

CLINICAL AND INFECTIVE OUTCOME OF PARASITOLOGICALLY CONFIRMED KALA-AZAR PATIENTS TREATED WITH SODIUM ANTIMONY GLUCONATE

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Abstract

A total of fifty consecutive cases of Kala-azar admitted in the medicine units of Rajshahi Medical College Hospital during the period from February 2006 to October 2006 were included in this study. The number of the patients clearly indicates that the burden of Kala-azar in this region is significant and expanding. Male to female ratio was 1.9:1. Fever (96%) and splenomegaly (100%) were the predominant features. Hepatomegaly was found in 82% of the cases. Other clinical manifestations were Hyperpigmentation (76%), weight loss (62%), pallor (60%), jaundice (10%), oedema (10%), cough (6%) and lymphadenopathy (4%). Fever of 75% cases subsided within one week of starting treatment. Weight of 89.6% cases increased after completion of treatment. After completion of treatment spleen size regressed in 95.8% cases and no LD (Leishmania donovani) body was seen in 46 (92%) patients splenic / bone marrow aspiration after completion of treatment. 2 (4%) patients remain LD body positive after completion of treatment and 2 (4%) patients died during treatment. Still sodium antimony gluconate (SAG) is very effective in the clinical and parasitologically confirmed Kala-azar patients. A combination of sand fly control, early detection and treatment of the patients is the best approach for controlling Kala-azar.

Keyword: Kala-azar, Sodium Stibogluconate, LD (Leishmania donovani) body, splenic or bone marrow aspiration.

Introduction

Kala-azar has re-emerged from near eradication in the last 3 decades. The current prevalence rate in Bangladesh is estimated at 40,000 cases. About 20 million (18%) of the total population are at risk of Kala-azar, with at least 27 districts affected (42%) and 88 upazila (19%) reporting Kala-azar cases in 1993-4.¹ Untreated cases of Kala-azar are associated with up to 90% mortality, which with treatment reduces to 15% and is 3.4% even in specialized hospital.² Toxicity related to anti Kala-azar drugs; resistance of the organism to sodium antimony gluconate (SAG); resistance of sandfly to DDT created extra burden on treatment, control and eradication of Kala-azar.² Definite diagnosis of Kala-azar is made

by observation of LD body in bone marrow or splenic aspirate.^{3,4} But due to requirement of technical skill & hazard of these invasive procedures, serological diagnosis of Kala-azar by DAT, ELISA, IFAT and ICT are drawing more and more attention of physician.^{1,2,3} Unfortunately these facilities are not available, in most of our largest medical centers including Rajshahi Medical College Hospital.

Antimony (Sb) compounds were the first drugs to be used for the treatment of Leishmaniasis and remain the mainstay of treatment in most parts of the world.⁵ Traditionally, pentavalent antimony is available as Sodium Stibogluconate (100mg/ml) and meglumine antimoniate (85mg/ml).⁵ The daily dose is 20mg/kg body weight, given either intravenously or

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intramuscularly for 28-30 days.⁵ Common Side effects are arthralgia, myalgia, pancreatitis, and ECG changes.^{5,6} Occasionally severe cardiotoxicity like prolongation of QT_c in ECG, ventricular ectopics, runs of ventricular tachycardia, torsades de pointes, ventricular fibrillation and sudden death can occur in excess dose or improperly manufactured or stored stibogluconate.^{5,6} Until a safe and effective vaccine is developed, a combination of sand fly control, early detection and treatment of the patients is the best approach for controlling Kala-azar.²

Materials and methods

This was a cross sectional study carried out in the medicine unit of Rajshahi Medical College Hospital, during the period of February 2006 to October 2006. A total number of 50 subjects between 13-50 years were included in this study. Relevant history, clinical findings, laboratory records and follow-up of every case was recorded in a pre-designed data sheet. Subsequently, data were analyzed by statistical software SPSS version 11. Suspected cases of Kala-azar that were admitted under all three medicine units of Rajshahi Medical College Hospital were studied. After taking detail clinical history, splenic aspiration or bone marrow study for Leishmania donovani body (LD body) were done in highly suspected cases. All the parasitologically positive Kala-azar cases were included in the study. All parasitic positive cases were treated with Sodium Antimony Gluconate (SAG) for 28 days. At the end of the treatment follow up splenic aspiration were done in all the patients to see infective outcome.

