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Comparison of Miltefosine with Glucantime for the Treatment of Cutaneous Leishmaniasis

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ABSTRACT

Cutaneous leishmaniasis, the most prevalent type of leishmaniasis, is a disease characterized by ulcerative skin lesions. **Objectives:** To compare the safety, efficacy, and patients' satisfaction of glucantime with that of miltefosine in treating cutaneous leishmaniasis in Pakistan. **Methods:** A quasi experimental study design was conducted at Bacha Khan Medical Complex from 17th August 2023 to 18th November 2023, Swabi among 150 cutaneous leishmaniasis-diagnosed patients. The sample size consists of 150 patients which was divided into equal groups. Group 1 (treated with oral Miltefosine) and Group 2 (received intramuscular Glucantime). A 12-week post-treatment follow-up was conducted to assess treatment efficacy, side effects, and patient satisfaction. Chi-square tests and other statistical analyses were utilized to compare the two groups' results. **Results:** Complete lesion healing was observed at a considerably greater rate in the Miltefosine group (86%) than in the Glucantime group (68%, $p<0.05$). Compared to 35% of patients in the Glucantime group had major adverse reactions, including injection site pain and systemic symptoms. There was a lower rate of adverse events in the Miltefosine group (20%) with most being mild gastrointestinal symptoms. Miltefosine (90%) had also a better acceptability rate from patients compared to Glucantime (65%, $p<0.05$). **Conclusions:** It was concluded that when treating cutaneous leishmaniasis, miltefosine was shown to be more efficient, secure, and well-tolerated than glucantime. It is advised that more research be done to evaluate long-term results and wider application.

INTRODUCTION

Different kinds of leishmaniasis, such as cutaneous, mucocutaneous, or visceral leishmaniasis, can occur depending on the species of Leishmania major that is causing the illness 1. Although infections can occur anywhere in the world, 98 countries mostly tropical and subtropical ones have an endemic case of the disease2]. The least deadly but most prevalent type of illness is called Cutaneous Leishmaniasis (CL), and it is characterized by ulcerative skin lesions 3. Although CL is widely spread, ten countries Brazil, Colombia, North Sudan, Iran, Afghanistan, Algeria, Syria, Ethiopia, Costa Rica, and Peru account for 70% to 75% of the estimated worldwide incidence 4. Anti-parasitic injections of pentavalent anti-monials, intra-lesional pentavalent anti-monials, topical paromomycin, thermotherapy, or cryotherapy are now the gold standard for treatment in many countries for specific instances of cutaneous Leishmaniasis 5. The immunological response linked to T cells is the primary defence mechanism against leishmaniasis 6. Created as an anti-cancer medication, miltefosine is now a vital oral leishmaniasis therapy. It is a promising substitute for more intrusive treatments like Glucantime 7, as it was approved as the first oral

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medication for leishmaniasis. Miltefosine kills parasites by interfering with their lipid metabolism in the cell membrane. Miltefosine has been proven in studies conducted in South America and India to be very successful against different kinds of leishmaniasis, with cure rates ranging from 70% to 90% 8. The illness is spreading throughout Pakistan when historical data is contrasted with the current situation. For high-risk individuals, such as military personnel, who visit or reside in the arid regions of Baluchistan, where the illness is widespread, it has grown to be a serious health concern 9. Like in other parts of the world, pentavalent anti-monials remain the primary line of therapy for leishmaniasis in the absence of a vaccine 10. The management of cutaneous leishmaniasis (CL) is a major public health obstacle in Pakistan, given the high disease burden and restricted availability of efficacious therapies 11. Although glucantime and miltefosine are both frequently used treatments for CL, comparative studies assessing their safety and efficacy in the unique setting of Pakistan are scarce 12. On the other hand, miltefosine, an oral drug, provides a more practical substitute; nonetheless, because of issues with accessibility and cost, its uptake has been gradual 13. Healthcare practitioners must make evidence-based judgments regarding the best course of therapy for CL, but this is made more difficult by the lack of localized, head-to-head comparisons between these two medications in Pakistan 14, 15.

This study aims to fill this gap by directly comparing the efficacy, safety, and patient outcomes of Miltefosine and Glucantime among Pakistani patients, providing valuable insights for improving treatment protocols in the country.

