Open Access

Original Article

# Comparison of Electrocardiographic Changes Induced by Injection Meglumine Antimoniate after Intravenous Versus Intramuscular Administration in Patients of Cutaneous Leishmaniasis

**Shafia Shaikh, Najia Ahmed, Hafiz Muhammad Umer*, Moniba Saeed**

Department of Dermatology, Combined Military Hospital Quetta/National University of Medical Sciences (NUMS) Pakistan,
*Department of Medicine, Combined Military Hospital Quetta/National University of Medical Sciences (NUMS) Pakistan

## ABSTRACT

***Objective***: To compare the electrocardiographic changes induced after intravenous versus intramuscular administration of injection meglumine antimoniate in patients with cutaneous leishmaniasis.
***Study Design***: Quasi Experimental Study.
***Place and Duration of Study***: Department of Dermatology, Combined Military Hospital, Quetta Pakistan, from April to October 2024.
***Methodology***: A total of 80 patients with biopsy-proven cutaneous leishmaniasis were divided into intravenous (Group-A) and intramuscular (Group-B) groups. The intravenous group received 15mg/kg/day of meglumine antimoniate diluted in 100 ml of 5% glucose solution over 60 minutes with cardiac monitoring, while the intramuscular group received a similar dose as per weight into the gluteal muscles. ECG was done before the start of treatment and then weekly. Only 03 patients lost to follow so data analysis was done on 77 patients.
***Results***: Mean age of the patients was 30.60±6.35 years. Out of 77, 24(30.0%) patients experienced ECG changes in both groups: T wave inversion in 14(17.5%), Bifid T-wave in 4(5.0%), and QT prolongation in 2(2.5%). A higher proportion of ECG changes occurred in the Group-A (n=14, 35.0%) compared to the Group-B (n=10, 25.0%), but the difference was not statistically significant ($p$=0.210). The ECG changes were statistically insignificant when stratified for route of administration, number of lesions, and number of injections except for QT prolongation ($p$=0.004)
***Conclusion***: Electrocardiographic changes were more frequent in patients using the intravenous route compared to intramuscular administration, but the results were statistically insignificant.

**Keywords**: Cutaneous Leishmaniasis, ECG, Meglumine Antimoniate, Sandfly.

***How to Cite This Article:*** *Shaikh S, Ahmed N, Umer HM, Saeed M. Comparison of Electrocardiographic Changes Induced by Injection Meglumine Antimoniate after Intravenous Versus Intramuscular Administration in Patients of Cutaneous Leishmaniasis. Pak Armed Forces Med J 2026; 76(Suppl-8): S1292-S1295. DOI: https://doi.org/10.51253/pafmj.v76iSUPPL-8.14124*



## INTRODUCTION

Leishmaniasis is a parasite-borne disease caused by the Leishmania protozoa, with sandfly as vector is sandfly.[1] Cutaneous, mucocutaneous, and visceral are the three presentations of disease. Americas, the Mediterranean basin, the Middle East, and Central Asia constitute about 95% of cases of Cutaneous leishmaniasis (CL).[2] According to WHO, each year around 600,000 to 1 million new cases occur globally.

CL can be treated by local or systemic therapy.[3] Systemic drugs are pentavalent antimonial, azole antifungals (fluconazole, itraconazole, ketoconazole), chloroquine, allopurinol, and dapsone.[4] Pentavalent antimonial, such as Meglumine Antimoniate (MA), remains the first-line treatment of CL and can be administered by various routes: intralesional (IL), Intramuscular (IM), and intravenous (IV).[5] Systemic administration of MA is associated with fever, fatigue, headaches, myalgias, raised amylase and lipase levels, gastrointestinal disturbance, and electrocardiographic (ECG) changes.[6] Common cardiac manifestations are alterations in repolarization, primarily impacting the T wave and the ST segment. Other cardiac side effects include QT interval prolongation, torsade de pointes arrhythmias, and sudden cardiac death.[7] Although these complications exist, MA can still be safely administered systemically, with careful cardiac monitoring (ECG), for the treatment of CL.[8] The recommended approach is that treatment can be continued until there are no arrhythmias in ECG, prolonged PR interval >500ms, or no ST-segment changes.[9]

Aim of our study was to compare the frequency of ECG changes between two different modes of drug delivery, IV versus IM.

