

LONDON  
SCHOOL of  
HYGIENE  
& TROPICAL  
MEDICINE



LSHTM Research Online

Lockwood, DNJ; (2001) Commentary (on treatment of Indian visceral leishmaniasis with single or daily infusions of low dose liposomal amphotericin B: randomised trial) Cost and resistance remain issues. BMJ (Clinical research ed). p. 422. ISSN 0959-8138  
<https://researchonline.lshtm.ac.uk/id/eprint/19464>

Downloaded from: <http://researchonline.lshtm.ac.uk/19464/>

DOI:

**Usage Guidelines:**

Please refer to usage guidelines at <https://researchonline.lshtm.ac.uk/policies.html> or alternatively contact [researchonline@lshtm.ac.uk](mailto:researchonline@lshtm.ac.uk).

Available under license: Creative Commons Attribution Non-commercial  
<http://creativecommons.org/licenses/by-nc/3.0/>

<https://researchonline.lshtm.ac.uk>

9. Sundar S, Agrawal NK, Sinha PR, Horwith GS, Murray HW. Short-course, low-dose amphotericin B lipid complex therapy for visceral leishmaniasis unresponsive to antimony. *Ann Intern Med* 1997;**127**:133-137.
10. Davidson RN, di Martino L, Gradoni L, Giacchino R, Gaeta GB, Pempinello R et al. Short-course treatment of visceral leishmaniasis with liposomal amphotericin B (AmBisome). *Clin Infect Dis* 1996;**22**:938-943.
11. Di Martino L, Davidson RN, Giacchino R, Scotti S, Raimondi F, Castagnola E et al. Treatment of visceral leishmaniasis in children with liposomal amphotericin B. *J Pediatr* 1997;**131**:271-277.
12. Berman JD, Badaro R, Thakur CP, Wasunna KM, Behbehani K, Davidson R et al. Efficacy and safety of liposomal amphotericin B (AmBisome) for visceral leishmaniasis in endemic developing countries. *Bull World Health Organ* 1998;**76**:25-32.
13. Sundar S, Jha TK, Thakur CP, Mishra M, Singh VP, Buffels R. Low dose liposomal amphotericin B (AmBisome) in refractory Indian visceral leishmaniasis — a multicenter study. *Am J Trop Med Hyg* (in press).
14. Sundar S, Goyal AK, More DK, Singh MK, Murray HW. Ultra-short-course amphotericin B lipid complex treatment for antimony-unresponsive Indian visceral leishmaniasis. *Ann Trop Med Parasitol* 1998;**92**:755-764.
15. *Drug topics redbook*. Montavale, NJ: Medical Economics, 1999.
16. Meyerhoff A. US Food and Drug Administration approval of AmBisome (liposomal amphotericin B) for treatment of visceral leishmaniasis. *Clin Infect Dis* 1999;**28**:42-48.
17. Thakur CP, Pandey AK, Sinha GP, Roy S, Behbehani K, Olliaro P. Comparison of three treatment regimens with liposomal amphotericin B (AmBisome) for visceral leishmaniasis in India: a randomized dose-finding study. *Trans R Soc Trop Med Hyg* 1996;**90**:319-322.

## Commentary: cost and resistance remain issues

**Diana N J Lockwood, consultant physician** ([Diana.Lockwood@lshtm.ac.uk](mailto:Diana.Lockwood@lshtm.ac.uk))

<sup>a</sup> Kala-Azar Medical Research Centre, Banaras Hindu University, Department of Medicine, Institute of Medical Sciences, Varanasi-211005, India,

<sup>b</sup> Department of Medicine, Weill Medical College of Cornell University, New York NY 10021, USA  
Hospital for Tropical Diseases, London WC1E 6AU

Leishmania are inoculated into humans by the bite of infected sandflies. In the Indian subcontinent the infection is anthroponotic; man is the only known reservoir. The close proximity of humans, cows, and sandflies in Indian villages provides ideal conditions for spread of the disease.

Control of the disease depends on controlling sandflies and detecting and treating human disease early. Since the end of the antimalarial campaigns there has been little systematic use of insecticides, and the proposal to ban the use of the cheap and effective dicophane (DDT) poses an extra threat to control measures. Treatment is therefore the mainstay of control. Pentavalent antimonials have been the treatment of choice since the 1920s, but resistance is increasing in India. Thus there is an urgent need for new drugs. Currently three drugs are being evaluated for visceral leishmaniasis in India, liposomal amphotericin B, paromomycin, and oral miltefosine.<sup>1</sup>

The exclusion criteria used in the study by Sundar et al show the degree of weight loss and the effects of disease and splenomegaly on the haemoglobin, granulocyte, and platelet counts. Splenic aspirate remains the best method of diagnosis. It is simpler and less painful than a bone marrow aspirate and is the only means of assessing the parasitic response to treatment.

This study shows that a one day course of treatment can cure the disease in 90% of very sick patients. This is good but tantalising news for patients, many of whom are landless peasants. Their earning capacities will have been seriously impaired by their disease. The families' financial losses are increased because relatives have to care for and feed patients while they are in hospital.

Nevertheless, we cannot be sure that a 90% cure rate would be adequate to prevent the emergence of resistance. Studying drug resistance in leishmaniasis is difficult. Amastigote-macrophage cultures have to be used because there are no molecular markers of resistance. But monitoring drug resistance is important, especially when monotherapy is used in an anthroponotic focus. Perhaps short combined regimens should be developed to ensure that the range of drugs for leishmaniasis remains adequate.

The drug treatment of leishmaniasis highlights the problems of delivering effective drugs to resource poor settings. Paromomycin has been shown to be more effective than antimony,<sup>2</sup> but the drug has still not yet reached patients. Four years ago, the drug had no manufacturer. An industrial partner has now been found, but the tropical disease research programme at the World Health Organization does not have the funds to complete the comparative studies needed for drug registration.

Liposomal amphotericin remains an extremely expensive drug that no patient or health service in the developing world is ever going to be able to buy, and there are no patient activists to pressurise the manufacturer into providing the drug at an affordable price.

## Footnotes

- Competing interests None declared.

## References

- 1.Jha TK, Sundar S, Thakur CP, Bachmann P, Karbwang J, Fischer C, et al. Miltefosine, an oral agent, for the treatment of Indian visceral leishmaniasis. *N Engl J Med* 1999;**341**:1795-1800.
- 2.Jha TK, Olliaro P, Thakur CPN, Kanyok TP, Singhanian BL, Singh IJ et al. Randomised controlled trial of aminosidine (paromomycin) v sodium stibogluconate for treating visceral leishmaniasis. *BMJ* 1998;**316**:1200-1205.