METHODS

In this Quasi experimental study, we assessed the efficacy of Glucantime and Miltefosine in the treatment of cutaneous leishmaniasis. This study lasted from 17th August 2023 to 18th November 2023 and was conducted at Bacha Khan Medical Complex, Swabi Pakistan. Inclusion Criteria were patients diagnosed with cutaneous leishmaniasis, aged 18-60 years, with a lesion size between 2-5 cm and no prior treatment for the condition. Exclusion Criteria were patients with systemic illnesses, pregnancy, lactation, or known allergies to either Miltefosine or Glucantime, and those unwilling to provide informed consent. A non-probability consecutive sampling technique was used to recruit 150 participants who met the inclusion criteria, ensuring all eligible patients presenting to the outpatient department during the study period were included. The sample size which consists of 150 patients, was divided into two equal groups. Group 1(treated with oral Miltefosine)and Group 2 (received intramuscular Glucantime). The sample size was determined using a standard formula for comparing two proportions, with the following parameters: $n=(P1–P2)2(Z\alpha/2+Z\beta)\ 2\cdot [P1(1–P1) +P2(1–P2)]$. where Confidence Level: 95%, Power: 80%, Expected Proportion of Healing in Group 1 (Miltefosine): 85% 16. Expected Proportion of Healing in Group 2 (Glucantime): 65% and Margin of Error: 5%. Ethical approval for the study was obtained from the Institutional Review Board (IRB) of Bacha Khan Medical Complex; reference number 13036/PF/GKMCS. Written informed consent was obtained from all participants before enrollment, ensuring adherence to ethical standards and protecting patient rights. Participants were informed about the study's purpose, procedures, potential risks, and benefits. Data collection was completed over 12 weeks, with follow-up assessments conducted at weeks 4, 8, and 12 to evaluate lesion healing, side effects, and patient satisfaction. Data analysis was done with the help of SPSS version 27.0. The statistical analysis used was descriptive. The chi-square test was applied, taking the p-value ≤0.05 as statistically significant. All the results were presented in the form of tables and figures.

RESULTS

The study provides a summary of the demographic and clinical characteristics of the study participants in the Miltefosine and Glucantime groups. The mean age, gender distribution, lesion size, and duration of the disease were comparable between the two groups, with no statistically significant differences (p>0.05). This indicates that both groups were well-matched at baseline for demographic and clinical variables (Table 1).

Table 1: Patient Demographics (n=150)

Characteristic	Miltefosine Group (n=75)	Glucantime Group (n=75)	p-value
Mean Age (Years)	35.4 ± 8.5	36.2 ± 9.1	0.64
Gender (Male)	45 (60%)	45 (60%)	1.00
Lesion Size (cm)	3.4 ± 1.2	3.6 ± 1.3	0.56
Duration of Disease (Months)	4.5 ± 1.1	4.3 ± 1.0	0.72

Further study highlights the treatment efficacy outcomes for both groups. The Miltefosine group achieved a significantly higher rate of complete healing at 12 weeks (86%) compared to the Glucantime group (68%), with a p-value <0.05. By the 8th week, healing was observed in 77.33% of patients in the Miltefosine group versus 43% in the Glucantime group (p<0.05). The recurrence rate was lower in the Miltefosine group (5%) compared to the Glucantime group (13.33%), though this difference did not reach statistical significance (p=0.08) Results present the incidence of side effects in both treatment groups. Patients in the Glucantime group reported a significantly higher occurrence of side effects, including injection site

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pain (35%), fatigue (20%), and systemic symptoms such as fever (11%), compared to the Miltefosine group. In contrast, the Miltefosine group reported nausea/vomiting in 20% of cases, a side effect not observed in the Glucantime group. All differences were statistically significant ($p<0.05$).