## METHODOLOGY

This quasi-experimental study was conducted at Combined Military Hospital Quetta, Pakistan after approval from the Institutional Ethical Review Board (CMH QTA-IERB/18/2024) from April to October 2024.

**Correspondence: Dr Shafia Shaikh,** Department of Dermatology, Combined Military Hospital, Quetta Pakistan
*Received: 12 Dec 2025; revision received: 06 Mar 2026; accepted: 09 Mar 2026*

**Inclusion Criteria**: Patients of either gender with age ranging from 15-70 years, biopsy-proven cutaneous leishmaniasis, and those fulfilling the requirement of systemic antimonial therapy with more than 3 lesions, plaque size over 4 cm, non-healing ulcer longer than 4 months, cutaneous sores which heal with disfiguring or disabling scars (such as on face, hand and large joints) and/or with sporotrichoid spread were included.

**Exclusion Criteria**: Patients with known comorbidity (diabetes, hypertension, tuberculosis, hepatitis, cardiovascular disease), pre-existing cardiac disease, known hypersensitivity to meglumine antimoniate, children, pregnant and nursing mothers, and those with abnormal ECG changes at the time of enrollment were excluded.

The sample size calculated was 80 using the WHO sample size calculator with an estimated prevalence of 2.7% of CL in Baluchistan.[9] Total of eighty patients were enrolled by non-probability consecutive sampling technique after informed consent.

Patients were divided prospectively by the investigator into two groups of 40 patients each. Complete blood count, liver function test, renal function test, serum amylase and ECG were done in each case before starting the treatment. For cardiac evaluation, we also performed serum electrolytes (serum Na+, K+, Ca++, Mg++), cardiac enzymes and echocardiography, evaluated by a medical specialist in each case before the start of treatment. WHO recommends both IV and IM MA for treatment of CL. It is available as Glucantime, by Sanofi Aventis. Group-A was given IV MA at a dose of 15mg/kg, diluted in 100ml of 5% dextrose water, for over 60 minutes. Group-B was given IM MA at a same dose of 15mg/kg until lesion cure was achieved. Three patients were lost to follow up.

ECG was done weekly. If any patient had a change in ECG, it was repeated daily to see the progression. Serum electrolytes, cardiac enzymes, and echocardiography were repeated if a patient developed an ECG change during treatment, and they were followed weekly until the lesion was completely cured. Eighty participants of biopsy proven leishmaniasis were recruited at the start of study out of which only 3 missed a part of intervention due to their personal reasons. The analysis was done on sample size of 77, 39 in Group-A and 38 in Group-B. Patient flow can be seen in Figure.

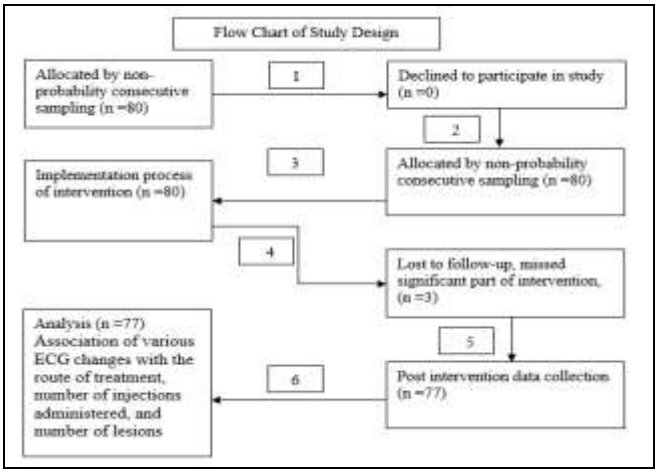


**Figure: Patient Flow Diagram (n=77)**

Data analysis was done using Statistical Package of Social Sciences version 27. Descriptive statistics were used to represent data. Data was stratified by treatment and potential side confounders. Post-stratification, the Chi-square test and Fisher's exact test were applied to compare the mean differences in efficacy of the two groups, wherever applicable. A *p*-value ≤0.05 was considered statistically significant.

## RESULTS

In this study we compared the cardiac implications of modes of drug delivery during treatment of cutaneous leishmaniasis. The mean age of patients was 30.60±6.35 years. The mean age in Group-A was 29.55±6.99 and in Group-B was 31.65±5.52 years. In both groups, all patients were male. Overall, patients had a median of 2.50 (1.00-4.00) lesions. The median number of days at which cure achieved was 40.00 (33.25-54.00) as shown in Table-I. A total of 24(30.00%) of patients experienced ECG changes.

