

Comparative study of testing the efficacy of injection meglumine antimoniate with oral itraconazole as first line treatment of cutaneous leishmaniasis

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Abstract

Background Cutaneous Leishmaniasis is caused by different species of a protozoa.¹ The disease is endemic in some areas of Pakistan like Baluchistan, Sindh, Khyber Pakhtunkhwa.² There are many treatment options including meglumine antimoniate, rifampicin, tetracyclines, sodium sitboglucanate and itraconazole etc.³

Objective The objective of our study was to compare the efficacy of injection meglumine antimoniate with cap Itraconazole as 1st line treatment of cutaneous leishmaniasis.

Methods This study on cutaneous leishmaniasis was conducted in the Dermatology Department at Punjab Ranger Teaching Hospital Lahore. All 20 male patients referred to us from the endemic area (Kashmore) were divided into two groups A and B after positive Slit Skin Smear test. Group A were given meglumine antimoniate 400mg/day intramuscular injection, group B were given Cap Itraconazole 200 mg per day for 4 weeks. Patients assessment was done on three criteria; 1: clinical resolution of lesions 2: side effects seen during the treatment 3: report of slit skin smear at 4 weeks.

Results According to study results Slit Skin Smear test was 100% positive for all 20 patients before treatment, but came negative for all 10 patients of group A and negative for only 2 patients of group B after 4 weeks. Some side effects were observed during treatment in both groups but they were more in group A patients. Clinical resolution of lesions was 100% in Group A as compared to group B 20%.

Conclusion Injection meglumine antimoniate is the preferred treatment of cutaneous leishmaniasis regards to its efficacy as compared to oral Itraconazole based on the clinical resolution & negative slit smear at the end of the course but the limitations to treatment are the poor patient tolerance & the increased side effects seen in this group.

Key words

Itraconazole; Meglumine antimoniate; Cutaneous leishmaniasis.

Introduction

Leishmaniasis is a widespread disease and has visceral, mucocutaneous and cutaneous manifestations. Cutaneous leishmaniasis is its most common form, caused by various species of phlebotomine sandflies which live in dark damp places and can fly only to 50 meters,

because they are smaller in size can easily enter mosquito nets and are most active in the evening

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and at night. Leishmaniasis is endemic in 88 countries; 90% of cases are reported in just six countries, Afghanistan, Brazil, Iran, Peru, Saudi Arabia and Syria.⁴ Leishmaniasis disease can be found in almost 40 of the 88 countries.⁵ Leishmaniasis is endemic in Pakistan and it is commonly reported in urban areas of Punjab, Baluchistan, Azad Jammu Kashmir, Khyber Pakhtunkhwa and Federally administrated tribal areas. Cutaneous leishmaniasis is the result of factors like parasite species (flagellated protozoa), site of inoculation and host immune status, patient may not recall the initial sand fly bites. It is localized to the site of infection within dermal macrophages, metastasis to lymphatic, mucosal and bone marrow sites can also occur.⁶ After parasites are inoculated into the mammalian host by the sand fly vector, they are engulfed by macrophages where the intracellular amastigotes survive and divide within the parasitophorous vacuole.⁷ First of all nodules form at the site of bite, which progress to ulcerative lesions, lasting from 3 months to three years. Epidermal changes are hyperplasia and epidermal thickening.⁸ Epidermal disruption results in discharge and eventually dries to form an encrusted ulcer, with a central depression and raised border.⁹ There are many treatment options for cutaneous leishmaniasis. The first line treatment is systemic pentavalent antimonials like sodium stibogluconate and meglumine antimoniate (Glucantime) even though they have various side effects like bone marrow suppression, deranged LFTS, deranged pancreatic enzymes, and disturbance in electrocardiogram. There are some 2nd line treatments like itraconazole which we used in our research, others drugs are Rifampicin, aminosidine, pentamidine and ketoconazole.¹⁰

Objectives

The objective of our study is to compare the

efficacy of meglumine antimoniate with itraconazole as 1st line treatment of cutaneous leishmaniasis

Methods

This study was conducted in Dermatology department of Punjab Rangers Teaching Hospital Lahore. Duration of our study was 4 weeks. Total number of twenty patients of cutaneous leishmaniasis, all males (21-45) referred to us from the endemic area(Kashmore) reported positive for Leishmania Donovan Bodies on the Slit Skin Smear examination were enrolled in the study. All patients were admitted indoor, divided into two equal groups of ten each, group A and group B. All patients had non-healing indurated scaly and crusted plaques ranging from two to six in number mainly over the upper and lower limbs. Group A were given a 4 week course of meglumine antimoniate 400mg/day intramuscular injection daily while the other group B were given Cap. Itraconazole 200 mg per day for 4 weeks. Effectiveness and safety of each drug was assessed on the improvement in the lesions, side effect profile and repetition of slit skin at the end of 4 weeks. Improvement in lesions were assessed on the basis of reduction in the size & induration of plaque. For the side effects subjective complaints of patients along with Liver functions, renal functions, pancreatic enzymes were assessed weekly. At the end of 4 weeks slit smears were repeated for presence of LD bodies.

