

Comparison of the Efficacy of Infrared Heat Therapy with Cryotherapy as an Adjunct to Meglumine Antimoniate in the Treatment of Cutaneous Leishmaniasis

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ABSTRACT

Objective: To compare the efficacy of infrared heat therapy with cryotherapy as an adjunct to Meglumine Antimoniate in the treatment of cutaneous leishmaniasis

Study Design: Quasi-experimental study

Place and duration of study: Combined Military Hospital, Quetta, Pakistan, from Jan to Jun 2024.

Methodology: Eligible participants were aged 18 years or older with confirmed cutaneous leishmaniasis. Participants were assigned to three treatment arms: cryotherapy with meglumine, meglumine alone, and infrared heat therapy with meglumine. The primary outcome was clinical cure after 2 months of therapy.

Results: The mean age of the participants was 28.6 ± 9.2 years. Most of the participants were male, comprising 87.5% of the patients. The duration of the disease among the participants was 3.6 months on average. On average, each participant had 4.7 lesions.

28 participants (87.5%) achieved a clinical cure in the group treated with cryotherapy and meglumine. 26 participants (81.2%) achieved a clinical cure in the group treated with infrared heat therapy and meglumine. Among those treated with meglumine alone, 22 participants (68.7%) achieved a clinical cure. The p-value indicates a statistically significant difference in clinical cure rates among the treatment groups, with a value less than 0.05.

Conclusion: Combination therapy of meglumine with infrared heat and cryotherapy achieved better clinical cure when compared to meglumine alone.

Keywords: Cutaneous Leishmaniasis; Cryotherapy; Meglumine Antimoniate; Leishmaniasis; Thermootherapy.

How to Cite This Article: Kazam Z, Ahmed N. Comparison of the Efficacy of Infrared Heat Therapy with Cryotherapy as an Adjunct to Meglumine Antimoniate in the Treatment of Cutaneous Leishmaniasis. *Pak Armed Forces Med J* 2026; 76(5): 661-664.

DOI: <https://doi.org/10.51253/pafmj.v76i5.12609>

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INTRODUCTION

Cutaneous leishmaniasis (CL) is a tropical disease caused by the *Leishmania* parasite, characterized by skin lesions, ulcers, and scars.¹ The treatment options for CL include systemic and topical medications, such as Meglumine Antimoniate.² However, these treatments have limitations, such as high toxicity, variable efficacy, and the emergence of drug resistance. Therefore, there is a need to explore alternative or adjunctive therapies to improve the treatment outcomes of CL.³

Infrared heat therapy (IHT) and cryotherapy are two physical modalities that have been used in various medical conditions, including inflammatory, infectious, and neoplastic diseases.⁴ In the context of CL, IHT and cryotherapy may have potential benefits by enhancing the penetration and efficacy of Meglumine Antimoniate, reducing inflammation and

scarring, and modulating the immune response.^{5,6}

A study by Asilane et al. showed promising results of efficacy when meglumine was combined with cryotherapy.⁷ The results showed a complete cure in 90.9% of cases in the meglumine and cryotherapy group, whereas it was 55.63% for patients treated with meglumine alone. The difference was statistically significant ($P < 0.05$).⁸

The study also aims to determine whether either adjunctive modality offers superior improvement in lesion healing, symptom relief, and overall treatment response. By comparing treatment efficacy and safety through a randomized controlled design, the study may help identify a more effective and practical adjunctive approach. The findings could contribute to evidence-based management of CL and support the development of standardized treatment protocols in clinical practice.

METHODOLOGY

A Quasi-experimental study was conducted to examine the effectiveness of infrared therapy and

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Received: 05 Sep 2024; revision received: 27 Aug 2025; accepted: 28 Aug 2025

cryotherapy in addition to intramuscular Meglumine Antimoniate for treating cutaneous leishmaniasis. The research was carried out at Combined Military Hospital, Quetta, Pakistan, from Jan to Jun 2024, after the endorsement of the Institutional Review Board and Ethics Committee (Reference number: _CMH QTA-IERB/20/2024) and IRCT number 76617. Participants provided written informed consent. Sample size was calculated using OpenEpi software. Power of the study was taken as 80% and significance level was set to 95. Using Asilian et al., study as a reference,⁷ where anticipated population proportions of 90.9% cure rate of cases in Group 1, 57.15% of cases in Group 2, and 55.63% of cases in Group 3. The sample size comes out to be 96 (32 in each arm)

Inclusion Criteria: Eligible participants were those who were 18 years or older, of either gender, who had been diagnosed with cutaneous leishmaniasis caused by *Leishmania* species that required intervention. The diagnosis was established through the evaluation of clinical symptoms, laboratory tests including Leishman Donovan bodies smear and microscopic/histopathological examination of skin lesions.

