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Original Article

The efficacy of intralesional metronidazole compared to intralesional glucantime in the therapeutic therapy of cutaneous leishmaniasis

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Abstract

Objective To assess the effectiveness of intralesional metronidazole vs. intralesional glucantime in the therapy of cutaneous leishmaniasis.

Methods Study design is Randomized controlled trial, conducted in the Department of Dermatology, Lady Reading Hospital, Peshawar from the 1st of February to the 10th of June 2020. A total of 60 patients of both gender with cutaneous leishmaniasis <3 months duration were included. 30 patients were in the intralesional metronidazole group (Group A) while 30 patients were in the intralesional glucantime group (Group B). Efficacy from both groups was noted.

Results The participants age ranged in this study from 15 to 50 years, with Group A having a mean age of 30.700± 6.13 years and Group B with a mean age of 30.500 ±5.72 years. In this study Group A having mean disease period of 1.4000±0.49 months, while Group B had a mean disease period of 1.6000±0.46 months. In Group A, the mean weight was 66.63±8.21 kg, whereas in Group B, it was 69.066±9.59 kg. Efficacy was demonstrated in 26.7 percent of Group A patients against 73.3 percent of Group B patients (p=0.000).

Conclusion In our study intralesional glucantime is more effective and safe in the treatment of cutaneous leishmaniasis. Despite the fact that metronidazole was found to be unsuccessful in this trial, we feel that the quest for a pain free, readily applied, and effective treatment modality with minimum adverse effects for the therapy of cutaneous leishmaniasis is essential.

Key words
Cutaneous leishmaniasis, intralesional metronidazole, glucantime.

Introduction

Leishmaniases are a group of infectious disorders produced by protozoa of the Leishmania genus that generate severe public health issues in endemic areas in 98 countries. Among the two main types of this disease cutaneous leishmaniasis is more common than visceral leishmaniasis.[1] In endemic areas CL is becoming more prevalent as a result of natural favorable environmental changes, which are amplified by human factors such as overcrowding, urbanization, deforestation, global warming, regional wars and mass migrations.[2] These results showing Leishmania's genomic instability in response to environmental factors due to haplotype selection mechanisms and high aneuploidy which contribute to the existing diversity.[3]

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High population concentrations and hunger, along with insufficient sanitary facilities, are prevalent variables in all CL endemic locations.[4,5] Aside from the financial cost imposed by CL morbidity, social stigmatization and mental distress caused by ulcers, particularly among infected women and children, are additional significant consequences of the disease.[6,7] In the treatment of cutaneous leishmaniasis, a research by Mapar MA *et al*. found that intralesional metronidazole was 16.6% effective compared to 81 percent with intralesional glucantime.[8] Another research by Somaratne VN *et al*. found that intralesional metronidazole was effective in treating cutaneous leishmaniasis in 48.9% of cases.[9] In a research by Jaffary F *et al*, intralesional glucantime was shown to be 38.5 percent effective in the treatment of cutaneous leishmaniasis.[10] In Pakistan, there is a scarcity of information about this topic. Because of the fluctuation in outcomes and differences in genetic makeup, the findings of global studies cannot be applied to our local population. This encourages me to compare the efficacy of intralesional metronidazole and intralesional glucantime in treating cutaneous leishmaniasis. The findings of my research will aid in determining which of these two therapy approaches is best for our general population.

Material and Methods

With due approval of the hospital ethical committee, Informed permission was taken and 60 patients included in this study from Department of Dermatology LRH Peshawar. The demographic data including patient's name, age, gender, duration of disease residential area, and weight on weighing machine was noted. Smears have been done to diagnose cutaneous leishmaniasis.

Lesions located on the face, neck, or joints, patients with previous leishmania treatment, pregnant women and hepatic disease patients were excluded to avoid any bias in study results. The subjects were then randomly assigned through the lottery method. There were 30 patients were in the intralesional metronidazole group (Group A) while 30 patients were in the intralesional glucantime group (Group B). In Group A, Weekly intralesional injections of metronidazole were given to all lesions. Intralesional injections (0.5-2 ml for each lesion) were given intradermally to blanch the lesion surface. (Metronidazole vials, 500 mg/100 mL) All members of Group B received weekly intralesional glucantime injections (150-600mg =0.5-2ml of glucantime injection for every skin lesion). The procedures were repeated twice a week for a maximum of 8 weeks. Efficacy in terms of complete re-epithelization of the ulcerated lesions at 8 weeks of treatment from both groups was noted.

Data were analyzed with the statistical analysis program (SPSS-V23). For quantitative variables Mean±SD was presented. For qualitative variables frequency and percentage were computed. The Chi-square test was applied for comparing the efficacy of both groups, taking $p \leq 0.05$ as significant.

