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Original Article

ECG manifestations of meglumine antimoniate in treatment of cutaneous leishmaniasis

Anila Panezai, Sara Inayat, Saifullah, Habib Ullah, Mehvish Afridi, Sehrish Ghani

Department of Dermatology, Bolan Medical College/ Sandeman Provincial Hospital, Quetta.

Abstract

Objective To determine ECG manifestations of Meglumine Antimoniate in treatment of cutaneous leishmaniasis for cutaneous leishmaniasis.
Study Design: Cross Sectional.

Setting & Study duration This study was conducted at the Department of Dermatology, Bolan Medical College/ Sandeman Provincial Hospital, Quetta from 20th August 2015 to 20th February 2016 (6 months).

Material and Methods A total of 245 patients were included in the study. All patients between the ages of 25 to 60 years diagnosed as leishmaniasis and on treatment for > 2 weeks were enrolled. The patients were treated with intra-muscular injections of MA (Glucantime; Aventis, France) at a dose of 20 mg/day for 21 days. ECG was captured on a standard 12 leads format. The diagnosis of ECG manifestations was made based on recording of ECG done at 1st and fourth week after starting treatment. Data was analyzed using Statistical package of Social Sciences (SPSS) version 19. Mean + SD were calculated for continuous variable of age, height, weight, BMI, daily dose and duration of treatment. Results on categorical variables of gender and patient outcome variable i-e Sinus tachycardia, sinus bradycardia, prolong QT interval, T inversion, ST Depression, Q wave were expressed in frequencies and proportions. Stratification of age, gender, duration of treatment, duration of disease and daily dose was done to see their effect on outcome variable.

Results A total of 245 patients were included in the study. Mean age of the patients was 54.34±5.02 years. Majority of the patients 189 (77.1%) were males. Mean duration of treatment and duration of disease was 4.98 ±1.56 weeks and 6.20 ±1.82 weeks respectively. Frequency of sinus tachycardia was found in 37 (15.1%) patients, sinus bradycardia 19 (7.8%), T wave inversion 12 (4.9%), prolong QT inversion 38 (15.5%), ST depression 13 (5.3%) while Q wave was observed in 67 (27.3%) patients.9.23 years.

Conclusion Our results showed that treatment with Meglumine antimoniate can induce many ECG changes. We suggest that ECG monitoring should be performed in high-risk patients undergoing Meglumine antimoniate treatment with special attention to ECG changes.

Key words
ECG manifestations, Meglumine Antimonate, cutaneous leishmaniasis.

Introduction

Leishmaniases are a group of parasitic diseases caused by several species of the genus Leishmania,[1] which display dermotropism or viscerotropism in the Old World (Southern Europe, the Middle East, Asia, and Africa) and New World (Latin America), while the subgenus Viannia, is exclusively dermotropic. The parasites are transmitted by the bite of different sandfly species.[2]

Address for correspondence
Dr. Sara Inayat
Head Department of Dermatology, Bolan Medical College/ Sandeman Provincial Hospital Quetta.
Ph: 0300-4641871
Email: drsaraderm@gmail.com

After 1 to 12 weeks incubation period, the lesion appears as a red papule enlarging to a nodule or plaque with an infiltrative border and central crust.[3] Spontaneous healing occurs after 6 to 12 months, with a remaining scar.[4] Despite the adverse effects and inconveniences of usage of pentavalent antimony derivatives, these drugs remain the mainstay of systemic treatment.[5] The reported efficacy of Meglumine antimoniate (MA) in the treatment of CL varies from 2-90% depending on dosage, duration of treatment and the responsible Leishmania species. Pentavalent antimonials are the first-line drugs for the treatment of the cutaneous form of leishmaniasis in the World.[6] The recommended dose range is 10–20 mg/kg/day for a minimum period of 3 weeks . Other therapeutic regimens are also used. The efficacy of different drugs seems to vary according to the Leishmania species involved.[7] Symptoms of antimonial toxicities are myalgia, joint stiffness, anorexia, bradycardia and other changes in electrocardiogram including prolonged QT, inverted T wave. Hepatotoxicity, haemolytic anaemia, nephrotoxicity, pancreatitis and anaphylaxis are the rare side effects. Initially there were small Q waves in 10 patients and with antimoniate treatment these changes were found in 18 (30%) patients. In 5 patients (8.33%) bradycardia was noticed and in 9 patients (15%) tachycardia, while QT interval was prolonged in 15% of the patients. Another study has shown sinus tachycardia and q waves in 8.3% and 30% of the patients taking antimonite treatment respectively.[8]

