KALADRUG-R: TOWARDS IMPROVED MONITORING OF DRUG RESISTANCE AND TREATMENT RESPONSE IN INDIAN VL

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Early treatment is a major pillar of the current Kala Azar elimination programme in the Indian subcontinent. The arsenal of available drugs is limited. Because of its toxicity and because of emerging drug resistance, the former first-line drug sodium stibogluconate (SSG) was recently replaced by miltefosine (MIL) in the Indian subcontinent, but MIL is an oral drug with a long half-life, and it is feared that resistance will rapidly emerge. Moreover, the region is confronted with an expanding HIV-epidemic,and we expect to see more HIV-VL co-infections which will generate major therapeutic challenges. Combination regimens for VL are under clinical development, but the drug policy will take several more years to change. Meanwhile, the effectiveness of current drugs needs to be safeguarded in order to cure patients and to sustain the control of VL. For this, the uninterrupted supply of quality drugs, the promotion of treatment adherence and the monitoring of treatment effectiveness and of drug resistance will be pivotal. There is a direct need for new tools to allow monitoring treatment effectiveness and drug resistance because (i) validated methods to monitor treatment effectiveness under routine conditions do not exist, (ii) there are discrepancies in assays for the assessment of drug resistance in Leishmania parasites, (iii) the knowledge on mechanisms of drug resistance's emergence, its dynamics and the impact of the introduction of new drugs is poor, and (iv) molecular tools for high throughput monitoring of drug resistance do not exist. Clinical and laboratory research is urgently needed to support the drug policy of the VL elimination programme. We aim in the KALADRUG-R project to develop, evaluate and disseminate new tools for evaluation of drug resistance in L. donovani as well as innovative methodologies for monitoring Kala-Azar treatment effectiveness in routine conditions.