Oral administration of zinc sulphate in treatment of acute cutaneous leishmaniasis

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Abstract

Background: Due to increasing unresponsiveness and significant side effects associated with antimonial compounds, alternative therapeutic modalities are suggested. Recently oral zinc sulphate has been reported to be effective in the treatment of CL. The aim of this study was to evaluate the efficacy of oral zinc sulphate in the treatment of CL.

Methods: The present study comprised 31 patients with clinical diagnosis of dry type leishmaniasis and parasitologically proven cutaneous leishmaniasis of which 22 patients received a full course of treatment. Patients were treated with 10 mg/Kg/day of oral zinc sulphate for 45 days and were followed through 20 and 45 days of treatment as well as 45 days after cessation of therapy.

Results: Only 2 (9%) of 22 patients were cured after 45 days of treatment with zinc sulphate.

Conclusion: The administration of zinc sulphate for the treatment of CL seemed to be of inadequate therapeutic value.

Keywords: Cutaneous leishmaniasis; Leishmaniasis, Zinc sulphate

Introduction

Leishmaniasis is one of the important protozoal infections in many countries with varying clinical manifestations based on the leishmania species and immunologic response of the host. Variable forms of cutaneous, mucocutaneous and visceral leishmaniasis are transmitted through the bite of infected sand fly. Worldwide, at least 12 million persons suffer from one type of disease and about 2 millions new cases are infected annually. Both cutaneous and visceral forms of leishmaniasis are endemic in different parts of Iran. Etiology of cutaneous leishmaniasis (CL) in Iran is usually Leishmania tropica and Leishmania major and its vector is Phlebotomus papatasi, Phlebotomus Serganti and Phlebotomus ansari. The city of Mashhad, northeastern Iran, is an endemic region for dry type of CL, where in 2002, an outbreak of Anthroponotic Cutaneous Leishmaniasis occurred with almost 4,900 cases detected by clinical and parasitological studies (Khorasan Health Centers Reports 2000-2002).

CL is a self-limiting disease, but must be treated because of its prolonged duration, the generation of ugly scars in exposed areas of the body and destruction of adjacent structures such as ear and nose. In addition chronic lesions or recidivans forms may occur in 4% of cases. World Health Organization has recommended pentavalent antimonials as intramuscular or intralesional injection for treatment of CL. There are several physical and medical therapeutic modalities for treatment of CL with variable results. Glucantime, a pentavalent antimony, is the first-line drug for the treatment of all forms of leishmaniasis in Iran. It prevents the growth of amastigote form of parasite by inhibition of glycolytic activity and fatty acid oxidation. However, some patients with CL who did not respond to pentavalent antimony, might require alternative treatments. L. tropica field isolates with primary resistance to Glucantime and accounting...
for treatment failure are now frequently found in Iran.\textsuperscript{9} Combination therapy, monitoring of therapy, and improved diagnostics could play an essential role in preventing the emergence of parasite’s resistance to newer drugs.\textsuperscript{10} Moreover, the knowledge about the mechanisms of drug action and resistance may allow the development of new medications.\textsuperscript{11-13} Cure rates of CL with Glucantime in different studies from Iran were reported to be 41.7\% (12), 50\% (13), 55.63 \% (14) and 72 \%.\textsuperscript{15} Potential role of zinc in diseases associated with impaired cellular immunity, such as leishmaniasis has already been reported.\textsuperscript{16,17} Zinc was postulated to act directly on the parasite’s enzymatic system.\textsuperscript{18} An in vitro study on axenic amastigotes of Old World CL species showed that both \textit{L. major} and \textit{L. tropica} were sensitive to zinc sulphate and the results were confirmed in an animal model for CL.\textsuperscript{19} Efficacy and safety of intralesional 2\% zinc sulphate has previously been demonstrated,\textsuperscript{18,21} and supported by the recent report on oral zinc sulfate used for treatment of CL in Iraq by sharquie et al.\textsuperscript{22} Considering the safety and the lack of serious side effect,\textsuperscript{14} it seemed likely that zinc sulphate was a useful drug for treatment of CL.

