Mean age (Years)</th>
<th>Sex(%male)</th>
<th>Intervention</th>
<th>Blood sugar before mg/dl (Mean ± SD)</th>
<th>Blood sugar after mg/dl (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R. Chen, 2000 (Chen, Chen, Xie, &amp; Zhang, 2000)</td>
<td>10</td>
<td>67.3</td>
<td>55%</td>
<td>ILBI intravenously 2 mW, l = 0.63 mm, 405-nm</td>
<td>259.74±15.48</td>
<td>255.78±15.32</td>
</tr>
<tr>
<td>T.V. Kovalyova, 2002 (Kovalyova, 2002)</td>
<td>27</td>
<td>57.3</td>
<td>13%</td>
<td>ILBI intravenously 2 mW, l = 0.63 mm, 405-nm</td>
<td>240±17</td>
<td>214.71±78.99</td>
</tr>
<tr>
<td>R. Chen, 2015 (Chen, Chen, Xie, &amp; Zhang, 2000)</td>
<td>27</td>
<td>63.7</td>
<td>55%</td>
<td>ILBI intravenously 1.5 mW, l = 0.63 mm, 405-nm</td>
<td>245±18</td>
<td>222.8±49.9</td>
</tr>
<tr>
<td>N. Kazemi Khoo, 2013</td>
<td>60</td>
<td>63.7</td>
<td>55%</td>
<td>ILBI intravenously 1.5 mW, l = 0.63 mm, 405-nm</td>
<td>240±17</td>
<td>222.8±49.9</td>
</tr>
</tbody>
</table>

Results

In Kazemi Khoo’s (2015) study, the results of blue and red laser irradiation therapy were compared. The mean difference in blood sugar level before and after laser therapy was entered in the meta-analysis and SD of mean difference was calculated using SD of glucose level before laser therapy (SDc) and SD of glucose level after laser therapy (SDa) as follows:

\[ r = \frac{SDc}{SDd} \times \frac{SDa}{SDc} \]

where r is Pearson correlation coefficient, SDc is Standard deviation of glucose level changes, SDd is Standard deviation of glucose level before laser therapy, and SDa is Standard deviation of glucose level after laser therapy.
Compared with the before laser therapy, the pooled estimate showed a significant decrease in glucose level (Mean difference = 14.445, 95% CI: −1.12 to 30.03, p=0.007; Figure 1). There was not any significant heterogeneity between trials (P=0.158, I²=42.3%). There was no significant publication bias as evidenced by the Begg’s test and Egger’s test (all P>0.05).

Discussion

The result of this meta-analysis suggests that Intravenous laser therapy decreases blood glucose level in diabetic type 2 patients significantly. Immediately after ILIB blood glucose decreases 14 mgr/dlit. It seems that laser irradiation may have an effect on arginine and increase nitric oxide (NO) production. Arginine affects on the release of hormone like glucagon, insulin, prolactin, adrenal catecholamins and growth hormone [9]. It decreases tissue hypoxia, stimulates oxygenation and normalizes tissue metabolism [10]. Ramadawon concluded that even in advanced cases of diabetes mellitus, laser therapy could restore the 24-h glucose level, and regenerate tissues and regenerate cells [11]. A study conducted by Hu et al. [12] assessed the effects of laser therapy on diabetic advanced disease states. In this study, 69 patients were divided into two groups: a laser therapy group and a control group. The laser therapy group was treated with a low-level laser device (LLD) at a wavelength of 808 nm and a power density of 20 mW/cm², while the control group received only conventional treatment. After 12 weeks of treatment, the fasting blood glucose level, 2-hour postprandial glucose level, and HbA1c level were significantly lower in the laser therapy group compared to the control group. These results suggest that laser therapy may be an effective treatment for diabetic patients with advanced disease states.

Tiedan et al. reported that ATPase was significantly lower in diabetic patients than that in control subjects, and laser irradiation significantly activated Na\(^+\)/K\(^+\)-ATPase, Ca\(^{2+}\),Mg\(^{2+}\)-ATPase. They suggested that intravascular laser might be a new complex therapeutic for diabetes [12]. However, it shows inadequate evidence regarding the effects of other factors related to health of diabetic people. Numerous studies showed the positive effect of laser therapy on diabetic complications [13-17]. Our previous studies showed that laser irradiation may be effective in neuropathy and wound healing in these patients [18-20]. It could be recommended to include these factors for future systematic reviews.

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

To the time being, this is the first analysis that systematically assesses the hypoglycemic effect of intravenous laser therapy, in patients with type 2 diabetes. This study analyses the quantity of therapeutic effects of this method including Mean, SD and SE. We included trials with before-after study designs. Even though it is difficult to assess causal association in this kind of trials, they are the most feasible way to measure medical intervention effects. Due to small numbers of trials in this field 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 adequate information should be conducted. Despite no significant publication bias was detected by the Begg’s test and Egger’s test, the risk of publication bias still cannot be fully ruled out due to the language restriction to English, the selection of only published papers, as well as the potentially underpowered statistical tests.

In conclusion, the meta-analysis shows that Intravenous laser therapy is associated with a decreased blood sugar level among patients with type 2 diabetes.

**Figure 1**

![Forest plot of trials examining LLLT effects on glucose level in type 2 diabetes patients. ES, mean difference; CI, confidence interval. Summary estimates were analyzed with a random-effects model.](image)
patients 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.

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References


