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TO EVALUATE SERUM POTASSIUM DURING AMPHOTERICIN B THERAPY IN VISCERAL LEISHMANIASIS

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ABSTRACT

OBJECTIVES

The present work is aimed to evaluate potassium level during Amphotericin B therapy is different stages of Kala–azar and to see whether potassium supplementation is required during therapy. Amphotericin B was used for 20 days after on initial base line estimation of potassium. Estimation were done during the treatment and again at follow up.

Material

The material for the present study were selected from MOPD and indoor Medical wards of Sri Krishna Medical College and Hospital Muzaffarpur Bihar from April 2019 to January 2020. A total of forty cases were undertaken for this study. The cases were of both sexes and from all age groups , except those below 10 years.

Methods

The suspected patients presenting with fever including those treated for kala-azar with sodium antimony gluconate were admitted and splenic aspiration was done . Bone marrow aspiration was done only in those cases where spleen was not palpably Enlarged .

Only LD positive patients were included in this study . A detailed history of every case was taken then a through clinical examination was performed.

Initial Assessment:

A detail history of every case was taken under the following heading Name , age ,sex, religion , Economic status , occupation , full address.
Complains of the patients with duration in chronological order.
Types of fever – with/without chills or rigor .
History of Patients illness , history of past illness , family history ,personal and social history , Drug history.

Systemic Examination

1. Abdomen , Liver – size consistency margin , tenderness.
Spleen – size , consistency , margin , notch surface tenderness.
Any other lump in the abdomen.
2. Other systems

Investigation

To establish the diagnosis splenic puncture was done . prior to doing splenic aspiration prothrombin time bleeding time and clotting time were done and the procedure was avoided if these were significantly increased. Size of the spleen and liver were also measured. TLC, DLC, Hb%, Platelet count, blood urea serum creatinine, serum potassium, R/E of urine X-ray chest, ECG, Fundoscopy were also done. Serum potassium was estimated by auto analyzer.

Introduction

Visceral Leishmaniasis has existed in india among the plains of rivers Ganga and Brahamputra. This disease is mainly distributed in the eastern sector of country viz West Bengal, Bihar and Assam .
The Incidence of Kalazar touched and all time low during 1958-64 mainly due to massive spraying of insecticides for Malaria Eradication. Since then the incidence has been steadily increasing . In the state of Bihar only 250000 cases were reported in DGHS Govt. of India (1992)

Kalazar in India is caused by the Parasite leishmania donovani and transmitted by sandfly and the reservoir in our country is thought to be anthroponotic . Many drugs have been tried for the treatment of Visceral leishmaniasis viz. Antimonials, Pentamidine Amphotericin B, Ketoconazoal,Gold salt , Allopuronol,Gabreomycin Gama interferon etc.

Sodium Antimony Gluconate is the treatment of choice . Unfortunately 25% Patients show unresponsiveness to stibogluconate . This can be either primary or secondary. WHO(TDR.December 1996) reported over 10,000 cases of visceral leishmaniasis only in the state of Bihar Pentamidine was used in these cases with great success . Although relapse have been reported that relatively high proportion of Patients with visceral leishmaniasis, failed to respond to Pentamidine in India , Kenya and China . The major disadvantage of Pentamidine is its serious adverse reaction .

The scenario has now shifted to Amphotericin B as the oyher second line . There are two forms of this drug –one is the conventional Amphotericin B and the other is Amphotericin B. Lipid complex

Although Amphhotericin B lipid complex is shown to be more effective with less adverse effects , but due to its high coast and non availability , is out of reach of most of the Patients of this country.

So the mainstay of treatment is still Amphotericin B. Amphotericin B has selective toxicity for leishmania. As it probably intercalates with parasite episterol precursours of ergosterol in presence to host cholesterol(Burman,1996) . This is a very effective second line drug and has resulted in substantial reduction in treatment failure.

Fever , Chills and phlebitis are few common side effects . Apart from these the major side effect is renal complication , which rarely occur during or after treatment of visceral leishmaniasis , as the renal failure is dose dependents , although permanent damage to renal tubules may occur in short courses.

Permanent functional deficit are uncommon in patients in whom renal function was normal prior to treatment, unless a total dose in excess of 3-4 gm is given to an adult (Goodman Gilman,1996).

Hypokalaemia occurs during treatment with this drug which is mainly due to renal wasting , and renal tubular acidosis.

About one third of patients on prolonged therapy require

supplementation of potassium(Goodman Gilman 1996),Davidson R.N.(Lancet,1991). Hypokalaemia is common with conventional Amphotericin B , and toxicities are low with liposomal Amphotericin B. Thakur C.P.(National med j.india showed a minor fall in potassium on treatment with Amphotericin B. Thakur c.p.in this report(National Med j. India 1995 vol 8) showed two patients of Kala-azar who developed caediac arrest after Amphotericin B infusion and both had electrolyte imbalance including Hypokalaemia . He also showed that correction of the imbalance prevented recurrence . Maddex et al observed that Hypokalaemia may develop in patients on Amphotericin B therapy within first two weeks.

