Original Article

Cutaneous Leishmaniasis

Efficacy and Safety of Glucantime for Cutaneous Leishmaniasis – Eight Years Experience at A Tertiary Care Hospital of Karachi

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ABSTRACT

Objective: To observe the efficacy and adverse effect profile of Glucantime in treatment of cutanous leishmaniasis.
Study Design: Cross sectional study
Place and Duration of Study: This study was conducted in Dermatology Department, JPMC Karachi from Jan 2007 to Jan 2015.
Materials and Methods: 252 patients of CL, diagnosed clinically and confirmed parasitologically were treated with injection glucantime. After taking history and physical examination, baseline complete blood count ,Liver function tests, Renal function tests and ECG were performed.76 patients were treated with intralesional injection and 156 patients were treated with intramuscular Glucantime. Treatment response was observed and adverse effects were noted. The data was recorded and analysed on SPSS version 16. Mean ±SD was calculated for continuous variables like age, duration of disease. Categorical values like gender, type, morphology, site of lesions efficacy and adverse effects were recorded as numbers and percentages.
Results: The mean age of I/L group was 31.4 ±11.6and for I/M group. Efficacy of intramuscular Glucantime was 76.3% in intralesional group and 86.9%in intramuscular group. Adverse effects were seen in 25 % of intralesional and 26.9 %of intramuscular group.
Conclusion: Glucantime is effective and well tolerated drug in Old World CL both by intramuscular or intralesional route.
Key Words: Cutaneous Leishmaniasis, glucantime, interalesional, intramuscular, efficacy.

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INTRODUCTION

Cutaneous Lieshmanisis(CL) is endemic in 98 countries of world. WHO Estimates annual incidence of 0.7 to 1.2 million new cases world wide.[1]In the Old World (the Eastern Hemisphere), CL is found in some parts of Asia, Middle East, Africa and Southern Europe.[2] In Pakistan CL is prevalent in certain belts of Khyber Pakhtunkhawa, coastal areas of Baluchistan, interior sindh and scattered areas of Punjab.[2]It is a parasite borne disease caused by protozoa Leishmania. Its incidence is increasing creating a major public health problem. Up to 20 species of CL have been found to be pathogenic. L.Major, L. Tropica, and L. infantum are major pathogens found in Asia and Africa. S. Ayub et al. conducted a study on thirty patients in multan for species identification and found all cases were caused by L. Tropica.[3]Incubation period is variable, ranging from few days to a year. Final outcome depends upon host immune status and pathogen interactions. Lesion may heal itself over a period of 1 to 2 years depending upon immune status of host, leaving a cribriform scar.

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[4]The main concerns are unsightly appearance, disfiguring scar and chances of spread. The aim of treatment is to speed up healing and limits scarring.[5]
Various Local and systemic treatment options have been used for its treatment over years. Pentavalent antimonials are, however, drug of choice. Although meglumine antimonite (Glucantime®, sanofi, France)have been used for about eight decades for treatment of cutaneous Lieshmiasis, both intralesional and intramuscular ,the main problems with this drug is its parenteral route, long duration of treatment and reports of many potentially serious adverse effects. Resistance to antimonials is also being reported from different regions of world.[6]There is paucity of data regarding efficacy and safety of this drug in Pakistan. Firdous et al conducted a study on troops deployed in Baluchistan which showed overall response rate of 81% and adverse effects in 14% of patients.[11]
The aim of present study was to observe the treatment response and adverse effect profile of intralesional and intramuscular glucantime for treatment of CL in our patients.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted in Dermatology Department Jinnah Postgraduate Medical

centre, Karachi, from January 2007 to January 2015. 252 patients of CL diagnosed by trained clinician and confirmed parasitologically by slit skin smear or histopathology were enrolled .Complete history was taken and physical examination was done. Age, duration, site and number of lesions, type and morphology, previous treatment used, co-morbid conditions like hepatic, cardiac or renal disease, any known drug allergy were recorded. Baseline Complete blood count, Liver function tests, renal function tests, ECG and chest x-ray were performed. These investigations were repeated weekly during course of treatment. Adverse effects symptoms were asked and recorded. Those patients having <3 lesions, sites not on face joints or adjacent to vital structures, sporotrichoid and Lupoid leishmaniasis were treated with Intralesional glucantime. Injection glucantime was infiltrated with an insulin syringe around the lesion till blanching of lesions.The injection was repeated every 3rd day. The patients who had >3 lesions, sites on face or near joints, sporotrichoid and lupoid Leishmaniasis and those who failed intralesional therapy were treated with intramuscular Glucantime, given intragluteally in doses of 20mg/kg of body weight for 21 days. Ulcer charting was done and infiltration was measured during the course of therapy to see the response. Responders were defined as at least 70%reduction in infiltration or ulcer size after 21 days of therapy. The patients were followed for 6 weeks after therapy.

The data was recorded and analysed on SPSS version 16. Mean ±SD was calculated for continuous variable like age, duration of disease. Categorical values like gender, type, morphology, site of lesions, efficacy and adverse effects were recorded as numbers and percentages.

