

## **Amphotericin B in Resistant Visceral Leishmaniasis**

**Ajit Sharan Sahay  
T.K.Jha**

Sodium stibogluconate (SSG) in the dose of 20 mg/kg body weight daily intramuscularly for 20-30 days is recommended by WHO as the first line drug for Indian visceral leishmaniasis (VL). Relapses following therapy and unresponsiveness to the higher doses of SSG are still a problem in north Bihar. Serious toxicity of SSG including myocarditis, sudden death and renal failure have also been reported(1,2). Pentamidine isethionate is also extensively used as a second line drug for VL. The drug, however, has to be imported, is costly and toxic. Pentamidine induced diabetes mellitus and myocarditis leading to sudden deaths are not uncommon(3-6).

Amphotericin B has been used in mucocutaneous and VL(7-9). This drug acts on the ergosterol containing cell-membrane of the protozoa thereby killing the parasite. We report the results of treatment of multi-drug resistant cases of VL with amphotericin B.

---

*From the Department of Medicine, S.K. Medical College, Muzaffarpur 842 004.*

*Reprint requests: Dr. Ajit Sharan Sahay, Assistant Professor of Pediatrics, Bank Road, Muzaffarpur.*

*Received for publication: July 8, 1994;*

*Accepted: September 21, 1995*

---

## **Subjects and Methods**

Thirty two patients of VL who were admitted in the Kala-azar unit of the Department of Medicine, S.K. Medical College, Muzaffarpur during January to December 1992 were studied. All these patients had failed to respond to WHO regimen of SSG and had relapsed after receiving pentamidine isethionate in the dose of 4 mg/kg given parenterally on alternate days for 15 to 20 injections. The mean age was 7.6 years and 28 patients were boys. The mean duration of illness was 7.8 months.

Patients with renal, cardiac or liver diseases and hemoglobin values below 7 g/dl were excluded. Following investigations were done: complete hemogram, liver function tests, renal function tests, serum electrolytes, ECG, radiograph of chest and splenic aspirate for parasites. Clinical evaluation was done daily and signs and symptoms of toxicity looked for. Weekly splenic aspirates, serum potassium, magnesium, creatinine, blood counts, ECG and weight were done. Splenic size was measured in cm from the 12th rib in the anterior axillary line to the tip of the spleen.

Amphotericin B containing 50 mg/vial (Fungizone, Squibb India) was dissolved in 10 ml of distilled water. Test dose of 5 mg dissolved in 500 ml of 5% dextrose was given intravenously over 6-8 hr. Daily increments of 5 mg was done till the full dose of 1 mg/kg was achieved. This full dose was given on alternate days till two successive splenic aspirates were negative.

## **Results**

All patients become afebrile before the

full dose of 1 mg/kg was achieved. All patients had clinical and parasitological cure after receiving 11 to 14 injections. None relapsed at 6 months follow-up. The mean dose required for full cure was 123.6 mgs (11.2 mg/kg). *Table 1* shows the clinical and hematological parameters before, at end of therapy and 6 months follow-up. Febrile reactions with chills

were found in all cases till the last injection. Gastrointestinal disturbances were seen in 8%, thrombophlebitis in 7.8%, transient albuminuria in 6.3% and reversible ST and T wave changes on ECG in 6% were observed. No significant nephrotoxicity and alteration of levels of magnesium and potassium were observed.

**TABLE I**—Clinical and Hematological Parameters Before, End of Therapy and at Six Months Follow-up.

|                   | 0 Day |      |      | End of Therapy |      |       | After 6 months |       |      |
|-------------------|-------|------|------|----------------|------|-------|----------------|-------|------|
|                   | Range | Mean | S.D. | Range          | Mean | S.D.  | Range          | Mean  | S.D. |
| Weight (kg)       | 6-14  | 12.5 | 3.6  | 5.5-14         | 11.0 | 3.2   | 6.5-18         | 15.6  | 2.9  |
| Splenic axis (cm) | 3-14  | 8.6  | 2.7  | 0.5-6          | 2.8  | 0-0.7 | 0.5            | 0.1   |      |
| Hb (g/dl)         | 5-9   | 7.6  | 1.2  | 7.0-12         | 9.3  | 1.1   | 9.0-14         | 11.07 | 2.06 |

## Discussion

Mishra *et al.*(9) first used amphotericin B in Indian VL in a dose of 0.5 mg/kg with satisfactory results. In our patients we used a dose of 1 mg/kg since all cases were non-responders to standard doses of SSG and relapsed after treatment with pentamidine isethionate.

Though gain in weight is one of the criteria of clinical response none of our patients gained weight at the end of therapy. All patients, however, started gaining weight at follow-up. This study also shows that there was further reduction in splenic size after completion of therapy. This could be due to cumulative effect of drug in addition to its immunodulatory effect.

Treatment was prolonged for a further three doses after the first negative splenic aspirate, to overcome the problem of relapse. Thus, amphotericin B used in a dose of 1 mg/kg for 11 to 14 injections cured all patients of multidrug-resistant VL. This drug is also more cost effective and less toxic than pentamidine isethionate.

Patients, however, require hospitalization and constant clinical, biochemical and electrocardiographic monitoring during therapy.

## REFERENCES

1. Singh NKP, Sharma D, Jha TK. Kala-azar mortality in hospitalized cases in north Bihar. *J Assoc Phy India* 1989, 37: 514-516.
2. Jha TK, Sharma VK. Prolonged sodium stibogluconate therapy in Indian kala-azar. *J Assoc Phy India* 1985, 34: 469-471.
3. Singh NKP, Agrawal SK, Jha TK. Persistent hyperglycemia requiring insulin therapy following the use of pentamidine in treatment of kala-azar. *J Assos Phy India* 1989, 37: 154-156.
4. Jha TK, Sharma VK. Pentamidine induced diabetes mellitus. *Trans R Soc Trop Med Hyg* 1984, 78: 252-253.
5. Jha TK. Evaluation of diamidine compound (pentamidine isethionate) in treatment of resistant cases of kala-azar occurring in north Bihar, India. *Trans R Soc Trop Med Hyg* 1983, 77:167-170.

BRIEF REPORTS

6. Jha SN, Singh NKP, Jha TK. Changing response to diamidine compounds in cases of kala-azar unresponsive to antimonials. *J Assos Phy India* 1991, 39: 314- 316.
  7. Sebastia A, Sanpaio P, Godoy JT, Lamartine P, Dillon NL, Lazaz CDS. The treatment of American (mucocutaneous) leishmaniasis with amphotericin B. *Arch Dermatol* 1960, 82: 627-635.
  8. Aluizio P. Treatment of kala-azar with amphotericin B. *Trans Royal Soc Trop Med Hyg* 1963, 57: 266-268.
  9. Mishra M, Singh MP, Choudhary D, Singh VP, Khan AB. Amphotericin B for second line treatment of Indian kala-azar. *Lancet* 1991, 337: 926.
-