Exclusion Criteria: The study did not include patients with an age less than 18 years, pregnant and breastfeeding women, patients allergic to antimonial, lesion is already self-healing, disfiguring lesions on the face or around eyelids, individuals with weakened immune systems, those with diffuse cutaneous or visceral leishmaniasis, and individuals with a medical history of liver, kidney, or heart disease, patients who refused to accept diagnostic procedures.

Patients were selected using convenience sampling. Participants were randomly assigned to one of three treatment arms by lottery method: Cryotherapy and Meglumine Arm, Meglumine Arm, and Infrared Heat and Meglumine Arm. Cryotherapy was done twice weekly. After explaining the procedure to the patient, an appropriately sized cotton wick was wrapped on an orange stick. The cotton wick was dipped in a disposable glass containing liquid nitrogen and applied over the lesion for 8-10 seconds. After thawing, a second freezing cycle was repeated. Infrared heat at 45 degrees C was also given twice weekly, comprising two sessions, each lasting 10 minutes, 3- 4 cm from the skin. Meglumine was administered intramuscularly at a dose of 15mg/kg if the dose exceeds 10ml then it should be divided into two doses given on each buttock.

The primary outcome was measured after 02 months of therapy. The outcome measure was the patients achieving complete healing. The cure was defined as complete re-epithelialization, the disappearance of edema, induration, and other signs of inflammation, and a negative smear. Failure was defined as incomplete re-epithelialization or a positive direct smear at the end of treatment or 6 weeks after treatment. Statistical analysis was done using the Statistical Package for Social Sciences version 21. It was conducted using appropriate methods to compare primary measures between the treatment arms. Descriptive statistics were used to summarize the baseline characteristics of participants. A chi-square test was used to determine the association between the groups. A p -value ≤ 0.05 was considered significant.

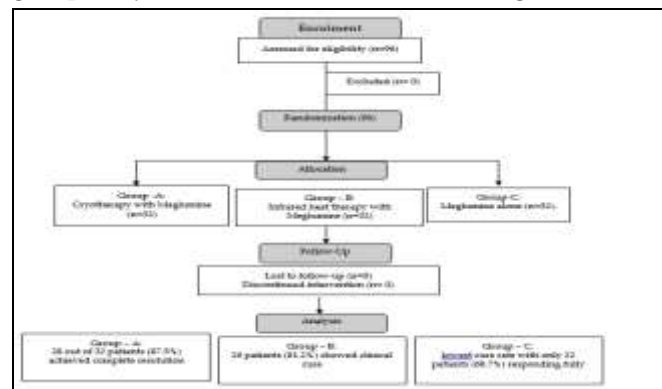


Figure-1: Patient Flow Diagram

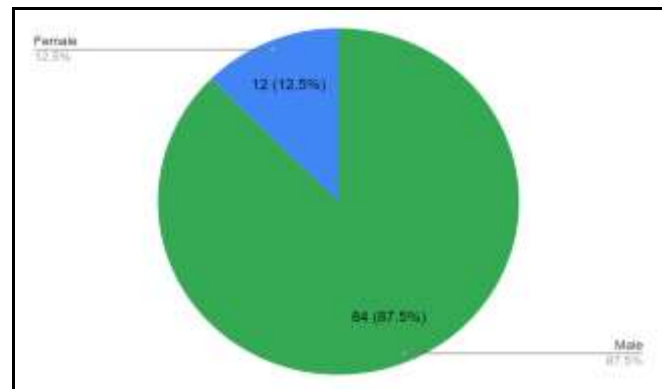


Figure-2: Gender Distribution Of The Patients

RESULTS

A total of 96 patients were enrolled in the study and evenly distributed into three groups: Cryotherapy with Meglumine ($n=32$), Infrared heat therapy with Meglumine ($n=32$), and Meglumine alone ($n=32$). The majority of patients were male 84 (87.5%) shown in Figure 2, and the mean age across the cohort was 28.6 ± 9.2 years (95% CI: 26.1–54.1). Duration of disease averaged 3.6 ± 1.6 months (95% CI: 3.2–3.9), and the

mean number of lesions was 4.7 ± 2.1 (95% CI: 4.3–5.1) shown in Table-I. The most frequently observed clinical presentation was erythematous nodular lesions, while the least common finding was ulcerative lesions with discharge. When evaluating treatment efficacy, the clinical cure rate was highest in the cryotherapy with meglumine group, where 28 out of 32 patients (87.5%) achieved complete resolution. In the infrared heat therapy group, 26 patients (81.2%) showed clinical cure, whereas the meglumine monotherapy group demonstrated the lowest cure rate with only 22 patients (68.7%) responding fully. Statistical analysis revealed a significant difference in clinical response among the groups, with a p -value <0.05 , indicating that adjunct therapies (cryotherapy or heat) were more effective than Meglumine alone shown in Table-II.

