

# Treatment of Cutaneous Leishmaniasis with Intense Pulsed Light: Is it Effective?

Amirhossein Siadat, Hamid Galehdari, Zabiholah Shahmoradi, Fariba Iraj, Azadeh Zolfaghari, Nazli Ansari

Department of Dermatology, Skin Diseases and Leishmaniasis Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

## Abstract

**Background:** Cutaneous leishmaniasis (CL) is a common parasitic disorder that is endemic in many countries. There is no completely effective treatment for this condition, but pentavalent antimony compounds are regarded as the main treatment. Different laser types have been used for treatment of CL with variable success but to our best knowledge, there is no published paper regarding use of intense pulsed light (IPL) for treatment of CL.

**Materials and Methods:** In this randomized, single-blind clinical trial study, we compared the efficacy of intralesional glucantime alone versus intralesional glucantime plus weekly IPL for treatment of 54 patients with confirmed cutaneous leishmaniasis for a maximum of eight weeks as a randomized, clinical trial.

**Results:** Although it was not statistically significant, combination treatment was more effective than intralesional glucantime alone ( $P > 0.05$ ). However, the velocity of healing was significantly higher in the IPL plus intralesional glucantime alone versus glucantime alone. No side effect was observed in both groups.

**Discussion:** To better evaluate the efficacy of IPL, more studies with a higher number of patients and using various IPL filters are recommended.

**Keywords:** IPL, leishmaniasis, treatment

**Address for correspondence:** Dr. Hamid Galehdari, Department of Dermatology, Skin Diseases and Leishmaniasis Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.

E-mail: drgalehdari@gmail.com

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## INTRODUCTION

Cutaneous leishmaniasis (CL) is a common parasitic disorder that is endemic in 98 countries,<sup>[1]</sup> with 90% of cases are reported from Afghanistan, Iran, Brazil, Saudi Arabia, and Syria.<sup>[2]</sup> The majority of cases in Iran are due to *L. Tropica* and *L. Major*.<sup>[3]</sup> The cutaneous lesion initially presents with a papule at the site of insect bite that gradually grows to nodule or plaque and may become ulcerated with a surrounding violaceous color.<sup>[4,5]</sup> The CL lesion usually persists for 6 to 12 months and heals with unsightly scar.<sup>[5]</sup>

Many treatment modalities have been utilized for therapy of CL lesions with variable success. These methods include

administration of different medications such as antimony compounds, sodium stibogluconate and azoles or physical methods such as cryotherapy, heat therapy, lasers, and radiofrequency.<sup>[6]</sup> Despite efforts to find more effective treatment, antimony compounds are still considered as the treatment of choice for CL lesions.<sup>[7]</sup> A recent study in Iran showed an efficacy of 55.63% of intralesional glucantime<sup>[7]</sup> for treatment of the CL, while another study showed complete healing of lesions in 41.7% and failure of response in 29.8% of the cases.

Intense pulsed light (IPL) has many applications in dermatology. This technology is a source of non-coherent light with a

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wavelength of 400-1200 nm. The IPL technology has been used in treatment of the various dermatological conditions such as hair removal, skin rejuvenation, acne and acne scars, rosacea, keratosis pilaris, and telangiectasia. Selective photothermolysis theory seems to be valid for IPL as the lasers.<sup>[8]</sup>

Previous studies have shown efficacy of lasers that were used to treat vascular lesions, such as pulsed dye laser (PDL) in treatment of CL.<sup>[9-11]</sup> IPL has been proved effective for manifold dermatological conditions when used in respective fluence, wavelength spectrum, and pulse duration. IPL has shown promise in treating nonvascular (such as melisma, acne vulgaris, and rosacea) and vascular (such as capillary, telangiectasia, and venous malformations, and infantile hemangioma) lesions with acceptable efficacy and safety.<sup>[12,13]</sup>

In a few cases, we observed promising results of the IPL alone in the treatment of resistant CL lesions (authors' personal observation). We also observed the efficacy of IPL on the live promastigotes *in vitro*. The present study was designed to better evaluate the efficacy of IPL in the treatment of CL.

## MATERIALS AND METHODS

This was a randomized, single-blind clinical trial that was performed in Isfahan University of Medical Sciences and Skin Diseases and Leishmaniasis Research Center clinics in 2018-2021 (Research no: IRCT20200825048515N14). The ethical committee clearance and informed consent was achieved.