**Table-I: Baseline Characteristics and Clinical Features (n=77)**

| Characteristic | Total Population (n=77) | Group-A (n=39) | Group-B (n=38) |
|---|---|---|---|
| Age in years (Mean ±SD) | 30.60±6.35 | 29.55±6.99 | 31.65±5.52 |
| Median number of lesions | 2.50 (1.00-4.00) | 3 (1.25-4.00) | 2.00 (1.00-4.00) |
| Median number of days at which cure is achieved | 40.00 (33.25-54.00) | 36.00 (33.00-40.00) | 53.00 (41.25-58.75) |

A higher proportion of patients suffered from ECG changes in the Group-B (n=14 35%) as compared to Group-A (n=10, 25%, *p*=0.210). The most common ECG change was T wave inversion in both treatment groups. Neither the presence of ECG changes nor any specific ECG morphology (bifid T waves, bradycardia, or T wave inversion) was statistically significant among the two treatment groups as shown in Table-II.

**Table-II: Association of ECG changes with the Route of Treatment, Number of Injections Administered, and Number of Lesions (n=77)**

| Stratification by Route of Administration | | | |
|---|---|---|---|
| **ECG Change** | **Group-A (n=39) n(%)** | **Group-B (n=38) n(%)** | ***p*-value** |
| T wave inversion | 8(20.00%) | 6(15.00%) | 0.556 |
| Bifid T wave | 3(7.50%) | 1(2.50%) | 0.305 |
| Tall T wave | 3(7.50%) | 1(2.50%) | 0.305 |
| QT Prolongation | 2(5.00%) | - | 0.152 |
| **Stratification by number of Lesions** | | | |
| | **Group-A (n=39) n(%)** | **Group-B (n=38) n(%)** | ***p*-value** |
| | **≤3 Lesion** | **>3 lesions** | |
| T wave inversion | 12(15.00%) | 2(2.50%) | 0.158 |
| Bifid T wave | 3(3.75%) | 1(1.25%) | 0.823 |
| Tall T wave | 3(3.75%) | 1(1.25%) | 0.823 |
| QT Prolongation | 1(1.25%) | 1(1.25%) | 0.532 |
| **Stratification by number of Injections** | | | |
| | **Group-A (n=39) n(%)** | **Group-B (n=38) n(%)** | ***p*-value** |
| | **≤30 Injections** | **>30 Injections** | |
| T wave inversion | 1(1.25%) | 13(16.25%) | 0.185 |
| Bifid T wave | - | 4(5.00%) | 0.305 |
| Tall T wave | - | 4(5.00%) | 0.305 |
| QT Prolongation | 2(2.50%) | - | 0.004 |

**ECG: Electrocardiography. T wave inversion: negative deflection after QRS complex more than 3mm. Bifid T wave: Notched or split T wave. Tall T wave: increase in amplitude of T waves. QT prolongation: QT interval >440ms*

## DISCUSSION

This study was conducted to compare the cardiac changes induced by intravenous (IV) versus intramuscular (IM) Meglumine Antimoniate (MA) in patients of Cutaneous Leishmaniasis (CL). Our study indicates that both IV and IM MA can cause ECG changes; however, the frequency and types of changes differ in both groups, though not statistically different. The median age of patients was 29.55±6.99 years in IV and 31.65±5.52 years in Group-B, while the mean age of patients in a study conducted by Afridi *et al.*, was 37.82 years, higher than our study population.[10] The difference may be attributable to the fact that in a far-flung area of Baluchistan, young people are more likely to reach for healthcare facilities. In our study, all patients were male, in contrast to the study by Sadhegian *et al.*, which had 46(35%) female and 85(65%) male patients.[11] This difference can be explained by behavioral, occupational, and socio-cultural factors. Increased exposure of male to sandfly is due to their more outdoor activities. In a study by Tahir *et al.*, the mean number of lesions were 3.03±1.072, similar to median number of lesions in our study that is 2.50 (1.00-4.00).[12]

