Comparison between efficacy of CO\(_2\) laser alone versus combination of cryotherapy and intralesional meglumine antimoniate in the treatment of cutaneous Leishmaniasis

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Abstract

Objective To determine the efficacy of CO\(_2\) laser therapy in comparison to combined cryotherapy and intralesional meglumine antimoniate therapy in the treatment of cutaneous Leishmaniasis.

Study Design Randomized controlled trial.

Place and duration of Study Department of dermatology CMH Peshawar from April 2016 to April 2017.

Methodology 136 patients between ages of 15 to 60 years with clinically diagnosed cutaneous Leishmaniasis, positive LT bodies in a skin smear or histopathology were included in the study. Patients with symptoms of 1-3 months’ duration were enrolled and two groups were formed. One treated with CO\(_2\) laser and retreated after 04 weeks if required. The second group was treated both with cryotherapy and intralesional meglumine antimoniate injection biweekly for 8 weeks. Clinical assessment for cure was done at 8\(^{th}\) week for both groups. Chi-square test was used to compare the efficacy in both the groups.

Results Mean age in group A was 28.5±4.9 years while in group B it was 29.5±4.8 years. The overall efficacy after 08 weeks in group A patients who had clinical cure was 79.4 % while it was 73.5% in group B.

Conclusion CO\(_2\) laser therapy in the treatment of cutaneous Leishmaniasis was found reliable and cost effective in comparison to combined cryotherapy and intralesional meglumine antimoniate therapy with benefit of less procedure work on patients.

Key words CO\(_2\) fractional laser, cutaneous Leishmaniasis, cryotherapy, intralesional meglumine antimoniate.

Introduction

Cutaneous Leishmaniasis (CL) is a common parasitic infection affecting humans, transmitted by the bite of an infected female sandfly. The overall incidence of CL have increased from 1.1 to 1.2 million cases per year from 2002–2009.\(^1\) Cutaneous Leishmaniasis is also a rising epidemic in Pakistan.\(^2\) The prevalence has been estimated at 2.7% in the north western part of Pakistan with incidence of 4.6 cases/1000 persons/ year over the last ten years.\(^3\) The drug of choice for CL is systemic pentavalent antimonials either sodium stilbogluconate (Pentostam) or meglumine antimoniate (Glucantime). Often its high cost, usually more than Rs.25000 per treatment and several side
effects like pain, burning sensation, secondary infection, body aches, renal failure, pancreatitis and hepatitis, limit it use.\textsuperscript{4,5}

Recently, treatment of CL with ablative CO\textsubscript{2} laser has shown negligible side effects and better cure rates than with combined cryotherapy and intralesional meglumine antimoniate.\textsuperscript{6} We conducted a study to see whether CO\textsubscript{2} ablative laser treatment is more effective than combined cryotherapy and meglumine antimoniate treatment in our population.

**Methodology**

The study was conducted in the department of dermatology, CMH Peshawar from April 2016 to April 2017 after approval from hospital ethical committee. A randomized control trial was carried out to determine the efficacy of CO\textsubscript{2} laser therapy versus the combined cryotherapy and intralesional meglumine antimoniate in the treatment of cutaneous Leishmaniasis.

All patients between ages 15 to 60 years having clinical cutaneous Leishmaniasis of 1 to 3 months duration as well as positive smear for LT bodies or positive histopathology were included in the study. Patient with history of hypersensitivity to meglumine antimoniate, those patients who had taken any form of treatment in the last 6 weeks, had major hepatic, renal, cardiac illness or had CL lesions around eye or body orifices were excluded from the study. We labeled them clinically cured if the lesion - nodule, ulcer, or crusted plaque was replaced by scar tissue with no evidence of erythema and induration.

A total of 136 patients were enrolled in the study that fulfilled inclusion/exclusion criteria. The purpose and benefits of the study were explained to the patients and written informed consent was obtained. The subjects were divided in two equal groups. Group A was treated with CO\textsubscript{2} laser with maximum power and continuous wave mode after giving local anesthesia with 2\% lignocaine. The lesions were ablated with CO\textsubscript{2} laser including 2-3 mm of surrounding normal skin. After the first ablation, the surface of the lesion was cleansed with normal saline soaked gauze and then second ablation was applied to the lesion. The procedure was repeated until ablated surface reached 2-3 mm below the normal skin level. After completion of the procedure the ulcer was covered with fusidic acid ointment dressing. Patients were called after 4 weeks for second session. If clinical cure was achieved after first CO\textsubscript{2} session, then patients were called after 8 weeks without performing 2\textsuperscript{nd} session for final assessment of result. Group B was treated first with cryotherapy followed by intralesional meglumine antimoniate injection. For cryotherapy liquid nitrogen was applied using cotton tipped applicator on the lesion until 2-3 mm ice halo formed beyond the lesion. The lesion was kept frozen for 15 to 25 seconds depending on the size of the lesion. After cryotherapy intralesional meglumine antimoniate was injected intradermally at about 0.1 ml per cm square area. This procedure was repeated twice weekly for 8 weeks and clinical cure was observed at the 8\textsuperscript{th} week of the treatment.