It is recommended that in patients under treatment with this drug, electrocardiogram (EKG) monitoring should be performed before treatment and weekly during the treatment, and therapy should be discontinued if the patients develop concave ST segment, prolongation of QT interval to more than 500 millisecond, or significant arrhythmias. Death has been reported in a few patients receiving very high daily dose.

Materials and methods

This Cross sectional was conducted at Department of Dermatology, Bolan Medical College/ Sandeman Provincial Hospital, Quetta. The Study duration was 6 months. The sampling technique used was Nonprobability consecutive sampling. Sample size was calculated using WHO calculator taking the of ST Segment depressions (least proportion) in patients on antimonate therapy i.e. 6.1%,[9] margin of error d=4% and 95% level of confidence. Sample size came out to be n=245.

Results

Mean age of the patients was 54.34 ±5.02 years. **(Table 1)**. There were 136 (55.5%) patients with >55 years of age **(Figure 1)**.

Table 1 Age of the patients (n=245)

Age of the patients (in years)	*Mean ±SD*	*Minimum*	*Maximum*
	54.34 ±5.02	45	63

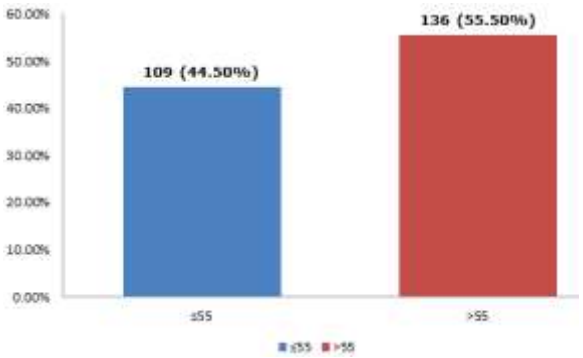

Figure 1 Age Group of the patients (in years)

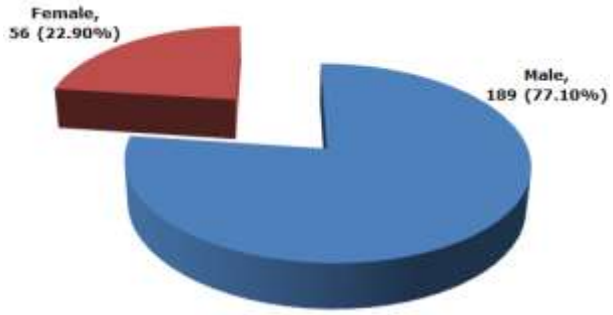

Figure 2 Gender distribution

Table 2 Duration of treatment

	Mean ±SD	*Minimum*	*Maximum*
Duration of treatment (in weeks)	4.98 ±1.56	3	7

Table 3 Duration of disease (n=245)

	Mean ±SD	*Minimum*	*Maximum*
Duration of disease (in weeks)	6.20 ±1.82	4	9

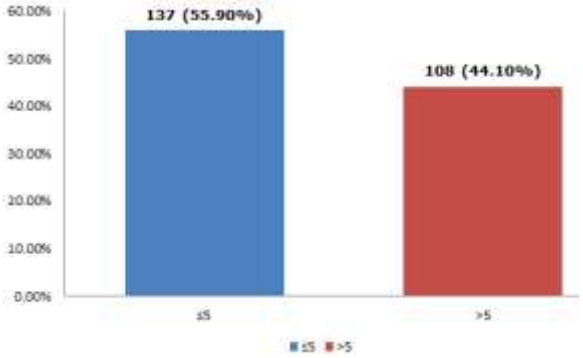

Figure 3 Categories of duration of treatment (in weeks).

