Kala-azar treatment failing in Nepal

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In a recent study, scientists have concluded that the cure rates of Miltefosine, the only oral drug for visceral leishmaniasis available, have significantly decreased. Miltefosine was introduced in the Indian subcontinent a decade ago. Despite adhering to the treatment, only 3 out of 4 patients treated with Miltefosine in Nepal today are being cured.

Visceral leishmaniasis, also known as 'kala-azar', is the most severe form of leishmaniasis and fatal if not treated. The disease is the second-largest parasitic killer in the world, after malaria, and is endemic in the Indian subcontinent, East Africa, Latin America and Southern Europe. Early diagnosis and treatment are essential to save patients' lives, and to control the spreading of the disease.

There are very few drugs available to counter this neglected infectious disease. By the end of the 20th century, the kala-azar parasite showed such an increased resistance to injectable antimonial drugs that its use had to be abandoned on the Indian subcontinent.

When Miltefosine was first introduced as part of a regional campaign in the Indian subcontinent for kala-azar elimination a decade ago, the drug proved to be very effective. The recent study shows that this effectiveness has now decreased significantly in Nepal.

The scientists used two methods to check whether the patients truly took the drug, but found that they adequately adhered to the treatment. They also explored whether drug-resistance could explain this high treatment failure, but so far no Miltefosine-resistant parasites were detected in

patients. This suggests that other mechanisms causing a reduction in the efficacy of Miltefosine may be at work.

"These results constitute an alarming signal for the kala-azar elimination campaign. Drug policies should be reviewed to achieve better cure rates and to protect the few available drugs. We are now investigating among other things what role super-parasites -very well adapted to manipulate human immune protection- may play and whether they are somehow responsible for the reduced efficacy of Miltefosine " said Jean-Claude Dujardin, coordinator of the Kaladrug-R project at the Institute of Tropical Medicine in Antwerp and senior author of the study.

The paper 'Increasing failure of miltefosine in the treatment of kala-azar in Nepal and the potential role of parasite drug resistance, re-infection or non-compliance' is published in the latest issue of *Clinical Infectious Diseases*.

More information: Rijal, S. et al. Increasing failure of miltefosine in the treatment of kala-azar in Nepal and the potential role of parasite drug resistance, re-infection or non-compliance. *Clin Infect Dis*. 2013 Feb 20. www.ncbi.nlm.nih.gov/pubmed/23425958

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