

Combination therapy for visceral leishmaniasis

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Visceral leishmaniasis (VL), also known as kala-azar, is a vector-borne disease caused by parasite *Leishmania donovani* and transmitted by the sandfly, *Phlebotomus argentipes*. The disease is characterized by fever for more than two weeks with splenomegaly, anemia, and progressive weight loss and sometimes darkening of the skin. The disease is fatal if not treated in time.

Nepal, India and Bangladesh are committed to eliminate VL with the target of VL incidence below 1 per 10,000 populations of the district by 2015. VL elimination is possible because: human being is only the reservoir; *P. argentipes* is only the vector; vector is sensitive to DDT and other synthetic pyrethroids; elimination strategy is in place; rK39 rapid diagnostic test is available for the diagnosis; and new efficacious drug are available.

The objective of treatment of VL is to cure the patient, prevent the complications of the disease, minimize the side effects of medicines, contain the risk of development of drug resistance and reduce the risk of spread of disease. A variety of drugs is available for the treatment of VL. Novel therapies such as single dose of liposomal amphotericin B (L-AmB) and multidrug therapy are important breakthrough for VL in the Indian subcontinent and have been recommended as the treatment of choice in this region.

AmBisome, a liposomal formulation of amphotericin B, has a demonstrated superior safety profile compared to conventional amphotericin B. It is safe, has minimum side effects, and treatment duration is the shortest amongst all drugs used for the treatment of VL. The short course ensures high drug compliance amongst the users. Studies have shown that a single dose of AmBisome given intravenous has a cure rate of more than 90%.^{1,2}

Paromomycin, an aminoglycoside antibiotic, is a promising new effective drug for the treatment of VL. The recommended dose is 15 mg/kg/day to be given by intramuscular injections for 21 days. The medicine is safe with minimal ototoxicity or nephrotoxicity.³ Paromomycin should be avoided in patients with severe anaemia with hemoglobin <5g/dl. Paromomycin can be administered intramuscularly according to body weight to patients with VL who have normal renal function including children without the need for therapeutic monitoring or dose adjustment.

Treatment for visceral leishmaniasis

Miltefosine is only oral drug available for the treatment of confirmed VL cases if there are no contraindications. It is a relatively safe drug; however, relapse of miltefosine treated VL cases has been reported in studies in Nepal, India and Bangladesh.⁴

Amphotericin B is excellent drug for the treatment of VL. The cure rate of this drug is very high, exceeding 90%. The patient must be admitted at level III health institution or special referral centers for administering Amphotericin B as it requires monitoring of renal parameters. The drug is given at 0.75-1 mg/kg daily dose as a daily intravenous infusion in 5% dextrose over 6 hours for 14 days. If there is poor response to the treatment, the drug has to be continued for a period of 21-28 days.

Sodium stibogluconate (SSG) was used for the treatment of VL during the previous years. The recommended dose is 20mg/kg body weight for daily dose, by intramuscular injection for 30 days. It is recommended that the patient should be admitted to the hospital for about 7 days. It has not been given to patients with liver, kidney or heart diseases. Among the side effects, cardiotoxicity is important. It has not been used for the treatment of VL since high level of resistance has been reported.

Although several drugs are available for the treatment of VL, the development of drug resistance and relapse have been reported within short period of use of the drugs. Therefore, it is important to keep the drug in reserve to use in future since currently there are no new drugs in pipeline for development. For this, combination therapy which will slow the development of drug resistance could be the recommendation for the treatment of VL.

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