Statistical analysis was performed using statistical program for social sciences (SPSS 21 for windows). Chi square test was used to compare the efficacy of both the groups. Mean and standard deviation were calculated for qualitative variables, while frequencies and percentage were calculated for quantitative variable.

**Results**

A total of 136 patients of CL fulfilling inclusion criteria were randomly allocated in two groups.
of 68 patients each by lottery method. The mean age of whole study sample was 29.05±4.87 years. The mean age of patient in groups A was 28.5±4.9 years while in group B it was 29.05±4.8 years. All of the study population was of male gender. All patients were assessed for efficacy after 8 weeks of treatment. The efficacy of the both groups was stratified with regards to age groups, site of lesions, size of lesions, number of lesions, type of lesions and duration of lesions to see the effect modifiers.

Data for site of lesion was stratified as lesions involving upper limb and it was 61.8% in group A versus 54.4% in group B. Lesions involving lower limb in group A were 35.3% versus 41.2% in group B while lesions involving all other sites in group A was 2.9% versus 4.4% in group B. The lesion types in group A was nodules 54.5 %, crusted plaque 17.6% and ulcer 27.9% while group B had 51.5% nodules, 27.9% crusted plaques and 20.6% ulcers.

Comparison of duration of lesion in both group was 4 weeks and 19.1 % in group A versus 27.9% in group B. Between 4 to 8 weeks 50% in group A versus 42.6 % in group in group B while duration of 8 to 12 weeks was observed in 30.9% in group A versus 29.5% in group B.

In group A single lesion was observed in 58.8%, two lesions in 35.3% and three lesions in 5.9%. In group B- single lesion in 55.9%, two lesions in 41.2% and three lesions in 2.9% were observed.

We observed clinical cure in 41% of patients (28 patients) in group A after 4 weeks i.e., just after the single session of CO₂ ablative treatment (Figure 1). After 8 weeks, 79.4% of patients had clinical cure in group A while 73.5% of patient in group B were evaluated disease free, p-value= 0.738.

Conclusion

The *Leishmania* species, causative agent of cutaneous Leishmaniasis are highly thermosensitive and these are killed at temperature of 39°C in vitro. CO₂ laser emits energy at 10600nm which is absorbed by water leading to tissue vaporization (>100°C) in the center and
surrounded by zone of tissue coagulation (>60°C).

In our study, we treated 68 patients with ablative CO$_2$ laser in group A at 0 and 4 weeks. In group B, 68 patients were treated with combination of cryotherapy followed by intrallesional meglumine antimoniate twice weekly for 8 weeks. All patients were assessed for clinical cure after 8 weeks of treatment. We observed cure rate of 79.4% (n=54) in group A while cure rate was 73.5% (n=50) in group B. The p value was 0.734 i.e. greater than 0.5 meaning that there was no significant difference in cure rates by both treatment modalities. Our study showed slightly better response in group A than the group B but this difference was not statically significant with this sample size.

Shamsi and co-authors$^6$ in a similar study reported 93.7% cure after a single session of CO$_2$ laser treatment in group A 78% cure rate in group B who received combined cryotherapy biweekly with intralesimal meglumine antimoniate for up to 12 weeks.

Esfandiarpour et al.$^8$ in Iran worked on 50 patients with lupoid or chronic Leishmaniasis, variants of CL that were resistant to various treatments. Patients were divided into two groups; the first group was treated with the CO$_2$ laser for one session and the second group was treated with glucantime (meglumine antimoniate) 50 mg/kg intramuscular for 21 days plus allopurinol 20 mg/kg for 30 days. They observed their patients for up to 72 weeks post-operatively. No significant difference in efficacy was observed between the two groups (p = 0.095).

Asilian et al.$^9$ evaluated the efficacy of CO$_2$ laser with glucantime 50mg/kg/day for 15 days and after 15 days of rest, this treatment was repeated. In their study the CO$_2$ laser was more effective in treating cutaneous leishmaniasis than glucantime (1.12 times), had fewer side-effects (4.5% vs. 24%) and resulted in a shorter healing time (1 month vs. 3 months), and treatment could be applied in a single session.

Advantages of CO$_2$ ablative treatment observed were fewer side effects, required few treatment sessions and cost effective. The side effects observed in group A were only pain during the procedure and pigmentation after healing.

**Conclusion**

Our study concluded that the both treatment modalities i.e. CO$_2$ laser therapy or a combination of cryotherapy and intrallesional meglumine antimoniate are equally effective in treating Cutaneous Leishmaniasis. However CO$_2$ laser is much cheaper, have fewer side effects and mostly produce cure in as early as 4 weeks when compare with other treatment modalities. More randomized controlled trials with larger sample sizes are highly recommended to draw more conclusive results and generate further evidence for uniform decision making in the treatment of Cutaneous Leishmaniasis.

**References**