Antezana *et al.*, observed that 45% of patients on antimony had ECG changes that principally affected repolarization (T wave and the ST segment), which is consistent with the majority of ECG abnormalities in our study, 26.3% out of 27.5% displaying T wave alteration.[13] In a study by Abid *et al.*, overall 41(68.33%) patients had ECG changes, 5(8.33%) of which had bradycardia and 9(15%) tachycardia, while in our study, only one patient (2.5%) in Group-A had bradycardia and none had tachycardia.[14] Sanehsaz *et al.*, also didn't observe any case of tachycardia with MA.[15] The variation can be ascribed to different demographics of study population and variation in sample size. Serious cardiac complications such as severe dilated cardiomyopathy as reported by Salah *et al.*, and sinoatrial block reported by Daadaa *et al.*, were not seen in our study.[16,17] Possible explanation to this may be vigilant ECG monitoring and adherence to treatment protocol, in addition to difference in sample size and study design. Rodrigues *et al.*, reported that 4(7.69%) of patients developed cardiac complications with IV MA, and Lyra *et al.*, documented cardiotoxic effects in 25.4% with IM drug delivery.[18,19] This is contrary to our study in which Group-A exhibited more cardiac complications 35% than Group-B 25%. Also, our study demonstrated early changes in IV (less than 30 days) while in intramuscular group, changes were more frequent after 30 days. This suggests that IV route was associated with more rapid onset of ECG changes, which may be attributed to higher plasma concentrations with IV route. This may not be as pronounced with IM injections, because the drug bioavailability with IM administration depends on blood flow.[20]

Our study is one of the first to compare ECG changes according to routes of administration of MA; IM and IV. To our knowledge, there is no prior study comparing the frequency and patterns of ECG changes with MA in relation to mode of drug delivery. It allows clear evaluation of how the route of drug administration influences cardiac electrophysiological functions. The absence of any statistical difference in the frequency of ECG changes highlights that the cardiac safety profile is similar in the two modes of delivery and decision of either route can be made according to patient suitability, tolerance and affordability.

## LIMITATION OF STUDY

There are few limitations of this study. It was a single center study with a small sample size and longer follow up was not done to see long term effects. Therefore, multicenter studies with larger sample size are needed to increase the generalizability of the findings. Further studies can also be done on special population like children, elderly and patients with comorbidities. Moreover, pharmacokinetics, pharmacodynamics, cost effectiveness and patient-centered outcomes can also be assessed.

## CONCLUSION

This study concludes that Meglumine Antimoniate causes ECG changes irrespective of the route of administration; however, these changes are more pronounced with the IV route compared to the IM route, with no statistically significant difference.

**Conflict of Interest:** None.

**Funding Source:** None.

**Authors' Contribution**

Following authors have made substantial contributions to the manuscript as under:

SS & NA: Data acquisition, data analysis, critical review, approval of the final version to be published.