Table-I: Baseline Characteristics of the Patients (n=96)

Baseline Characteristics	Mean $\pm$ SD
Mean Age (years)	28.6 $\pm$ 9.2
Duration of disease(months)	3.6 $\pm$ 1.6
Mean number of lesions	4.7 $\pm$ 2.1

Table-II: Comparison of Clinical Cure Rates Between Treatment Groups (n=96)

Response	Group-A Cryotherapy and Meglumine (n=32)	Group-B Infrared heat therapy and meglumine (n=32)	Group-C Meglumine alone (n=32)	p -value
Clinical Cure (%)	28 (87.5%)	26 (81.2%)	22 (68.7%)	<0.05

DISCUSSION

In the present study, 28(87.5%) patients achieved clinical cure with cryotherapy combined with meglumine, compared with 26(81.2%) with infrared heat therapy combined with meglumine and 22(68.7%) with meglumine alone ($p<0.05$). These findings indicate higher clinical cure rates with both adjunctive therapies than with meglumine monotherapy. Cryotherapy, a well-established treatment modality, exhibited a slightly higher clinical cure rate of 87.5% compared to the clinical cure rate of 81.2% observed with infrared heat therapy. These results suggest that cryotherapy may have a slight advantage over infrared heat therapy when used in conjunction with Meglumine Antimoniate for treating cutaneous leishmaniasis.

A meta-analysis showed that the efficacy of cryotherapy was comparable to antimonial. They showed that in 271 patients treated with cryotherapy and in 199 with pentavalent antimonial,⁹ respective per protocol and intent-to-treat efficacies of 63.6% and 54.2% were found in the first group, and per protocol and intent-to-treat efficacies of 74.7% and 68.3% were found in the second group.¹⁰ This was similar to the efficacy of pentavalent antimonial drugs, with a relative risk of 0.73 (0.42-1.29) compared to cryotherapy. This is consistent with findings in the literature, which report similar outcomes.¹¹

A large, pooled meta-analysis of 131 studies compared various treatment regimens for cutaneous leishmaniasis was conducted by Sridharan *et al.*, who concluded that parenteral Pentamidine had the highest statistical probability of being the best in the pool.¹² A study by Etemadifar *et al.* compared Meglumine Antimoniate and cryotherapy with Meglumine Antimoniate and Niosomal Dapsone Gel. Despite the initial better response with adjunct cryotherapy, 29(82.9%) patients in the adjunct cryotherapy group showed a complete response as compared to 33(86.8%) in the adjunct Niosomal Dapsone Gel group.¹³ During the twelve months of post-treatment follow-ups, no recurrence was reported in the adjunct cryotherapy group. Still, in the Niosomal Dapsone group, one patient developed lupoid leishmaniasis and was treated with systemic Meglumine Antimoniate. This shows that other adjuncts may confer better or similar benefits when compared to cryotherapy, which had also been highlighted in a study by Alidosti *et al.*¹⁴

Despite its prevalence, CL can still carry a social stigma due to its visible symptoms such as skin lesions. People with CL may face discrimination or social exclusion, especially in communities where there is a lack of understanding about the disease, as mentioned by Zabala *et al.*¹⁵ There is no widely available vaccine for leishmaniasis. However, research into vaccine development has started, research into various kinds of vaccines such as Whole parasite vaccines, Subunit vaccines, DNA vaccines, and Recombinant vaccines.¹⁶ There is an urgent need for updated treatment regimens to combat this disease.^{17,18}

This study demonstrates that Cryotherapy combined with meglumine produced the highest cure rate, followed by infrared heat therapy combined with meglumine, whereas meglumine alone achieved a lower cure rate; the overall difference among the

treatment groups was statistically significant ($p < 0.05$). These findings suggest that both cryotherapy and infrared heat therapy are useful adjunctive options, with cryotherapy showing a modest numerical advantage in this study.

LIMITATION OF STUDY

However, the relatively small sample size, short follow-up period, and limited assessment of lesion characteristics, disease severity, adherence, adverse effects, and recurrence restrict the generalizability of the results. Larger, adequately powered studies with longer follow-up and standardized evaluation of safety, cosmetic outcomes, recurrence, and patient-related factors are therefore needed before definitive treatment recommendations can be made.

CONCLUSION

In conclusion, our study provides valuable insights into the comparative efficacy of cryotherapy and infrared heat therapy as adjuncts to Meglumine Antimoniate in the treatment of cutaneous leishmaniasis. While both adjunctive therapies demonstrated effectiveness in achieving clinical cure, cryotherapy exhibited a slightly higher clinical cure rate compared to infrared heat therapy. Further research with larger sample sizes and comprehensive evaluation of patient-related factors is warranted to validate these findings and inform clinical practice guidelines for the management of cutaneous leishmaniasis.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

ZK & NA: Data acquisition, data analysis, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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