Overall, 54 patients with confirmed CL lesions were selected using simple sampling method and were randomized to receive either intralesional glucantime alone or intralesional glucantime plus IPL.

Inclusion criteria were diagnosis of leishmaniasis was confirmed by direct smear, pathology, or culture, the maximum number of the lesions in each patient was less than 5, the lesion had been present for less than 100 days, the size of lesions were less than 3 cm, the lesion was not located on the face, the age of patient was more than 5-year-old and the lesion was not located on the joint or cartilage.

Pregnancy and lactation, sporotrichoid and satellite lesions, use of immunosuppressive treatment in the past six months and history of local or systemic anti-leishmaniasis treatment in the past 6 months were regarded as exclusion criteria.

Demographic characteristics of the patients including age and sex along with lesions characteristics including number of the lesions, type, location, induration, diameter, and surface area were collected. Any observed or reported side effect was also recorded.

Parasitological diagnosis was performed by direct smear and Giemsa staining and was performed at the start of treatment and end of week 8. Patients were followed three and six months after treatment for signs of recurrence and the resulting scar.

Photography was also obtained using Canon digital camera (8.3 megapixel, Lexus 6015) at the start, at the follow-up visits and at the end of study.

Lesions with roughly similar characteristics were selected and randomized to be treated with intralesional glucantime or intralesional glucantime plus IPL.

In the both groups, each of the CL lesions was infiltrated on a weekly basis with 1-2 cc of Glucantime (Sanofi Company) injection until complete blanching of the lesion and its 1 mm peripheri. This treatment was continued for complete healing of the lesion for a maximum of eight weeks.

In the combination treatment group, in addition to the intralesional glucantime, lesions were treated with IPL (Filter: 570 nm, power: 16 watt) 3 times a week for a total of 10 sessions at the intensity of 48 J/cm<sup>2</sup> for 30 seconds and then at the intensity of 9.6 J/cm<sup>2</sup> for 2 minutes.<sup>[4]</sup> SOLARI™ (Lutronic Corporation, Ilsan, Korea) system was used for IPL administration.

It should be noted that the duration of the laser depends on the diameter of the wound and a maximum of five shots, which lasted a maximum of 5 minutes. Also, to avoid measurement errors, the lesions and endurance were measured by the clinician of Skin Diseases and Leishmaniasis Center.

Patients were followed at 1 week intervals for up to 12 weeks after treatment initiation and were finally categorized according to their response to three different groups of complete healing, partial healing, and no healing.

Complete healing was defined as elimination of all inflammatory reactions (swelling or induration), scar formation, or complete re-epithelialization of the lesion. Partial healing was defined as reduction in the size or induration of the lesion and no healing as no significant change in the lesion size or worsening of the lesion.

At the end of week 8, patients were followed for four more weeks, and in the case of partial or no healing, patients were treated with alternative methods of treatment including systemic glucantime.

Finally, the collected data were entered into SPSS software (ver. 26). Data were represented as means ± standard deviation (SD) or n (%). At the level of inferential statistics, Chi-squared test was used to compare the frequency distribution of qualitative variables between the two groups. Moreover, an independent samples *t*-test was run to compare the mean of quantitative variables between the two groups. In addition, the repeated measures ANOVA was used to compare mean of lesions size in each of the two groups over time. The significance level of less than 0.05 was considered in all analyzes.

## RESULTS

Overall, 27 patients in the intralesional glucantime alone group and 27 patients in the glucantime plus IPL group were

evaluated. 22.2% of the patients in the glucantime alone group were male and 77.8% were female, whereas in the combination treatment group 33.3% were male and 66.7% were female. The mean of age were  $46.41 \pm 16.44$  and  $41.37 \pm 17.54$  in the glucantime alone group and glucantime plus IPL group, respectively [Table 1].

In the glucantime alone group, the mean of lesion size was  $8.52 \pm 4.14$  at the start of the study that significantly reduced to  $0.64 \pm 0.78$  at the end of treatment ( $P < 0.001$ ). In the glucantime plus IPL group, the mean of lesion size was  $8.30 \pm 6.73$  at the start of the study that significantly reduced to  $0.35 \pm 0.39$  at the end of treatment ( $P < 0.001$ ). At the start of the study, there was no significant difference regarding lesion size between the two groups ( $P = 0.885$ ). However, at the end of study, our results showed a significant difference between the size of induration of the lesions ( $P < 0.001$ ) [Table 2].

