ORIGINAL RESEARCH PAPER

Volume-7 | Issue-11 | November-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

SINGLE DOSE INTRAVENOUS LIPOSOSOMAL AMPHOTERICIN B—A NEW APPROACH IN THE TREATMENT OF RESISTANT KALA AZAR

General Medicine

Dr Binay Kumar Professor(general Medicine),jawaharlal Lal Nehru Medical College ,bhagalpur ,bihar

Dr Kumar Ujjwal* M.B.B.S(HONS),Kasturba Medical College Mangalore,karnataka.*Corresponding Author

ABSTRACT

Human VL is a life theartening protozoan parasitic disease caused by LD complex.There are more than 20 leishmanial species which can be . transmitted by at least 30 different species of phlebotomin sandflies. VL is the second largest parasitic killer in the world after Malaria.It infects around 200,000 to 500,000 people each year world wide.The aim of this study was to ascertain the efficacy of single intra-Venous dose of liposomal amphotericin B in resistant cases of KA.

KEYWORDS

Kala azar(KA),Leishman Donovani(LD) bodies,Visceral leishmania sis(VL),Sodium stibogluconate(SSG),Liposomal Amphotericin B (LAMPB)

INTRODUCTION :-

LD bodies is an intracellular protozoan parasite.It causes VL.
VL is a disseminated and most serious form of leishmaniasis.VL

Causes approximately 500,000 new cases and 60,000 deaths each Year.Ninety percent of the cases are found in India,Bangla Desh,Sudan, and Brazil ,Ethiopia.

The treatment of VL has many limitations.Except Miltefosin all the antileishmanial drugs have to be given parentally.The duration of therapy too is long.All most all the drugs used for treating VL are potentially toxic and has to be given under the supervision of qualified doctors for which the patients have to be admitted in the hospital.Indiscriminate use of Pentavalent SSG resulted in the emergence of SSG resistence in India. Presently SSG has been found to be ineffective for the treatment of KA.Liposomal amphotericin B has been used to treat SSG resistant KA. It is the treatment of choice in KA cases with immunocompromised state or HIV infection.With the availability of Intravenous LAMPB in Govt. hospital there is a ray of hope in the treatment of resistant KA.

Liposomal Amphotericin B is a lypholised formulation of amphotericin B incorporated into small unilamellar liposomes composed of hydrogenatedsoy phosphodylcholine,distearoyl phosphatidylglycerol,and cholesterol.

In aqueous solution LAMPB is quite stable,less than 5% of the drug dissociates from the liposomes during a 72 hours incubation period in human plasma.The stability to loss of drug is the key factor,accounting for the ability of LAMPB to markedly reduce the well known acute and chronic toxicities associated with the administration of AMPB.The primary site of action of AMPB on LD promastigote cells appears to be membrane sterols that result in aloss of the permeability barriers to small metabolites.

AIMS AND OBJECTIVES:- The place of study J.L.N.Medical College Bhagalpur Bihar is a teaching hospital providing specialized treatment to the patients coming from surrounding districts (Munger,Banka,Purnia, Katihar,etc) and states like Jharkhand ,West Bengal and Nepal.The patients of Kalazar in the above mentioned areas are first treated at PHC level.It has been found that majority of these patients who were treated with SSG at PHC level were resistant to SSG.After various time these patients visited our hospital for evaluation and treatment thereafter.As LAMPB is available in our hospital free,it was with this objective to assess the efficacy of a single dose of Liposomal AmphotericinB in these resistant cases of KA.The other objective was to have a shorter stay of the patients in the hospital so that they can be with their family at the earliest to perform other social activities which was not possible with other mode of treatment in which the patient had to be in the hospital for at least 28 days.

METHODS:- 31 patients of resistant KA who attended the Hospital since Dec 2016 were included in this study .At the time of admission a detailed history was taken regarding duration of fever,investigation done to diagnose KA,treatment and duration of medicine received .Follow up state of persistence of fever and other constitutional symptoms wre too taken into consideration.

It was found that all these patients were febrile,loss of appetite was present.On clinical examination pallor was present, spleen was moderately palpable.

The CBC showed Anaemia,CXR(PA) was normal,USG/WA showed Splenomegaly and mildly enlarged liver, RK39 showed positive result and the splenic puncture showed presence of LD bodies . On the basis of history ,clinical examination and lab.tests it was proved to be a case of KA.All the patients had received full dose and course of SSG prior to the admission in this hospital.Those patients who had history of intercurrent infection,allergy, underlying chronic diseases as severe cardiac, pulmonary,renal,hepatic impairement or pregnancy were not included in the present study.

All these patients were admitted in the wards.The dose of LAMPB was calculated as 10mgm/Kg single dose Intravenous infusion in 5% Dextrose.Each vial of LAMPB contained 50 mgm of amphotericin which was slowly reconstituted with 12ml of water for injection.Dispersion was done in a circular motion to avoid formation of foam.Inspection of the suspension was done to see that the reconstituted solution was yellow,translucent,without particular matter.The solution then was diluted in 5% Dextrose.Infusion was started at a rate of 2drops/min for 5min to see for any adverse reaction , then the rate of infusion was fixed between 15-120drops/min.Vital parameters were taken every 30 min ,2 hr and 24 hr after treatment after which the patients were discharged.The patients were advised to visit the hospital 1month after the discharge. Each patient treated ,came for follow up after one month.At that time full history regarding fever,loss of appetite,weight gain,and other symptom if any were noted. Full clinical examination was done to ascertain the size of spleen,liver, presence of pallor.RK39 was again repeated in all the patients ,while splenic pucture was done in 8 cases.

