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Miltefosin - A Noble Protector

Medicine

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DR. BINAY KUMAR — ASSOCIATE PROFESSOR (MEDICINE) J. L. N. MEDICAL COLLEGE, BHAGALPUR, BIHAR.

DR (MRS) BONTI BORA — Professor and Head, Department of Physiology, Gauhati Medical College, Guwahati, Assam, India

ABSTRACT

Visceral Leishmaniasis (VL) is a major public health problem in India, Nepal, Bangladesh, Sudan, Europe, the Middle East, South and Central America and Brazil. Thousands of cases of KA are seen world over every year. If untreated, KA is almost always fatal as a result of intercurrent infection.

The standard drug treatment for KA is pentavalent antimonial sodium antimony gluconate (SAG), to be given parenterally. Those who donot respond to SAG, in them amphotericin B desoxycholate is given again parenterally. These drugs are too toxic for the patients. Liposomal amphotericin B is effective and safe but it is very expensive. Miltefosin (Hexadecyclophosphocholine) is an oral drug that is 100% effective not only against newly diagnosed cases of KA but also against those cases who are resistant to either SAG or amphotericinB. Miltefosine has proved to be ray of hope to all those KA patients who are either new cases or resistant to SAG or AMPB.

INTRODUCTION

Leishmaniasis is caused by unicellular eukaryotic obligatory intracellular protozoa of the genus Leishmania and primarily affects the host's reticuloendothelial system.The protozoa is transmitted by the bite of infected female Sand flies (SF) of the genera Phlebotomus and Lutzomyia. The transmission may be anthroponotic (i. e. the vector transmits the infection from infected humans to healthy humans) or zoonotic (i. e. the vector transmits the infection from an animal reservoir to humans. Human to human transmission may possibly be by transfusion, sexual contact, salivary or nasal secretions (where mucosae is involved) and very rarely congenital transmission. In the vertebrate host the parasites are found as oval amastigotes known as Leishman Donovan bodies (LD Bodies). These multiply inside the macrophages and cells of reticuloendothelial system. When these cells rupture the LD Bodies are released in the circulation. Once female sand fly bites such persons they suck these LD bodies which then go in sand fly's gut where they develop into flagellate promastigote. These then migrate into the salivary gland of the sand fly to be inoculated in a noninfected human during a bite. Leishmaniasis denotes a disease, which has four major clinical syndrome.

VISCERAL LEISHMANIASIS

CUTANEOUS LEISHMANIASIS

MUCOCUTANEOUS LEISHMANIASIS

POST KALA AZAR DERMAL LEISHMANIASIS

Visceral Leishmaniasis is also known as KALA AZAR caused by L. Donovani, L. Infantum or L. Chagasi. Man is the main host. VL has been reported from 66 countries to affect 500,000 people world over every year, 90% of these cases are in India, Nepal, Bangladesh, Brazil and Sudan.

The data given above itself depicts the grave situation of the disease. Initially these cases were treated with parental SAG or AMPB for a period of 28 days. But these drugs were very toxic and could not be given to patients who had preexisting heart, kidney, lung or liver disease. It was the demand of the time to have a noble drug which could be given orally with no or minimal side effect. Miltefosin is one of such drugs which full fills all the requirement.

AIMS AND OBJECTIVES - J. L. N. Medical College Bhagalpur (Bihar) is a tertiary hospital rendering medical services to many districts of Bihar e. g. Bhagalpur, Munger, Banka, Khagaria, Purnia, Katihar, Kishanganj, Saharsa, Madhepura, Araria and many districts of Jharkhand e. g. Sahebganj, Pakur, Godda, Rajmahal, Dumka. Many KA patients were reffered to J. L. N. Medical College from majority of these districts. These KA patients had already received full course of SAG at their native place but had not been cured. The aim of this study was to treat all such cases with Miltefosin and see its clinical and parasitological improvement.

METHODS- From January 2014 to October 2016, total of 82 KA cases were admitted in this hospital. They were reffered from different districts of Bihar and Jharkhand. Detailed history of each and every patient along with the treatment received was taken into consideration. Those patients who received full course therapy of SAG but were not cured were included in this study. In this hospital each case was thoroughly examined. There was history of prolonged fever, on examination pallor and hepatosplenomegaly were present. Diagnosis of KA was confirmed by rK39 dip-stick and by splenic puncture smear examination for LD Bodies.

In all these confirmed KA cases which did not respond to parental SAG previously, were given Miltefosin 50mgm twice daily after food for 28 days. After the full course of treatment the clinical response was judged by disappearance of fever, improvement in anaemia and decrease in hepatosplenomegaly.

RESULT - All the patients who received Miltefosin showed clinical response by having decrease in temperature, improvement in appetite from day 7 to 10. By the 14th to21st day of treatment they all became afebrile, there was considerable decrease in the size of liver and spleen. At the end of the treatment i. e 28th day all the patients were completely fever free, no hepatosplenomegaly and significant improvement in haemoglobin concentration. The splenic puncture repeated after the end of the treatment showed absence of LD Bodies in the smear indicating parasitological cure. With the 100mgm of total dose of Miltefosin the side effects observed in the patients were mild and tolerable. These adverse effects were nausea, belching, fullness in the abdomen and at times vomiting. These symptoms subsided by giving the drug after meals.

DISCUSSION - KA infection is endemic in many districts of Bihar. Bhagalpur and adjoining districts of Jharkhand also, have fresh KA cases in good number round the year. These cases were first treated with conventional parenteral SAG or AMPB with variable or no response before coming to this medical college. Later after their referral these cases were admitted in Medical College Bhagalpur for further investigation and treatment. As miltefosin is available free in this hospital for the admitted KA patients, their treatment became easy and complete. The disease was completely cured by treatment with miltefosin. As Miltefosin was given orally, compliance by the patients was excellent, furthermore the side effects were minimal and whatever side effects appeared they were very mild in the form of nausea and vomiting, and were prevented by giving Miltefosin after food. In the present study all the 82 KA patients who received Miltefosin were clinically and parasitologically cured after full treatment. Hence it is worth mentioning that MILTEFOSIN today is the first line treatment for all types of KA cases.

SUMMARY- Miltefosin is a broad spectrum antimicrobial. Chemically it is an alkylphosphocholine. It was developed in the late 1980s as an experimental cancer treatment by German scientists Hansjorg Fibl and Clemens Unger. In 1987 S. L. Croft and his team at the London School of Hygiene and Tropical Medicine reported that Miltefosin was effective against Leishmania Donovani amastigotes in cultured mouse peritoneal macrophages. On 19 March 2014, the U. S. Food and Drug Administration approved Miltefosin for the treatment of any form of Leishmaniasis for people of 12 years of age and older. It is the first drug approved drug for cutaneous and mucosal leishmaniasis. So far as the side effects of Miltefosin treatment is concerned nausea and vomiting are the only ones and milder in intensity checked by giving it after food. It is embroyotoxic and fetotoxic in rats and rabbits and teratogenic in rats but not in rabbits. It is therefore contraindicated for use during pregnancy and contraception is required beyond the end of treatment in women of child bearing age.

With the above discussion and summary it is concluded that Miltefosin is a NOBLE PROTECTOR against any form of leishmaniasis and should be used at the first stage of KA infection for a smooth and complete cure from this disease.

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