Results

There are 2 groups in our research.

Group A: Injection Glucantime was given to 10 patients of this group.

Group B: Cap Itraconazole 200mg BD was given to this group patients.

Table 1 Slit skin smear test.

Group A		Group B	
At time of admission	After 4 weeks	At time of admission	After 4 weeks
100% positive	100% negative	100% positive	20% negative

All 20 patients were male in our study and lied in the 21-45yr age group.

Slit Skin Smear Test was positive for all 20 patients of group A and group B at time of admission. After 4 weeks of treatment it was 100% negative for group A, but for group B it was only negative for 2 patients which is 20% (Table 1).

At 2 weeks >30% reduction in size was observed in all 10 (100%) patients of group A, while in group B 7 (70%) patients showed <30% reduction in size of lesion and 3 patients showed >30% reduction in size. From this we can conclude that 100% group A patients showed >30% reduction as compared to group B which is only 30%. At 4 weeks >60% reduction was observed in 100% patients of group A, while in group B 8 patients showed <60% reduction and only 2 patients showed >60% reduction (Table 2).

During treatment with injection glucantime some side-effects were observed which were

deranged liver function tests in 6 patients, raised amylase and lipase in 50% and 60% of patients, headache, body-aches in all 10 patients, pain at injection site in 70% patients others were loss of appetite, fever (Table 3).

Ten patients were given tablet itraconazole. Side effects of the tablet itraconazole are non-healing ulcers, multiple papular eruptions in 100% of the patients. Only one patient complained of body-aches and headache (Table 4).

Discussion

Cutaneous leishmaniasis is endemic in developing countries. Although the drug of choice & the first line treatment are pentavalent antimonials, however they have high intolerance and toxicity. Some patients find its mode of administration highly inconvenient. It is the need of the hour to study the effect of second line orally administered drugs for the treatment of cutaneous leishmaniasis. The rationale of the current study was to carry out factual visualization of the effects of oral itraconazole as an alternative treatment for the cure of this disease.

Literature surfing shows limited data on this drug. One study testing the efficacy of Itraconazole (400mg/day) in mucocutaneous

Table 2 Clinical resolution of lesions.

Group A				Group B			
Week 2 (reduction in size)		Week 4 (reduction in size)		Week 2 (reduction in size)		Week 4 (reduction in size)	
<30%	>30%	<60%	>60%	<30%	>30%	<60%	>60%
0%	100%	0%	100%	70%	30%	80%	20%

Table 3 Side effects in Group A.

Headaches and body aches	Fever	Pain at injection site	New papular eruptions	Deranged LFTs	Serum amylase	Serum lipase	Loss of appetite
100%	70%	70%	10%	60%	50%	60%	70%

Table 4 Side effects in Group B.

Headaches and body aches	Fever	New papular eruptions	Deranged LFTs	Serum amylase	Serum lipase	Loss of appetite
10%	0%	100%	0%	10%	0%	0%

leishmaniasis on 10 patients in the University of Sao Paulo, Brazil for a period of 6 weeks, showed healed lesions in 60 % patients.¹¹ These results are somehow different from the current study as in our study 20% patients in itraconazole group showed complete resolution of plaques. Reason could be the difference of dose of itraconazole in both studies, longer duration of treatment and the type of leishmaniasis being treated.

In another study conducted in the Isfahan University of Medical Sciences on 140 randomly selected patients from hyperendemic areas of Iran, Itraconazole was given in a dose of 7 mg/kg per day for 3 weeks. 59% patients showed complete resolution after this period compared to 20 % patients of our study with no reported side effects similar to the current study.¹²

One more study carried out in 2017 on 69 patients in Combined Military Hospital Quetta comparing the effect of intralesional meglumine antimonials with oral Itraconazole 200 mg once daily with the other group given (MA) alone proved no additional benefit of the combination therapy, showing that itraconazole in the dose of 200mg/day has no effective coverage against cutaneous leishmaniasis.¹³ This study shares similarity with the current study in terms of poor response to itraconazole with the same dosage being used.

The paucity of available data with the variation of response to treatment stresses on the need of further randomized studies to assess the benefits of the second line drugs in the treatment of cutaneous leishmaniasis.

Conclusion

Injection meglumine antimoniate is the preferred treatment of cutaneous leishmaniasis regards to

its efficacy as compared to oral Itraconazole based on the clinical resolution & negative slit smear at the end of the course but the limitations to treatment are the poor patient tolerance & the increased side effects seen in this group.

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