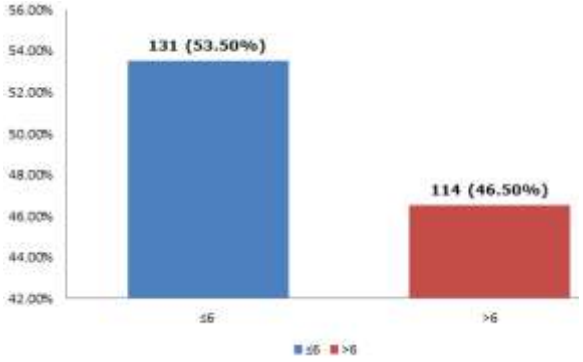

Figure 4 Categories of duration of disease (in weeks).

Majority of the patients 189 (77.1%) were males **(Figure 2)**. Mean duration of treatment and duration of disease was 4.98±1.56 weeks and 6.20 ±1.82 weeks respectively **(Table 2 & 3)**. Majority of the patients 137 (55.9%) were presented with ≤5 weeks of duration of treatment whereas duration of disease of majority of the patients 131 (53.5%) was ≤6 weeks **(Figure 3 & 4)**. Frequency of sinus tachycardia was found in 37 (15.1%) patients, sinus bradycardia 19 (7.8%), T wave inversion 12 (4.9%), prolong QT inversion 38 (15.5%), ST depression 13 (5.3%) while Q wave was observed in 67 (27.3%) patients **(Figure 5-10)**.

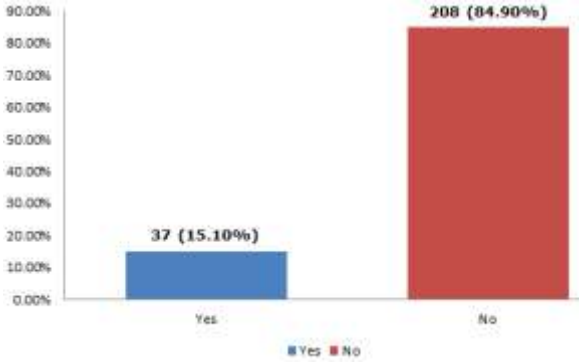

Figure 5 Sinus Tachycardia.

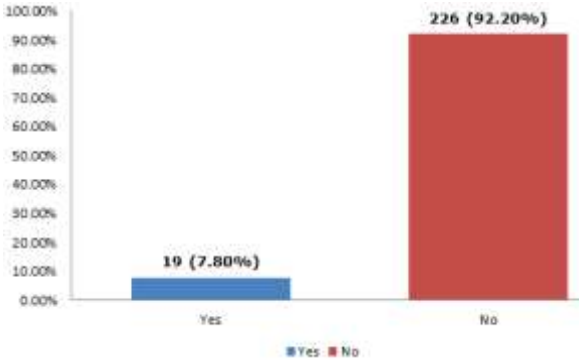

Figure 6 Sinus Bradycardia.

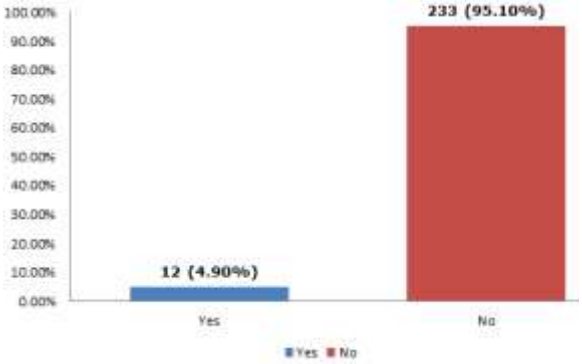

Figure 7 T wave Inversion.

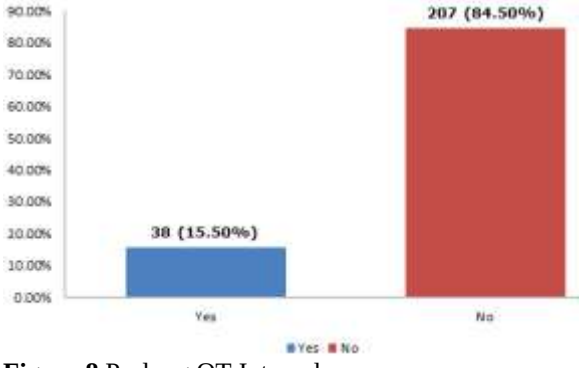

Figure 8 Prolong QT Interval.