RESULT:- After one month of the treatment the fever in all the cases had subsided except in two case. The spleen was palpable in just 3 cases and in rest it was not palpable .The liver was also not enlarged. Overall the haemoglobin rose from average 7.5gms to 11gms.RK 39 was negative in all the treated cases. Splenic puncture done in 8 cases also did not show LD bodies complex. There was satisfactory clinical improvement in all the cases except in two case.

DISCUSSION:- Resistant KA is found in abundance today in and around Bhagalpur.Misuse and improper dose of SSG given at the level of PHC,at times discontinuation of the treatment before completion led to the emergence of resistant strain of KA.WHO recommended monotherapy with LAMPB in resistant cases which rapidly reduce the burden of the disease.The use of LAMPB in Bihar was carried over by Dr.T.K.Jha at Muzaffarpur with 98% of success rate in resistant KA.In our study the cure rate was 95%.Similar study was done by Dr.Shyam Sunder et.al. from Varanasi which showed promising result with

LAMPB.Around the globe KA is worrying the health pesonals for its effective cure so that maximum number of sufferer of KA could be saved.Main reasons for ineffectivity of the older drugs were longer duration of treatment,toxicity,and at times cost of the medicine if not available in Govt. hospitals.In this context it is worth mentioning that treatment with LAMPB is also very expensive.It the the noble endeavour by the the Govt to supply the drug free in Hospitals where the needy patients could get it free.Simultaneously the monetary incentive to the KA patients by the Govt. is also worth praising.With all the good benefit of LAMPB in curing resistant KA patients we undertook this study and found its use promising.One day stay in the hospital makes it convenient for the patient to be present and get rid of the dreaded disease for sure.

SUMMARY:- With all round development around the globe in all the sphere of Medical science,it is very unfortunate to find KA in abundance till today.Approximately 500000 new cases of KA are added with 60000 deaths each year.To contain the disease effort has been taken from the prevention of bite by vector sand fly, to early diagnosis of cases in endemic areas by blood examination,RK39, bone marrow and splenic puncture. All the positive cases are being treated by SSG,Pentanidine,amphotericinB,Miltefosin with variable results. Failure to achieve complete cure of the disease is multifactorial.To mention some important causes, are heavy doses of SSG for 28 days is not only painful but but are associated with many toxic effects like kidney damage,activation of dormant TB foci , sensitivity to the drug.Pentamidine too is associated with incidence of hyper and hypo glycaemia,duration of treatment and availability of drugs are another reasons. Miltefosin a very good drug to be given orally ,is very expensive,cannot be administered in pregnancy limit its use ,recently cases of KA resistant to Miltefosin has also been reported.LAMPB is acceptable,safe and above all efficacious.The present recommendation of WHO for its use as first line drug for VL in southeast Asia also supports this study.The major hinderance in its use is its cost.LAMPB is very expensive and not available in open market so a common person cannot get or purchase the same which will limit its use in KA. It is very encouragimg to note that this costly drug is supplied free to the Govt. Hospitals from where it is being given to the KA patient free. Another major advantage of LAMPB is a single day treatment,which a person of KA can easily afford and can stay in the hospital.The most important aspect of the treatment is that only a single dose has to be given as full course, there is no chance of treatment failure. With the introduction of LAMPB it can be hoped that now KA can be contained.

REFERENCES

1. Thakur CP,Pandey AK,Sinha GP,et al comparision of three treatment regimens with liposomal Amphotericin B for visceral leishmaniasis in India a randomised dose finding study.Trans R Soc Trop Med Hyg 1996;90:319-22.
2. Thakur CP A single high dose treatment of Kala Azar with Ambisome:A pilot study.Int J Antimicrob Agents.2001;17:67-70.
3. Sunder S,Jha TK,Thakur CP,Mishra M,Singh VP,Buffles R.Low dose Liposomal Amphotricin B in refractory Indian visceral Leishmaniasis; a multicentre study.Am J Trop Med Hyg.2002;66:143-6
4. Sunder S,Agrawal G,Rai M,Makharia MK,Murray HW.Treatment of Indian Visceral leishmaniasis with single dose or daily infusion of low dose liposomal amphotericin B;A randomised trial BMJ.2001;323:419-22.
5. Report of a WHO informal Consultation on "Liposomal Amphotericin B in the treatment of Visceral Leishmaniasis".Rome,Italy,16 April2005
6. Davidson RN,di Martino L,Gradoni L,Giacchino R,Gaeta GB,Pempinello R et al Short course treatment of Viceral leishmaniasis with liposomal amphotericin B.Clin.Infect Dis.1996;22:938-43.
7. Bern ,Alder –Moore J,Berenguer J et al.Liposomal Amphotericin B for the treatment of visceral leishmaniasis.Clin.Infect.Dis.2006;43:917-24.
8. Sunder S,Chakravarty J,Agrawal D,Rai M,Murray H. Single dose liposomal Amphotericin B for Visceral leishmaniasis in India.N Eng.J Med 2010;362:504-12.