Results

Table I

Sex distribution in different age groups of Kala-azar cases (n=50)

Age in years	Male		Female		Male : Female
	No	%	No	%	
13-20	12	24%	4	8%	3 : 1
21-30	7	14%	6	12%	7 : 6
31-40	8	16%	5	10%	8 : 5
41-50	6	12%	2	4%	3 : 1

Table I shows age distribution of studied patients varied from 13 to 50 years. Maximum numbers of the patients were in the age group of 13-30 years (58%). In all age group male preponderance is more than female.

Table II

Symptoms of Kala-azar (n=50)

Symptoms	Number of patients	Percentage
Fever	48	96%
Weight loss	31	62%
Loss of appetite	20	40%
Generalized Weakness	12	24%
Abdominal pain	10	20%
Lump in abdomen	7	14%
Cough	3	6%
Jaundice	2	4%

Table II shows that fever (96%), weight loss (62%) and loss of appetite (40%) were the predominant symptoms in most of the cases.

Table III

Sign of Kala-azar (n=50)

Signs	Number	Percentage
Splenomegaly	50	100%
Hepatomegaly	41	82%
Hyperpigmentation	38	76%
Anaemia	30	60%
Jaundice	5	10%
Oedema	5	10%
Lymphadenopathy	2	4%

Table III shows most of the patient presented with splenomegaly (100%), hepatomegaly (82%), hyperpigmentation (76%), and anaemia (60%).

Table IV

Haemoglobin level (n=50)

Haemoglobin (gm/dl)	Number of cases	Percentage
<6	1	2%
6-8	16	32%
8-10	15	30%
>10	18	36%

Table IV shows that one third of study cases had moderate to severe anaemia.

Table V
Total leukocyte count (n=50)

Total count/cumm	Number of patients	Percentage
<2000	4	8%
2000-3000	21	42%
3000-4000	7	14%
4000-5000	5	10%
>5000	13	26%

Table-V shows that 32 (64%) cases had leukocytopenia.

Table VI
Platelet count (n=50)

Platelet count /cumm	Number of patients	Percentage
<1,00,000	5	10%
1,00,000-1,50,000	21	42%
1,50,000-2,00,000	10	20%
>2,00,000	14	28%

Table VI shows that 52% cases had thrombocytopenia.

Table VII
ICT strip test (n=50)

Results	Number of patients	Percentage
Positive	47	94%
Negative	3	6%

Table VII shows 47 (94%) cases were ICT strip test positive. 3 (6%) cases were ICT strip test negative.

Table VIII
Remission of fever after starting treatment (n=48, 2 patients had no history of fever)

Remission of fever	Number of patients.	Percentage
Within 1 weeks	36	75%
Within 2 weeks	8	16.7%
Within 3 weeks	4	8.3%

Table VIII shows all (100%) the patients became afebrile within 3 weeks of starting treatment. Among them 36 (75%) patients became afebrile within 1 week.

Table IX
Amount of weight increased after treatment. (n=48, 2 patients died during treatment)

Amount of weight increase (in Kg)	No. of patients	Percentage
0	5	10.4%
<1	4	8.3%
1-2	9	18.8%
2-3	20	41.7%
3-4	6	12.5%
>4	4	8.3%

Table IX shows weight of 43 (89.6% cases increased after completion of treatment. Weight of 20 (41.7%) patients increased 2-3 Kg. Weight of 9 (18.8%) cases increased 1-2 Kg and none of the patients lost weight after treatment.

Table X
Regression of spleen after treatment (n=48, 2 patients died during treatment)

Spleen size	No. of patients	Percentage
Regressed	46	95.8%
Did not regress	2	4.2%

Table X shows spleen size of 46 (95.8%) patients regress after treatment.

Table XI
Side effects observed during treatment with Inj. Sodium Stibogluconate (n=50)

Side effects	No. of patients	Percentage
Gum bleeding	3	6%
Epistaxis	2	4%
Sudden death	2	4%
No side effect	43	86%

Table XI shows 43 (86%) patients developed no side effect. 3 (6%) patients developed gum bleeding, 2 (4%) patients developed epistaxis, 2 (4%) patients died suddenly.