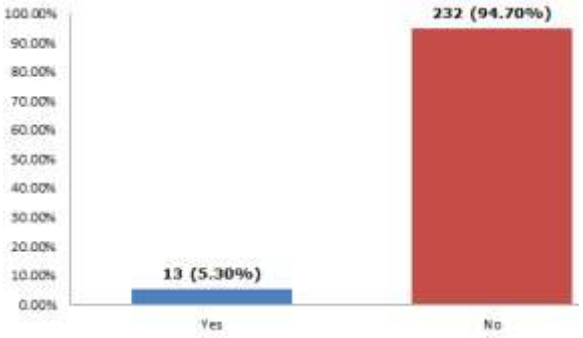

Figure 9 ST Depression.

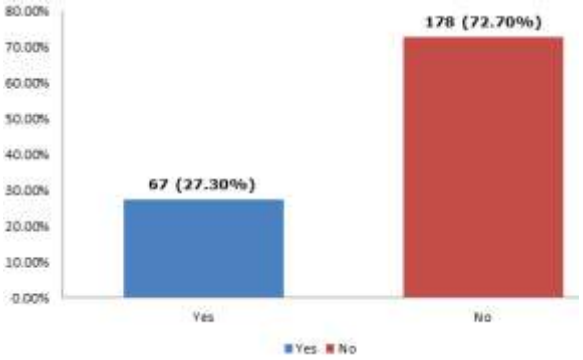

Figure 10 Q-wave

Comparison was done to see the effect of general characteristics on ECG manifestation of Meglumine Antimoniate treatment. Details of the results are shown in **Table 4-9**.

Table 4 Comparison of sinus tachycardia with general characteristics of the patients n=245.

	Sinus Tachycardia		*p-value*
	Yes	*No*	
Age, in years			
≤55	17 (45.9)	92 (44.2)	0.847
>55	20 (54.1)	116 (55.8)	
Gender			
Male	30 (81.1)	159 (76.4)	
Female	7 (18.9)	49 (23.6)	0.536
Duration of treatment, in weeks			
≤5	21 (56.8)	116 (55.8)	
>5	16 (43.2)	92 (44.2)	0.911
Duration of disease, weeks			
≤6	15 (40.5)	116 (55.8)	
>6	22 (59.5)	92 (44.2)	0.087

Table 5 Comparison of sinus bradycardia with general characteristics of the patients n=245.

	Sinus Bradycardia		*p-value*
	Yes	*No*	
Age, in years			
≤55	9 (47.4)	100 (44.2)	0.703
>55	10 (52.6)	126 (55.8)	
Gender			
Male	17 (89.5)	172 (76.1)	
Female	2 (10.5)	54 (23.9)	0.183
Duration of treatment, in weeks			
≤5	11 (57.9)	126 (55.8)	
>5	8 (42.1)	100 (44.2)	0.857
Duration of disease, weeks			
≤6	5 (26.3)	126 (55.8)	
>6	14 (73.7)	100 (44.2)	0.013

Table 6 Comparison of prolong QT interval with general characteristics of the patients n=245.

	Prolong QT Interval		p-value
	Yes	*No*	
Age, in years			
≤55	17 (44.7)	92 (44.4)	0.973
>55	21 (55.3)	115 (55.6)	
Gender			
Male	31 (81.6)	158 (76.3)	
Female	7 (18.4)	49 (23.7)	0.479
Duration of treatment, in weeks			
≤5	22 (57.9)	115 (55.6)	
>5	16 (42.1)	92 (44.4)	0.789
Duration of disease, weeks			
≤6	16 (42.1)	115 (55.6)	
>6	22 (57.9)	92 (44.4)	0.127

Table 7 Comparison of T wave inversion with general characteristics of the patients n=245.

