

Efficacy of Oral Azithromycin for the treatment of Cutaneous Leishmaniasis

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ABSTRACT

Objective: To determine the effectiveness of oral azithromycin for the treatment of cutaneous leishmaniasis.

Study Design: Randomized controlled trial

Place and Duration: outpatient dermatology department nishtar hospital multan, 6 months

Methodology: Fifty six smear positive patients of cutaneous leishmaniasis of either gender were enrolled. Patients ages were 18 to 70 years. All the patients were categorized equally into two groups. Group I with 28 patients received oral azithromycin 500mg/day for 25 days and group II with 28 patients received placebo. Efficacy of oral azithromycin was considered as complete healing leaving behind post inflammatory pigmentation, scarring or normal skin. Patients were followed for 3 months. Data was analyzed by SPSS 24.0.

Results: There were 20 (71.43%) males and 8 (28.57%) were females in group I and in group II 21 (75%) and 7 (25%) patients were male and females. Mean age of patients in group I was 34.26±12.85 years and in group II it was 35.14±12.74 years. At final follow-up 19 (67.86%) patients who received oral azithromycin were cured while in placebo group 12 (42.86%) patients were cured, a significant difference was observed between both groups with p-value <0.05.

Conclusion: Oral azithromycin is safe and effective for the treatment of cutaneous leishmaniasis with no side effects.

Keywords: Cutaneous Leishmaniasis, Azithromycin, Cured.

INTRODUCTION

Leishmaniasis has been found in 98 countries in tropical and subtropical regions of the world to be a neglected vector-borne tropical infection. Every year, worldwide, there are about 2 million new leishmaniasis cases¹. Two main syndromes, visceral and cutaneous leishmaniasis, are the clinically complex disease (VL and CL). Further clinical submissions, such as mucocutaneous, diffuse, and disseminated CL and dermal leishmaniasis post-kala-azar, also occur².

There are few proven treatment options for CL. There are many. While the therapeutic efficacy of standard schemes (20 mg antimony -1 per day 20 days) recorded in some studies in Brazil or 40 percent in Iran, pentavalent antimonials are still first line medicines³⁻⁴.

It will be very necessary to ensure the availability of an appropriate oral drug to treat leishmaniasis effectively. Azithromycin was developed in late eighties at 80^{5,6} and used in the clinical practice for the treatment of a variety of infections⁷, a macrolide derivative structurally associated with erythromycin. Its oral administration, quick transfer into the intracellular compartments, slow release (2-6 days in half-life) and accumulation in various tissues and organs in high concentrations, especially in phagocytic cells, make this medicinal product an attractive treatment choice for intracellular infectious microorganisms. Furthermore, this drug is therapeutic up to 5 days after the final dose given⁸⁻¹⁰.

Azithromycin shows good oral toleration for both children and adults and has been successfully utilised as a single dose in clinical practice for treating diseases, particularly nongonococcal urethritis as well as ocular infections, including trachoma, of the respiratory tract and the skin and for sexually transmitted disorders¹¹⁻¹². This research has been conducted to establish the successful treatment of cutaneous leishmaniasis with oral azithromycin.

MATERIALS AND METHODS

This randomized controlled trial study was conducted at outpatient department of Nishtar hospital Multan for duration of six months from 15 November 2019 to 14 May 2020. The sample of this study comprised of 56 patients. Patients detailed demographics age, sex, and residency details were recorded after taking written consent. Patients with hepatic and renal failure, pregnant women, and those who were medically sick were excluded from this study.

Fifty six smear positive patients of cutaneous leishmaniasis of either gender were enrolled. Patients ages were 18 to 70 years. All the patients were categorized equally into two groups. Group I with 28 patients received oral azithromycin 500mg/day for 25 days and group II with 28 patients received placebo. Efficacy of oral azithromycin was considered as complete healing leaving behind post inflammatory pigmentation, scarring or normal skin. Patients were followed for 3 months. Data was analyzed by SPSS 24.0.