\textbf{Materials and Methods}

This is an open pilot study performed on patients with dry type of CL in Dermatology Clinic of Ghaem Hospital, Mashhad, Iran. The duration of study was five months from Jan 2002 to Jun 2002. Patients with maximum of 3 months duration of CL participated in the study. All cases had positive smears of leishman body and had not taken any effective medication for CL. There was no age restriction with respect to safety of zinc sulfate. The informed consent was obtained from patients or parents of children. Zinc sulfate was administered as 10mg/Kg/day in the form of solution for children and 220 mg capsules for other patients in divided daily doses to reduce GI intolerance. There were no problematic side effects such as nausea and vomiting in any of the patients. Duration of treatment was 45 days and the patients were followed through 20 and 45 days of treatment and 45 days after the end of therapy. The same physician visited all patients and the size of lesions were recorded upon first visit and reevaluated in the ensuing follow-ups. The final clinical response at the end of 45\textsuperscript{th} days of zinc sulfate administration was determined by reduction in size of lesions and graded as follows: No response: no reduction in size, Mild: by up to 30\%, Moderate: by 30-60\%, Marked: by > 60\%, in which parasite were not detected in the smears prepared from affected areas, and complete disappearance of the lesion.

Both marked reduction and total clearance were considered as cured.

\textbf{Results}

A total of 31 patients, 10 males (32\%) and 21 (68\%) females, were included in this study. The patients aged from 1-80 years (22.4\pm7.3). The numbers of lesions were 1-4 (2.1\pm0.3). The most common form of lesions was plaque (64\%) with face being the most frequent site of lesion (67\%), followed by hand as the second site (28\%). All patients had clinical features of dry or urban type of cutaneous leishmaniasis. A total of 22 patients, 7 (32\%) males and 15 (68\%) females, completed the course of treatment and follow up period. However, 9 cases were excluded from the study because of not completing the follow up period, and concomitant use of other drugs or traditional therapy. Patients who completed the treatment and follow up period were between 1 to 80 years old (18.9\pm6.5). Numbers of lesions were 1 to 4 (2.3\pm0.2) with mean duration of disease being 2.4\pm0.2 months. Cure rates in terms of reduction in size of lesion upon 45 days of treatment with zinc sulfate involved 17 cases (77.5\%) with no reduction in the size of lesions, one case (4.5\%) with up to 30\%, and 2 cases (9\%) with 30-60\% reduction in size of lesion. However, only two cases (9\%) were cured, one with > 60\% reduction in the size of lesions in which parasite were not detected in the smears prepared from affected area and another with complete disappearance of the lesion. The drug did not have any serious side effects, except in one case that developed swelling around the lesion. The lesions remained unchanged in 20 cases that were not cured 45 days after cessation of treatment.

\textbf{Discussion}

Cutaneous leishmaniasis is endemic in some regions of Iran with Khorasan Province, northeastern Iran, being an important focus of CL.\textsuperscript{6} Suburbs of Mashhad city (Capital of Khorasan Province) are common sites for CL. Several physical modalities such as cryotherapy, local heat, excision, curettage or laser and systemic
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drugs such as Glucantime, ketoconazole, Itraconazole, Rifampin, Dapson, Metronidazol, Chloroquine, and miltefosine, are used for treatment of CL with variable results. Antimonials are recognized as standard treatment for CL. With respect to adverse effects of drug and unacceptable route of administration of this compound for children, who are at great risk of developing serious side effects, it seemed necessary to find a safe and cost-effective topical or oral treatment. According to the study of sharquie et al., oral zinc sulfate in 10 mg/Kg/day with a mean of 28.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeutic results (96.9 % cure rate). 22.32±1.35 days was safe with excellent therapeuti...