At the end of week 8, partial or complete improvement was seen in both groups and no one was left without improvement. In glucantime alone group 88.9% had complete healing and 11.1% partial healing and in glucantime plus IPL group 96.3%

had complete healing and 3.7% had partial healing. There was no significant difference between the two groups in the healing percentage ( $P = 0.299$ ). In fact, both groups were shown to improve significantly. But the velocity of complete response in glucantime plus IPL group was significantly higher than glucantime alone group. In glucantime plus IPL group, 12 patients had complete healing in the sixth week, 13 patients in the seventh week, and 1 patient in the eighth week, while in glucantime alone group in the sixth and seventh weeks, 4 and 8 patients had complete healing, respectively. And in the eighth week, 12 patients had complete healing. Therefore, it shows that the velocity of complete response in the glucantime plus IPL group was higher than the glucantime alone group ( $P < 0.001$ ) [Table 3].

## DISCUSSION

In the IPL technology, bandpass filters and flashlamps are used to emit polychromatic incoherent light with specific wavelength, fluence, and pulse duration. This will provide selective thermal damage of the target with results comparable to lasers. Appropriate selection of wavelength, fluence, pulse duration, and pulse intervals in the IPL devices would yield the capacity to treat many skin conditions. Different skin conditions, including but not limited to unwanted hair growth, vascular lesions, pigmented lesions, acne vulgaris, and aging skin, have IPL device been treated with IPL technology.<sup>[13]</sup> In fact, the ability to cutaneous leishmaniasis is the most common type of leishmaniasis caused by leishman body and transmitted by sandfly.<sup>[14]</sup> The common causes of CL are *L.tropica*, *L.major*, *L.aethiopica*, *L.braziliensis*, *L.amazonensis*, and *L.mexicana*.<sup>[15]</sup> Leishman bodies are sensitive to heat, makes them as a candidate for treatment with laser technology and heat therapy.

For the first time in 1981, Babajev KB used CO<sub>2</sub> laser in six patients with CL lesions with encouraging results.<sup>[16]</sup> Asilian *et al.* also used CO<sub>2</sub> laser in 123 Iranian patients with CL lesions with promising results.<sup>[17]</sup> Combination of CO<sub>2</sub> laser with other methods of treatment such as intralesional or systemic glucantime, topical TCA, and topical paromomycin have been

**Table 1: Demographic characteristics of the patients and lesions in the glucantime alone group and glucantime plus IPL group**

Characteristics	Glucantime group	Glucantime plus IPL group	P
Sex			
Male	6 (22.2%)	9 (33.3%)	0.362
Female	21 (77.8%)	18 (66.7%)	
Age; year	46.41±16.44	41.37±17.54	0.281
Count of wound			
1	19 (70.4%)	15 (55.6%)	0.078
2	8 (29.6%)	5 (18.5%)	
3	0 (0%)	4 (14.8%)	
4	0 (0%)	3 (11.1%)	
Place of wound			
Leg	5 (18.5%)	11 (40.7%)	0.115
Hand	18 (66.7%)	15 (55.6%)	
Finger	4 (14.8%)	1 (3.7%)	

**Table 2: Comparison of the lesions size in the two groups**

The lesion area	Glucantime group	Glucantime plus IPL group	P <sup>1</sup>
Before intervention	8.52±4.14	8.30±6.73	0.885
One week after the intervention	8.14±0.77	8.16±0.92	0.931
Two weeks after the intervention	7.62±0.80	7.64±1.03	0.936
Three weeks after the intervention	7.23±0.86	6.80±0.89	0.076
Four weeks after the intervention	6.80±0.85	6.45±0.86	0.138
Fifth weeks after the intervention	5.36±0.69	3.62±0.80	<0.001
Sixth weeks after the intervention	3.45±0.66	2.23±0.86	<0.001
Seventh weeks after the intervention	1.62±0.80	1.08±0.85	0.019
Eight weeks after the intervention	0.64±0.78	0.35±0.39	<0.001
P <sup>2</sup>	<0.001	<0.001	

<sup>1</sup>Significance level obtained from independent sample *t*-test comparing the mean between the two groups in each of the studied times. <sup>2</sup>Significance level obtained from repeated measure analysis after eight weeks of intervention in each of the two groups

**Table 3: Frequency distribution of lesion improvement in the two groups**

Improvement of lesion	Glucantime group	Glucantime plus IPL group	P
Complete improvement	24 (88.9%)	26 (96.3%)	0.299
Sixth/Seventh/Eighth weeks	4/8/12	12/13/1	
Partial improvement	3 (11.1%)	1 (3.7%)	
Non-improvement	0 (%)	0 (0%)	

described.<sup>[18,19]</sup> In another study, CO<sub>2</sub> laser with 50% local TCA in the treatment of cutaneous leishmaniasis was investigated and the results showed that the recovery time in combination treatment is shorter.<sup>[20]</sup> In the current study, to ensure that patients were not deprived from the standard treatment, both groups received intralesional glucantime.

