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ORIGINAL ARTICLE

Comparison of Use of Intralesional Artemether with Intralesional Meglumine Antimoniate in Cutaneous Leishmaniasis

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ABSTRACT

Objective: The objective of this study is to compare the efficacy and safety of Intralesional Meglumine Antimoniate and Intralesional Artemether in the Treatment of Cutaneous Leishmaniasis.

Patients and Methods: Total 168 patients of cutaneous leishmaniasis were assigned randomly and equally to intralesional meglumine antimoniate (group A) and intralesional artemether (group B). The study outcome was measured after 6 weeks of therapy and treatment was considered efficacious if the lesion reduced more than 75% from its baseline size. The side effects in terms of pain, redness and swelling at the site of injection, fever, hepatitis and renal impairment were also noted.

Results: Intralesional meglumine antimoniate achieved complete healing in 75 (89.3%) cases compared to 62 (73.8%) cases in intralesional artemether (p= 0.01).

Conclusion: Intralesional meglumine antimoniate is better than intralesional artemether in the treatment of cutaneous leishmaniasis. Both drugs were found safe and no significant side effects were noted.

Key words: Artemether, Cutaneous leishmaniasis, Efficacy, Meglumine antimoniate, Safety.

Author`s Contribution
[1] Conception, synthesis, planning of research and manuscript writing Interpretation and discussion, [2-4] Data analysis, interpretation and manuscript writing, [Active] participation in data collection.

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Introduction

Leishmaniasis is one of the protozoan skin infections caused by an intracellular parasite of the genus *Leishmania* which is transferred by the bite of sand fly, *Phlebotomine*. According to WHO, disease is native in 98 countries, having 350 million people at risk and currently 1 to 1.3 million cases are reported yearly.[1] The disease is endemic in Pakistan with a rising incidence in northern hilly areas and in Lasbella and Makran coastal areas in the southern parts of the country along with scattered foci in Punjab, KPK and Azad Kashmir.[2] The clinical continuum of leishmaniasis varies from cutaneous disease to disfiguring mucocutaneous disease and to a deadly systemic ailment. Cutaneous leishmaniasis generally heals spontaneously within a year, but resulting morbidity and disfiguring scar make it a serious health hazard especially in the endemic areas. Pentavalent antimony compounds like meglumine antimoniate and sodium stibogluconate are considered to be the mainstay of therapy for cutaneous leishmaniasis.[3] A study documented that efficacy of intralesional Glucantime was 80%, and was significantly higher than the 33.3% rate of healing in the group treated with intralesional 2% zinc sulfate.[4] However there have been several reports of emerging resistance to antimony compounds.[5, 6]

Artemether is an established drug for the treatment of malaria and this drug has also been found to be effective against cutaneous leishmaniasis caused by *leishmania major* in BALB/c mice.[7] A study showed that injection artemisinin when injected within the lesion of cutaneous leishmaniasis along-with sodium stibogluconate is effective in reducing the duration of healing in cutaneous leishmaniasis in 93.2% of individuals.[8] It was considered that intralesional meglumine antimoniate is more effective and safer than intralesional artemether.This study was designed to compare the efficacy and safety of Intralesional Meglumine Antimoniate and Intralesional Artemether in the treatment of Cutaneous Leishmaniasis.

Patients and Methods

This randomized controlled trial was carried out in Dermatology department, Pakistan Institute of Medical Sciences, Islamabad from 1st January 2015 to 31st October 2015. Total 168 patients of cutaneous leishmaniasis were registered. Patients above 14 years of age of either gender, having lesion duration for less than two months and lesion count equal to or less than three were included in the study. Those patients taking antileishmanial therapy within last two months, pregnant or lactating females, patients with hepatic or renal derangement, those with known allergy to the drug used and those having lesions localized to or near the joints were excluded. Permission was taken from the hospital's ethical committee. Skin biopsy was done for making a diagnosis. Venous blood samples were collected for baseline LFTs and Serum creatinine. The patients were divided randomly into two groups. Group A was given intralesional meglumine antimoniate, till blanching of lesion, weekly for 6 weeks and group B received intralesional artemether in same dosage schedule.

The study outcome was measured after 6 weeks of therapy and treatment was considered efficacious if the lesion reduced more than 75% from its baseline size. The data was analyzed with the help of Statistical Package for Social Sciences (SPSS) version 17. Chi square test was applied to compare complete healing after 6 weeks and safety (pain, hepatitis and renal impairment) between two groups. P value <0.05 was considered significant.