HMU & MS: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## REFERENCES

1. Ghatee MA, Sharifi I, Mohammadi N, Moghaddam BE, Kohansal MH. Geographical and climatic risk factors of cutaneous leishmaniasis in the hyper-endemic focus of Bam County in southeast Iran. Front Public Health 2023; 11: 1236552. https://doi.org/10.3389/fpubh.2023.1236552
2. Abadías-Granado I, Diago A, Cerro PA, Palma-Ruiz AM, Gilaberte Y. Cutaneous and Mucocutaneous Leishmaniasis. Actas Dermosifiliogr 2021; S0001-7310(21)00108-3: S1578-2190. https://doi.org/10.1016/j.ad.2021.02.008
3. Uribe-Restrepo AF, Prieto MD, Cossio A, Desai MM, del Mar CM. Eligibility for local therapies in adolescents and adults with cutaneous Leishmaniasis from southwestern Colombia: a cross-sectional study. Am J Trop Med Hyg 2019; 100(2): 306-310. https://doi.org/10.4269/ajtmh.18-0643.
4. Ahmed N, Malik S, Tahir M, Rahman A, Fayyaz I, Raza N, et al. Comparison of oral dapsone with intramuscular meglumine antimoniate in cutaneous leishmaniasis. J Ayub Med Coll Abbottabad 2022; 34(4): 802-806. https://doi.org/10.55519/JAMC-04-10265
5. World Health Organization. (2014). Manual for case management of cutaneous leishmaniasis in the WHO Eastern Mediterranean Region. [cited January 5th 2025] Available from: https://www.who.int/publications/i/item/9789290219453
6. Saffarian Z, Razavi Z, Ghanadan A. Erysipeloid leishmaniasis, a rare case of atypical cutaneous leishmaniasis misdiagnosed initially as rosacea. JAAD Case Rep 2025; 60: 15-18. https://doi.org/10.1016/j.jdcr.2025.01.048
7. Martin R, Lee VR. Antimony toxicity [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2025 Apr 22]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK608003
8. Gonçalves RS, Ladeira RT, Garcia AF, Teixeira Júnior P, Dias BK, Côrtes MA. Electrocardiographic changes in patients with American tegumentary leishmaniasis treated with meglumine antimoniate: integrative review. J Medicine Biomedical Sci 2021; 20(1): 131-136. https://doi.org/10.9771/cmbio.v20i1.37087
9. Ghandi Y, Mehrabi S, Safaei M. Electrocardiography Adverse Effects Systemic Glucantime in a Child With Cutaneous Leishmaniosis: A Case Report and Brief Review. J Pediatr Rev 2022; 10(2): 155-160. http://dx.doi.org/10.32598/jpr.10.2.913.3
10. Afridi IU, Bibi S, Shiraz Z, Ullah N, Khan WZ, Khan M. Effects of systemic meglumine antimoniate on ECG in patients with cutaneous leishmaniasis. J Pak Assoc Dermatol 2024; 34(4): 829-835. https://doi.org/10.66344/jpad.34.4.2024.2840
11. Sadeghian G, Ziaei H, Sadeghi M. Electrocardiographic changes in patients with cutaneous leishmaniasis treated with systemic glucantime. Ann Acad Med Singap 2008; 37(11): 916-918.
12. Tahir M, Bashir U, Ahmed N, Mumtaz J. Electrocardiographic changes with standard dose of meglumine antimoniate therapy in cutaneous leishmaniasis. Pak Armed Forces Med J 2021; 71(4): 1235-1238. https://doi.org/10.51253/pafmj.v71i4.4048
13. Antezana G, Zeballos R, Mendoza C, Lyevre P, Valda L, Cardenas F, et al. Electrocardiographic alterations during treatment of mucocutaneous leishmaniasis with meglumine antimoniate and allopurinol. Trans R Soc Trop Med Hyg 1992; 86(1): 31-33. https://doi.org/10.1016/0035-9203(92)90427-e
14. Abid R, Haleem S, Ghani S, Ahmed N, Farman M, Bukhari M, et al. Electrocardiographic changes during treatment with cutaneous leishmaniasis. Pak Heart J 2013; 46(1): 51-56. https://doi.org/10.47144/phj.v46i1
15. Shanehsaz SM, Ishkhanian S. Electrocardiographic and biochemical adverse effects of meglumine antimoniate (MA) during treatment of Syrian cutaneous leishmaniasis patients. J Pak Assoc Dermatol 2013; 23(4): 412-417. https://doi.org/10.66344/jpad.23.4.2013.289
16. Daadaa N, Youssef S, Haggui A, Harbaoui S, Jaber K, Doss N, et al. New onset of sinoatrial block in a young patient treated with systemic meglumine antimoniate. Clin Case Rep 2021; 9(3): 1797-1798. https://doi.org/10.1002/ccr3.3768
17. Salah NB, Aounallah A, Manaa L, Lahouel M, Mkhinini H, Belajouza C, et al. Systemic meglumine antimoniate-induced severe dilated cardiomyopathy. Dermatol Ther 2022; 35(12): e15896. https://doi.org/10.1111/dth.15896
18. Rodrigues BC, Ferreira MF, Barroso DH, da Motta JO, de Paula CD, Porto C, et al. A retrospective cohort study of the effectiveness and adverse events of intralesional pentavalent antimonials in the treatment of cutaneous leishmaniasis. Int J Parasitol Drugs Drug Resist 2020; 14: 257-263. https://doi.org/10.1016/j.ijpddr.2020.11.002
19. Lyra MR, Oliveira LF, Schubach AO, Sampaio RN, Rodrigues BC, Hueb M, et al. A Randomized, Controlled, Noninferiority, Multicenter Trial of Systemic vs Intralesional Treatment With Meglumine Antimoniate for Cutaneous Leishmaniasis in Brazil. Clin Infect Dis 2023; 77(4): 574-582. https://doi.org/10.1093/cid/ciad253
20. Carvalho SH, Frézard F, Pereira NP, Moura AS, Ramos LM, Carvalho GB, et al. American tegumentary leishmaniasis in Brazil: a critical review of the current therapeutic approach with systemic meglumine antimoniate and short-term possibilities for an alternative treatment. Trop Med Int Health 2019; 24(4): 380-391. https://doi.org/10.1111/tmi.13210