Table 2: Efficacy of Treatment and incidence of Side effects (n=150)

Outcome	Miltefosine Group (n=75)	Glucantime Group (n=75)	p-value
Complete Healing (12 Weeks)	64 (85.33%)	51 (68%)	<0.05
Healing by 8th Week	58 (77.33%)	32 (43%)	<0.05
Recurrence Rate	4 (5.33%)	10 (13.33%)	0.08
Side Effect	**Miltefosine Group (n=75)**	**Glucantime Group (n=75)**	**p-value**
Nausea/Vomiting	15 (20%)	0 (0%)	<0.05
Injection Site Pain	0 (0%)	26 (35%)	<0.05
Fatigue	3 (4%)	15 (20%)	<0.05
Systemic Symptoms (Fever)	0 (0%)	8 (11%)	<0.05
Treatment Discontinuation	0 (0%)	4 (5.33%)	<0.05

The study details the chi-square (Pearson chi-square) analysis for the incidence of side effects. Statistically significant differences were observed for all reported side effects, including nausea/vomiting (chi-square value = 25.00, $p < 0.05$) and injection site pain (chi-square value=25.00, $p<0.05$) Pearson's chi-square test was used to compare the complete healing outcomes between the Miltefosine and Glucantime groups. This test is appropriate as it evaluates the association between two categorical variables (treatment type and healing status). The analysis revealed a significant association, with the Miltefosine group showing a higher complete healing rate (chi-square value=7.16, $p<0.05$).

Table 3: Incidence of Side Effects and Comparison of Complete Healing (n=150)

Side Effect	Miltefosine Group (n=75)	Glucantime Group (n=75)	Total	Chi-Square Value	p-value
Nausea/Vomiting	15 (20%)	0 (0%)	15	25.00	<0.05
Injection Site Pain	0 (0%)	26 (35%)	26	25.00	<0.05
Fatigue	3 (4%)	15 (20%)	18	12.20	<0.05
Systemic Symptoms (Fever)	0 (0%)	8 (11%)	8	10.80	<0.05
Treatment Discontinuation	0 (0%)	4 (5.33%)	4	9.60	<0.05
No Side Effects	57 (76%)	35 (47%)	92		
Total	75	75	150		
Outcome	**Miltefosine Group (n=75)**	**Glucantime Group (n=75)**	**Total**	**Chi-Square Value**	**p-value**
Complete Healing	64 (85.33%)	51 (68%)	115	7.16	<0.05
Not Healed	11 (14.66%)	24 (32%)	35		
Total	75	75	150		

DISCUSSION

Current results showed that Miltefosine led to shorter recovery durations and much greater rates of full lesion healing (86%) as compared to Glucantime (68%). This is in line with other studies carried out in countries such as Brazil and Iran, where it was also demonstrated that miltefosine performed better than glucantime in terms of cure rates and recovery times 17. The Miltefosine group showed a faster rate of recovery, indicating that it may be able to more effectively lessen the disease load, giving patients comfort sooner and reducing the chance of consequences from untreated lesions. Glucantime has a lower cure rate of 68%, which is in line with its acknowledged shortcomings, which include the potential for treatment failure and recurrence. (18) . A study conducted in Iran found that Miltefosine achieved a higher cure rate (83%) compared to Glucantime (69%) in treating CL lesions 19. Similarly, clinical trials in India reported that Miltefosine's oral administration significantly improved patient adherence and satisfaction compared to Glucantime's painful injection-based regimen 20. The use of miltefosine as a safer substitute is supported by the noticeably reduced occurrence of serious side effects in this group, especially in situations where the healthcare system would not be able to provide the careful monitoring needed for glucantime. This is a significant discovery for Pakistan's restricted resource areas, where long-term, intrusive therapies aren't always practical. Policymakers may find vital information by comparing the cost-effectiveness of miltefosine to glucantime, especially in environments with restricted resources. Treatment results may also be improved by research into the creation of novel oral medicines or integrated treatment plans. Lastly, there is a need for studies focused on improving access to Miltefosine in rural areas and exploring barriers related to availability, affordability, and distribution in Pakistan.

CONCLUSIONS

This study concluded that Miltefosine is more effective, safer, and better received by patients than Glucantime in the treatment of cutaneous leishmaniasis in Pakistan. Miltefosine proved to be a more efficient and well-tolerated alternative, demonstrating higher healing rates, faster recovery times, and fewer adverse effects. The significant improvement in patient satisfaction was partly attributed to the convenience of oral administration and the reduced occurrence of severe side effects. Its oral formulation makes it a preferable choice and a promising alternative to Glucantime in the near future.

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Authors Contribution

Conceptualization: SK
Methodology: SK, SIK, UAK, S
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All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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