RESULTS

A total of 252 patients of CL were studied during the period of 8 years, among them 156 were treated with intramuscular glucantime and 76 were treated intralesional injection.: The mean age of I/L group was 31.4 ±11.6and for I/M group. Efficacy of Intramuscular Glucantime was 76.3% in intralesional group and 86.9%in intramuscular group. Adverse effects were seen in 25 % of intralesional and 26.9 %of intramuscular group. Clinical and demographic profile of patients is presented in table 1. Efficacy was recorded for I/Land I/M group and is shown in table -2,adverse effects are shown in Table 3.

DISCUSSION

Glucantime has been considered as the drug of choice for CL since it was first used in 1929.[7] The active compound of glucantime is Pentavalent antimony.[8] Although CL is a self-healing condition, treatment is indicated to reduce the duration of illness, and morbidity caused by persistent lesion, on face or near joint and to prevent dissemination to skin, mucosa and viscera. Exact mechanism of its Leishmanicidal action is not known how ever it is postulated that it is converted into active trivalent compound and inhibits parasitic phosphofructokinase, glycolytic and oxidative pathways of therefore reducing ATP synthesis required for parasite survival resulting in death of parasite.[8]It may be given intramuscularly or intralesionally in selected patients. Intarlesional injection for cutaneous leishmaniasis was first used in Algeria and was approved by WHO. It is popular and effectively used for selected cases.[9]

Table No.1: Clinical and demographic characteristics of patents (n=252)

Parameter	Intralesional group(I/L) N=76	Intramuscular group(I/M) N=156
Age(years)		
Mean±SD	31.4 ±11.6	29.1 ±13.4
Min-Max	10 -60years	2-60 years
Gender		
Male	46	98
Female	30	58
Duration of disease		
<3months	32	88
>3months	24	68
Mean ±SD	7.4±4.2	6.36±5.2
Site of lesion		
Lower Limb	30	91
upper limb	24	40
Face	-	16
Trunk	2	3
Type of Lesion		
Dry	24	50
Wet	52	106
Morphology of lesion		
Volcano ulcer	35	88
Nodular	12	12
Plaque	14	23
Ulcerated	08	14
sporotrichoid	0	07
Verrucous	07	05
Lupoid	0	04
Others	01	03
Total	**76**	**156**

Table No.2: Efficacy of glucantimeintralesional(I/L) and intramuscular (I/M) group

Response	Intralesional group (I/L) n=76	Intramuscular group (I/M) n=156
Responders	58(76.3%)	140(89.7%)
Non-responders	18(23.7%)	16(10.3%)
Total	76	156

Table No.3:- Adverse effects of Intralesional(I/L) and Intramuscular group(I/M)

Adverse effects	Intralesional group(I/L) n=76	Intramuscular group(I/M) n=156
Local reaction	7	8
Secondary infection	6	4
Arthralgia and myalgia	3	12
Headache	2	10
Fever	-	8
Anorexia	-	1
Anaphylactic Reaction	-	1
Haematological	-	-
Raised ALT	-	4
Cardiac	-	-
Vasovagal syncope	1	-
Total	19(25%)	42(26.9%)

There are variable results of studies regarding efficacy of drug in old world CL.In Pakistan Firdous et al conducted a study on troops deployed in Baluchistan which showed overall response rate of 81%.[10]A study in Iran by Mohammadzadeh M et al showed overall high failure rate (22.6%).[11]There are reports of increasing overall resistance of Leishmaniasis for Glucantime. .B. Parmochanadi et al in Iran found 34.9% were clinically unresponsive. [12]The difference in treatment response might be due to different species of leismania and genomic variation.[13]. In this study we found the response rate to be 76.3% for intramuscular group and 86.9% for intralesional group.

Treatment with glucantime has been associated with many adverse effects..The commonly observed adverse effects are however mild like fever, arthralgias and myalgias, anorexia.[14] Few serious complications like renal failure, pancreatitis, cardiac and haematological have been reported.[15,16,17]Side effects are dose dependant and are directly related to concentration of antimony in plasma and skin of patient. [18]Malika RB etal reported adverse effects 17 out of 67 patients (25%) in Tunisia.[19]Another study by masmoudi A et al found adverse reactions in 19% of patients.[20]Dar NR etal observed Glucantime fever to be common side effect which may result in massive investigations to search cause of fever if drug fever is not kept in mind.[21] In our study we found that the frequency of adverse effects in I/L group to be 25% .Local reactions and secondary infections are common which can be treated with antibiotics and NSAIDS. One case of vasovagal syncopy with bradycardia was observed who recovered. Systemic adverse effects with I/Lglucantime are minimal. Among the patients treated with I/M injections, adverse effects were 26.9% Most of these adverse effects were mild, arthralgia and myalgia being most common followed by headache, fever and anorexia. Two cases of injection site necrosis following I/M injection were observed which required surgical debridement. One case of non- fatal anaphylactic reaction immediately after test dose was observed. No case of severe adverse event like cardiac, renal or pancreatitis was recorded. ALT was deranged in four patients.

The limitations of study are retrospective study design, species identification of parasite was not done due to limited resources and origin of patients could not be done as resistance may be prevalent in certain regions than others.

CONCLUSION

Therefore our study concludes that Glucantime is effective and well tolerated drug in Old world CL. However, search for alternative drugs should be continued as to avoid development of resistance against this drug.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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