CO<sub>2</sub> laser, in addition to heat, can provide tissue destruction which eliminates the environment leishman body residing in. The IPL technology that we used in the current study is not tissue destructive but, in our opinion, mostly works through heat generation and selective photothermolysis theory.

Several studies have reported IPL's promising efficacy in treating various skin disorders, especially vascular lesions, in some of which IPL presented as the treatment of choice.<sup>[12,13]</sup> However, no prior study has assessed IPL in treatment of CL lesions. On the other hand, pulsed dye laser (PDL), which is also an efficient laser therapy in treating of vascular lesions, has shown promising results in treatment of CL. Therefore, we hypothesized that IPL, which shares efficacy in treating vascular lesions with PDL, might be as well efficacious in treatment of CL. Although the exact mechanism of the effects of IPL and lasers on CL lesions is unknown, some factors have been stated as possible underlying mechanisms. Vascular nature of lesions and thermal effects of light on Leishman bodies in superficial dermis are thought to be involved. Thermal effects can potentially cause vascular injury and trigger immune responses that might eventually lead to inflammation and elimination of the parasites. However, the maximum penetration depth of vascular lasers is often less than the depth of CL lesions, and thus, thermal effects cannot be solely responsible for this processes.<sup>[21-23]</sup>

Argon laser, Erbium-Glass laser and long-pulsed ND-YAG laser have also been used for treatment of the CL with various success.<sup>[24,25]</sup> Except long-pulsed ND-YAG laser, all these methods are ablative and possibly associated with more side effects.

PDL laser, which is also non-ablative as IPL, has been successfully used recently by Radmanesh *et al.*<sup>[26]</sup> in 2-week intervals for 1-4 sessions. The scar of leishmaniasis in PDL group was slightly less than intralesional glucantime group. Heat generation, stimulation of inflammatory response and immunity along with cytokine change and vascular injury are some possible mechanisms of this treatment.<sup>[9,23]</sup> PDL technology is somehow similar to IPL as both of them are

non-ablative. The duration of treatments in this study and our study was similar (i.e., 8 weeks).

The results of our study showed that although it was not statistically significant, the efficacy of combination treatment with IPL plus intralesional glucantime higher than intralesional glucantime alone.

In addition, the velocity of response of CL lesion to treatment was significantly higher in the combination group versus glucantime alone group. As it is obvious, duration of CL lesions correlates with the size of ensuing scar and faster complete healing of the lesion is associated with smaller scar which is of the major cosmetic concern for the patient.

IPL may have some advantage over laser for treatment of CL. IPL devices are generally less expensive than laser devices and therefore more affordable. IPL devices are also need less maintenance care and cost and therefore seem to be used more practically in the distant areas that are usually foci of CL. In addition, the non-ablative nature of IPL seems to provide less side effect profile as compared with more invasive ablative lasers.

Few studies have evaluated the efficacy of IPL in the treatment of CL alongside conventional therapy (glucantime administration), which can be considered as a strength of our study. In the current study, we did not observe any side effect with use of IPL or IL glucantime. In addition, one of the major possible mechanisms of IPL for treatment of the CL lesions is heat production in the target tissue. It is therefore could be concluded that increasing the frequency of treatment may yield better response rate and this issue may be a good subject for the future studies.

In addition, the type of filter that was used in this study was determined by personal observation of the authors in a few cases of CL lesions who were resistant to all conventional treatment. Performing more studies using different filters to determine the best filter for this objective seems necessary. On the other hand, assessing the efficacy of IPL alone and without any parallel treatment could be a possible subject for the further studies. We did not use IPL for lesions very close to the eye region and face to avoid any possible complication of irradiation. It could be a possible minor drawback to use of this technology for treatment of CL.

## CONCLUSION

Use of IPL might be effective for treatment of the CL. More studies are recommended to better determine the optimum parameters and to evaluate the efficacy of this treatment for cutaneous leishmaniasis.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients

understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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