RESULTS

There were 20 (71.43%) males and 8 (28.57%) were females in group I and in group II 21 (75%) and 7 (25%) patients were male and females. Mean age of patients in group I was 34.26 ± 12.85 years and in group II it was 35.14 ± 12.74 years. Out of 56 enrolled cases, 39 (69.64%) patients of rural areas were found and 17 (30.36%) cases of urban areas were found. (table 1)

Table 1: Baseline detailed demographics of enrolled cases

Characteristics	Frequency	Percentage
Group I		
Male	20	71.43
Female	8	28.57
Group II		
Male	21	75
Female	7	25
Mean age		
Group I	34.26 ± 12.85	
Group II	35.14 ± 12.74	
Residence		
Rural	39	69.64
Urban	17	30.36

Single or multiple lesions of skin leishmaniasis were found mostly over the limbs, 31 (55.36%) were upper limbs, 14 (25%) were lower limbs and 11 (19.64%) were on face. (table 2)

Table 2: Distribution of lesions on skin

Variables	frequency	%age
Lesions		
Upper limbs	31	55.36
Lower limbs	14	25
face	11	19.64

At final follow-up 19 (67.86%) patients who received oral azithromycin were cured while in placebo group 12 (42.86%) patients were cured, a significant difference was observed between both groups with p-value < 0.05 . (table 3)

Table 3: Distribution of effectiveness among both groups

Variables	Group I	Group II	P value
Efficacy			
Yes	19 (67.86%)	12 (42.86%)	< 0.05
No	9 (32.14%)	16 (57.14%)	

DISCUSSION

The concentrate of azithromycin in tissues, especially in macrophages that are infected with *Leishmania* parasites, is 100 - 200 times higher than the concentration of serum. For decreasing L, azithromycin is successful. In cell-free culture, major promastigotes and L. Count big amastigotes in the society of macrophages.¹³ In this study fifty six biopsy proven patients of cutaneous leishmaniasis of both genders were presented. Patients were equally divided into two groups, group I with 28 patients received oral azithromycin 500mg/day for 25 days and group II with 28 patients received placebo. Efficacy of azithromycin group was 67.86 % was greater than that of placebo group 42.86%. Our results were comparable to the previous some studies.¹⁴ In two little L. brasiliensis series. 85% infected patients were cured identified having azithromycin (500–

1000 mg/d, 2 to 10 d/mo and maximum 4 month therapy).^{15,16}

Mean age of the patients in group I was 34.26 ± 12.85 while in group II was 35.14 ± 12.74 . Most of the patients 69.64% were from the rural areas and the frequency rate of urban areas were 30.36%. Patients aged between 18 to 70 years. In 2016, intralesional compared to oral chloroquine, Hanif MM et al considered oral chloroquine to be most effective in skin leishmaniasis.¹⁷ In macrophage infected cultures, chloroquine has been found active against intracellular amastigotes.¹⁸ These findings were comparable with our research somehow. In the treatment of old-world CLs (*L. major* and *L. tropica*), two previous studies with azithromycin have been released.^{19,20}

Single or multiple lesions of skin leishmaniasis were found mostly over the limbs, 31 (55.36%) were upper limbs, 14 (25%) were lower limbs and 11 (19.64%) were on face. This can be attributed rather to the effect of associated bacterial infections on the lesions as rapidly as possible. It was possible to determine that the reaction with this medicament occurs more slowly than classically observed with antimonials on the basis of the lesion evolution and the number of cycles used, indicating a leishmaniostatic effect. A recent research has supplemented azithromycin assessment, showing that the models used have a dose-dependent activity.²¹ Other effects of this medicinal product, including phagocytosis stimulation, chemotaxis, cytotoxic activity as well as its immunomodulative action have also been identified.^{22,23}

The efficacy of azithromycin found in this patient series indicates, particularly given the costs-benefit ratio and the fact that the drug is easy for oral use with a single daily dose, that it can be used as a therapeutic choice to treat skin leishmaniasis caused by *L. vi*.

CONCLUSION

Oral azithromycin is safe and effective for the treatment of cutaneous leishmaniasis with no side effects.

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