	T wave Inversion		p-value
	Yes	*No*	
Age, in years			
≤55	5 (41.7)	104 (44.6)	0.840
>55	7 (58.3)	129 (55.4)	
Gender			
Male	12 (100)	177 (76)	
Female	0 (0)	56 (24)	0.053
Duration of treatment, in weeks			
≤5	8 (66.7)	129 (55.4)	
>5	4 (33.3)	104 (44.6)	0.442
Duration of disease, weeks			
≤6	2 (16.7)	129 (55.4)	
>6	10 (83.3)	104 (44.6)	0.009

Table 8 Comparison of ST depression with general characteristics of the patients n=245.

	ST Depression		*p-value*
	Yes	*No*	
Age, in years			
≤55	5 (38.5)	104 (44.8)	0.653
>55	8 (61.5)	128 (55.2)	
Gender			
Male	13 (100)	176 (75.9)	
Female	0 (0)	56 (24.1)	0.044
Duration of treatment, in weeks			
≤5	8 (61.5)	129 (55.6)	
>5	5 (38.5)	103 (44.4)	0.675
Duration of disease, weeks			
≤6	2 (15.4)	129 (55.6)	
>6	11 (84.6)	103 (44.4)	0.005

Table 9 Comparison of Q wave with general characteristics of the patients n=245.

	Q Wave		*p-value*
	Yes	*No*	
Age, in years			
≤55	29 (43.3)	80 (44.9)	0.816
>55	38 (56.7)	98 (55.1)	
Gender			
Male	53 (79.1)	136 (76.4)	
Female	14 (20.9)	42 (23.6)	0.654
Duration of treatment, in weeks			
≤5	38 (56.7)	99 (55.6)	
>5	29 (43.3)	79 (44.4)	0.877
Duration of disease, weeks			
≤6	32 (47.8)	99 (55.6)	
>6	35 (52.2)	79 (44.4)	0.272

Discussion

Cutaneous leishmaniasis is endemic in more than 70 countries worldwide, and 90% of cases occur in Afghanistan, Algeria, Brazil, Pakistan, Peru, Saudi Arabia, and Syria.[13]

Surveillance data indicate that the global number of cases has increased during the past decade, as documented in Afghanistan,[14] Bolivia,[15] Brazil, Colombia,[15] Peru,[15] and Syria.

Such increases can be explained in part by improved diagnosis and case notification, but are also a result of inadequate vector or reservoir control, increased detection of cutaneous leishmaniasis associated with opportunistic infections (eg, HIV/AIDS), and the emergence of anti-leishmanial drug resistance.

However, because many infections are symptomless or misdiagnosed, the global burden of cutaneous leishmaniasis is likely to be underestimated. Transmission cycles are adapting to peridomestic environments and are spreading to previously non-endemic areas as a result of urbanisation and deforestation, with domestic animals as potential reservoirs. Additionally, economic hardship, natural disasters, armed conflict, and tourism cause susceptible populations to migrate to areas endemic for cutaneous leishmaniasis, where exposure to infection results in noticeable epidemics.

The reported efficacy of Meglumine antimoniate (MA) in the treatment of CL varies from 2-90% depending on dosage, duration of treatment and the responsible Leishmania species Pentavalent antimonials are the first-line drugs for the treatment of the cutaneous form of leishmaniasis in the World.[6] The recommended dose range is 10–20 mg/kg/day for a minimum period of 3 weeks. Other therapeutic regimens are also used. The efficacy of different drugs seems to vary according to the Leishmania species involved.[7]

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in 8.3% and 30% of the patients taking antimonite treatment respectively.[8]

In this study, frequency of sinus tachycardia was found in 37 (15.1%) patients, sinus bradycardia 19 (7.8%), T wave inversion 12 (4.9%), prolong QT inversion 38 (15.5%), ST depression 13 (5.3%) while Q wave was observed in 67 (27.3%) patients.

It is recommended that in patients under treatment with this drug, electrocardiogram (EKG) monitoring should be performed before treatment and weekly during the treatment, and therapy should be discontinued if the patients develop concave ST segment, prolongation of QT interval to more than 500 millisecond, or significant arrhythmias. Death has been reported in a few patients receiving very high daily dose.

Conclusion

Our results showed that treatment with Meglumine antimoniate can induce many ECG changes. We suggest that ECG monitoring should be performed in high-risk patients undergoing Meglumine antimoniate treatment with special attention to ECG changes.

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