Discussion

During study normal level of serum potassium was taken as (3.5-5 mEq/L). During treatment serum potassium estimated and ECG were done at weekly intervals.

Those patients who developed hypokalemia were kept into two groups.

Group I included those patients in whom serum k+ level was between 3-3.4 mEq/L and group II patients had serum k+ level <3 mEq/L. This was done because only group II patients were given high potassium diet, from the day they became hypokalemic.

This was done on the basis of treatment guideline given in Oxford text book of Medicine 1996, (Vol.3) which whise "in otherwise healthy subject most physicians will treat" those in whom potassium concentration are consistently below 3 mEq/L. Both the groups of were closely monitored thereafter in group II patients, who were received potassium rich diet, estimated of potassium level was done on alternate days from the day of hypokalemia to the end of therapy. Patients of group I were not given high potassium diet. At the end of therapy, spleenic aspiration for LD bodies was done to establish parasitalogical cure and all the test were repeated. Patients were followed up and all the test including serum potassium estimation were again core on 60th days.

TREATMENT

Amphotericin B available as 50 mg yellow lyophilizes powder vial. The vial were kept in refrigerator until used. 10 ml of sterile water for injection was added to reconstitute the drug so the prepared concentration was 5 mg/ml. The required amount of drugs was added to 500 ml of 5% glucose.

On first day 30 ml of reconstitute drugs was given through intravenous infusion and hypersensitivity reactions were notes. If no reaction occurred the rest of the drug was infused over 2hrs in a peripheral vein. The drug was given daily and in full dosage from the first day of treatment and adverse reaction if any was noted.

This dose schedule was according to Thakur etal (Ann. Trop. Med. Parasitol 1994, 88: 365-70). The regime was continued for 20 days total dose was 20 mg/kg only weight and was in accordance with Crofts at (1976) and Thakur C.P (1993).

Fever with shaking chills were treated by stopping infusion for sometimes in mild cases and with paracetamol tablets for more severe cases. After this the infusion was restarted at a very slow rate. Care was taken to a bid the use of steroid injections although they were cupt ready for use in emergency since these drugs always causes hypokalemia.

Physical examination:

General built	Anemia	Nutrition
Mental Status	Jaundice	Pulse
Respiration	Lymphadenopathy	Temperature
Weight in kg	Neck Veins.	Cyanosis
Clubbing.	Thyroid	

Results

40 cases of visceral leishmaniasis were taken up for the study. It was observed that maximum number of patients were in 10-20 years age group and minimum in 51-60 years age group. These were 28 males (70%) and 12 females (30%).

The mean level of total leukocyte count, haemoglobin concentration and body weight increased markedly after treatment.

Mean serum potassium level of all the forty patients before treatment and 1st ,2nd and 3rd week and follow up were 4.24+0.40mEq/L, 4.11=0.40 mEq/L, 4.18+0.37 mEq/L, 4.26+0.38 mEq/L respectively, 15 out of forty patients developed hypokalemia (37.5%), 6 patients become hypokalemic from 1st week (15%). One of these six patients attained normal serum potassium level in 2nd week without potassium supplementation. Rest of the five plus eight more patients become hypokalemic in 2nd week.

The mean level of serum potassium of 15 hypokalem patients before treatment in 1st,2nd and 3rd week and follow up were 3.98+0.34, 3.6+0.29, 3.08+0.34, 3.86+0.20 and 4.12+0.30 mm/l respectively.

Hypokalemic patients were divided into two groups. Group II patients (serum K+<3mEq/L) were monitored on alternate days and were given potassium rich diet. Group I patients (serum + 3-3.4 mEq/L) were not given high potassium diet. Level of serum potassium come to normal in both the groups at the end of therapy and remained normal at follow up.

Over all six patients showed ECG changes of hypokalemia. No significant change like heart block or arrhythmia were seen. ECG change did not correlate well with level of hypokalemia and become normal at the end of therapy.

The change in serum potassium level on the day was not significant ($p>0.05$) but on 14 day became significant ($p<0.01$). Thereafter at the end of therapy and follow up the level was not significant.

CONCLUSION

Therapy with Amphotericin-B caused mild to moderate hypokalemia mainly during first two weeks and the overall incidence was 37.5% Supplementation of Potassium was not necessary for all hypokalemic patients. Only 20% patients in whom Serum K + level went below 3mEq/L, were given potassium rich diet. This was sufficient to correct hypokalemia.

In subsequent check up i.e. at the end of treatment and at follow up the potassium levels of all the forty patients were within normal limits.

So keeping in mind the enormous burden of kala-azar patients both due to ongoing endemicity and epidemic, blind potassium therapy in all patients being treated with Amphotericin B is not required.

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