Table XII

*Clinical outcome after completion of treatment
(n=50)*

Clinical outcome	No. of patients	Percentage
Clinical improvement	48	96%
Death during treatment	2	4%

Table XII shows 48 (96%) patients clinically improved after treatment. 2 (4%) patients died during treatment.

Table XIII

*LD body in Splenic / Bone marrow aspiration after
completion of treatment (n=50)*

LD body	No. of patients	Percentage
Negative	46	92%
Positive	2	4%
Death during treatment	2	4%

Table XIII shows no LD body was seen in 46 (92%) patients splenic / bone marrow aspiration after completion of treatment. 2 (4%) patients remain LD body positive after completion of treatment and 2 (4%) patients died during treatment.

Discussion

A large number of studies were carried out on Kala-azar including its clinical profile worldwide especially in Bangladesh, India and Sudan. The total numbers of Kala-azar cases were fifty, which constituted 1.9% of total admission in the department of Medicine, Rajshahi Medical College Hospital for a period of 8 months. In this series, majority (58%) of the patients were in the age of 13-20 years. As the patients less than 13 years of age were admitted in the Pediatrics department, they were not included in this study. So, incidence of the age group in this study is not consistent with other series, where majority of the cases were of 11-20 years of age.^{7,8,9}

Male to female ratio was 1.9:1 in our series. Male preponderance was also reported by other studies.^{7,9,10,11} In a study of 89 cases, Sharma et al found that sex incidence of Kala-azar at pre-puberty age group was equal but in the reproductive age group, there were significant less cases in females than males.¹⁰ Fever was the predominant symptom

in this study (96%). Thakur found fever in 98.1% of the cases and Kager et al in 73.77% for the cases.^{12,13} In this study, intermittent fever was noted in 60% of the cases. Weight loss was the second most common presenting symptom (62%). Similar result was also reported by different studies.^{7,8,9} Splenomegaly was the most prominent sign (100%). This is consistent with the observations of others.^{8,11,12} Hepatomegaly was found in 82% of the cases which is in agreement with others, where hepatomegaly was present in 96.36% and 91% of the cases respectively.^{7,8}

Jaundice related to Kala-azar was noted in 10% of the patients. Study of Chowdhury et al reported jaundice only in 6.6% of the patients.⁸ Hyper pigmentation of the skin found 76% of the cases. Study of Choudhury et al and Starker et al reported hyper pigmentation in 46.2% and 21.81% of the cases respectively.^{7,8} In this series, lymphadenopathy was found only in 2 (4%) cases. Similar finding was reported by other series in Bangladesh.^{7,8} Though lymphadenopathy rare in Indian Kala-azar.^{14,15} It is one of the prominent clinical presentations in African Kala-azar patients.¹⁴ 64% of the cases in this series had haemoglobin level of less than 10gm/dl, majority (50%) being in the range of 6-8 gm/dl. High ESR was noted in almost all the cases, 94% having >50mm in first hour. Progressive leucopenia with relative lymphocytosis is a characteristic finding of Kala-azar. 74% of the patients had lower total leukocyte count (<5000/cu mm) of which 64% were leukopenic (<4000/cu mm). All the above investigation results work in agreement with other reported data.^{7,8,11,12,16}

Fever of 75% cases subsided within one week of starting treatment. Weight of 89.6% cases increased after completion of treatment. After completion of treatment spleen size regressed in 95.8% cases. Epistaxis occurred during treatment in 4% cases. Gum bleeding occurred in 6% cases. 2(4%) patients remain LD body positive completion of treatment. But they were clinically cured. They were advised for follow up after one and six months. In our study 2(4%) patients died during treatment. Study of Bora D shows mortality is 3.4% even in specialized hospital.² This is consistent with our study. Recently in India, they have found many cases of SAG resistant Kala-azar, though it is the first line treatment of Kala-azar.¹⁷ In our study we have found that SAG is still effective in our parasitologically confirmed Kala-azar patients.

Conclusion

In endemic areas, high grade of clinical suspicion with the help of commonest clinical features, such as fever, anaemia, generalized weakness, weight loss with splenomegaly and with minimum laboratory aids, like decrease hemoglobin, high ESR, progressive leucopenia with relative lymphocytosis and positive ICT test, it is easy to come to clinical diagnosis. Sodium antimony gluconate, after 60 years of its use, still remains very effective in the treatment outcome of Kala-azar clinically and parasitologically.

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