Results

The mean age of patients was 27.3±12.1 in group A and 28.2±13.2 years in group B. The mean number of lesions was 1.2±0.43 in group A and 1.1±0.42 in group B. The lesion size was found to be 10.6±7.4 cm in group A and 6.7±5.5 cm in group B (Table 1). The efficacy of interventions was measured after 6 weeks of treatment in terms of 75% reduction in size of lesion from its pre intervention measurement. In this study it was found that the drug used in group A was significantly more efficacious than group B in the treatment of cutaneous leishmeniasis (p-value, 0.01) (Table 2)

Discussion

Cutaneous leishmaniasis is not a life threatening illness and it does not cause significant morbidity, however the disfiguring scar caused by it, is a source of mental distress and thus impairs quality of life of the patients. For this reason, dermatologists always try to treat it, using different treatment modalities. The mean age of patients was 27.3 ± 12.1 in group A and 28.2 ± 13.2 years in group B and was found comparable. In a comparative study by Anderson EA on meglumine antimoniate the mean age of patients was found to be 30 years.[9]

Table 1: Cutaneous lesions before treatment in the two study groups

	Group A (n=84)	Group B (n=84)	p-value
No. of lesions			
Mean + SD	1.2 ± 0.43	1.1 ± 0.42	0.63
Lesion size (cm2)			
Mean + SD	10.6 ± 7.4	6.7 ± 5.5	0.02

Table 2: Comparison of efficacy of interventions between the two study groups

Efficacy (complete healing after 6 weeks)	Group A (n=84)	Group B (n=84)	p-value
Achieved	75 (89.3%)	62 (73.8%)	0.01
Not achieved	9 (10.7%)	22 (26.2%)	

Another RCT (randomized control trial) by Nilforoushzadeh MA on comparison of meglumine antimoniate alone with combination of trichloroacetic Acid 50% and intralesional meglumine antimoniate in the treatment of acute cutaneous leishmaniasis witnessed the mean age of their patients to be 11.0 years with age range of 5 to 32 years as they also enrolled paediatric and adolescent age groups.[10] A local study by Jamal Q et al witnessed that most of their cases of leishmaniasis were between 11 and 20 years.[11]

In the present study, male gender was predominantly affected by cutaneous leshmaniasis in both genders. A study by Al Samarai and Abolaidi witnessed a similar trend with male majority in their study.[12] Other previous studies also reported male preponderance, however, there are contrast reports as well where both genders have been found equally affected and even in some trials female gender was found predominant.[13] In this study most of the lesions were found on forearm, followed by legs and face whereas the mean number of lesions were 1.2 per patient. Goyonlo VM witnessed that most of their patients had lesions on head and neck followed by upper limbs.[14] In the present study Intralesional meglumine antimoniate achieved complete healing in (89.3%) cases compared to (73.8%) cases in Intralesional arthemeter group after 6 weeks of treatment and this difference was significant (p-value,0.01). We could not find any study comparing intralesional meglumine antimoniate and intralesional artemether in humans, however, studies on animals (mice) were available.

In a study, conducted by Ghaffarifar F et al, the antiparasitic activity of artemisinin on L.major, both in vitro and in vivo, was assessed by finding the cytokine pattern as well as the percentage of apoptosis induced by artemisinin. It was concluded that artemisinin induces cytotoxic effects on L.major via apoptosis related mechanism.[15] it was reported that oral artemether is an effective and simple method and may be used to treat visceral leishmaniasis.[16] The current study has many advantages, firstly, there have been very few studies on cutaneous leishmaniasis nationally and internationally and this study is certainly very informative in this regard. Secondly, two therapeutic drugs i.e. intralesional meglumine antimoniate and intralesional artemether for the management were investigated. Thirdly, a reasonable number of study population was enrolled in both study groups. Although, the current study found no local side effects (pain, redness and swelling at the site of injection), fever and renal impairment with both interventions, there were 2 cases of Hepatitis in meglumine antimoniate and 1 case in artemether group. Intralesional artemether can be considered as a safe and effective treatment option in localized cutaneous leishmaniasis. Although the cure rate was better in the intralesional meglumine antimoniate group, but intralesional artemether is much cheaper, readily available and at the same time is effective and safe. There is a need to conduct further comparative trials on artemether and meglumine antimoniate, so that findings of current study could be validated.

Conclusion

Intralesional meglumine antimoniate is superior to intralesional artemether in the management of cutaneous Leishmaniasis. Both drugs have very few toxic effects and were found safe for treatment.

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