Result

The age in this study ranged from 15 to 50 years with mean age of 30.700±6.13 years in Group A while 30.500±5.72 years in Group B. The mean period of disease was 1.400±0.49 months in Group A while 1.600±0.46 months in Group B. Mean weight was 66.633±8.21 Kgs. in Group A and 69.066±9.59 Kgs. in Group B. All the parameter in both the groups were statistically insignificant as shown in **Table 1**. Male gender was dominant in both groups i.e. 83.3% and 80% respectively. There were 47 (78.3%) patients belonging to rural areas while 13

Table 1 Age, duration of disease and weight in both groups.

	Group A Mean ± SD n=30	*Group B Mean ± SD n=30*	*p-value*
Age(years)	30.700± 6.13	30.500± 5.72	0.8965
Duration of disease (months)	1.400±0.49	1.600±0.46	0.1085
Weight (Kg)	66.633±8.21	69.066±9.59	0.2955

Table 2 Comparison of efficacy in both groups.

Efficacy	*Group A n=30*	*Group B n=30*	*P value*
Yes	8 (26.7%)	22 (73.3%)	0.000
No	22 (73.3%)	8 (26.7%)	
Total	30 (100%)	30 (100%)	

(21.7%) were presented from urban areas. Both were insignificantly distributed among the groups with p-value=0.739 and 0.105 respectively. Among all patients 66.7% of patients were having 1-2 lesions in group A while 76.7% in group B. Similarly 33.3% of patients have lesions of 3-4 in group A while 23.3% were found in Group B, but this difference was found statistically insignificant with p=0.567. In group A efficacy was seen in 26.7% of patients while in group B it was 73.3% (p=0.000) as shown in **Table 2**.

Discussion

Cutaneous leishmaniasis is an endemic parasite disease that is a major public health issue in several countries, including Pakistan. Although it is normally self-limiting, it can leave scars and disfigurements. The therapy of leishmaniasis is a significant medical issue. Unfortunately, there is no perfect treatment for cutaneous leishmaniasis. Several topical, intralesional and systemic treatment modalities have been advocated for cutaneous leishmaniasis, with glucantime being the primary choice.[11] The efficacy of intralesional glucantime injections for the treatment of cutaneous leishmaniasis has been established,[12-14] it is associated with a different adverse effects i.e. acute discomfort and reactions at injection site. Aching, arthralgia, weariness, gastrointestinal disturbance, elevated liver enzyme levels, lipase and amylase, anemia, leukopenia and electrocardiographic abnormalities are some of the other adverse effects that can occur with intravenous or intramuscular injections.[11,15] According to recent circumstantial data, a growing percentage of individuals with cutaneous leishmaniasis are resistant to glucantime.[16] In addition, if many skin lesions develop, the aggregate dose of intralesional medication administered might be comparable to intramuscular or intravenous injections. As a result, each injection technique may have the same systemic side effects. Patients in Pakistan and other endemic countries are developing resistance to pentavalent antimonials, hence a new therapeutic strategy is required.[17] Metronidazole was developed in 1957 in France and quickly became the first choice of treatment for trichomoniasis. In further research it was shown to be efficacious for giardiasis and amebiasis as well as cutaneous leishmaniasis,[17-20] however, its efficacy in cutaneous leishmaniasis was not substantiated in subsequent trials.[21-23] As a result, the efficacy of oral metronidazole in the therapy of cutaneous leishmaniasis is still up for debate. As a result, we decided to put the intralesional metronidazole injection procedure to the test on a few of our patients. But the intralesional injection was quite painful, and all of the patients complained of extreme discomfort. The six patients who dropped out of this group did so possibly owing to acute injection discomfort and/or unsatisfactory outcomes. Only eight (26.7 percent) of the patients in this group exhibited full recovery. In the treatment of cutaneous leishmaniasis, a research by Mapar MA *et al.* found that intralesional metronidazole was 16.6% effective compared to 81 percent with intralesional glucantime.[8] Another research by Somaratne VN *et al.* found that intralesional

metronidazole was effective in treating cutaneous leishmaniasis in 48.9% of cases.[9] In a research by Jaffary F. *et al.* intralesional glucantime was shown to be 38.5 percent effective in the treatment of cutaneous leishmaniasis.[10] The success of intralesional metronidazole injection was substantial in a recent clinical trial in Iraq, with 85-87 percent of patients treated with 1-3 doses. The results of this study differ significantly from ours, these discrepancies might be attributable to changes in drug manufacturing methods, different criteria for defining cure, or variable sensitivity of different geographical variants of parasite species to metronidazole. The solutions of metronidazole were made in the Iraqi study by dissolving powder in 100 ml of distilled deionized water. The medication in our trial was a typical intravenous injection vial. Our findings are consistent with those who found oral metronidazole to be ineffective.[21-23] Our study has several flaws, including a limited number of patients, absence sore culture and undetermined strains and species of the genus Leishmaniasis. Similar investigations with more patients should be conducted by other researchers due to considerable variations among outcomes of study in Iraq and our study.

Conclusion

In conclusion intralesional glucantime is more efficaeous and safe for the treatment of cutaneous leishmaniasis. Despite the fact that metronidazole was found to be unsuccessful in this trial, we feel that the quest for a painless, readily applied, and effective therapy for cutaneous leishmaniasis with low side effects is essential.

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