Efficacy of polymeric micelles for amphotericin B delivery against murine visceral leishmaniasis

Débora V.C. Mendonça[1]; Mariana C. Duarte[1,2]; Letícia M. R. Lage[2]; Daniela P. Lage[1]; Lourena E. Costa[1]; Beatriz C.S. Salles[1]; Thaís T.O. Santos[1]; Fernanda F. Ramos[1]; Mariana P. Lima[1]; Miguel A. Chávez-Fumagalli[1]; Vívian T. Martins[1]; Danniele L. Vale[2]; Daniel S. Dias[1]; Patrícia A.F. Ribeiro[1]; Grasiele S.V. Tavares[1]; José M. Barichello[3]; Eduardo A.F. Coelho[1,2]

[1]Programa de Pós-Graduação em Ciências da Saúde: Infectologia e Medicina Tropical, Faculdade de Medicina. [2]Departamento de Patologia Clínica, COLTEC, UFMG, Brazil. [3]Centro de Ciências Químicas, Farmacêuticas e de Alimentos. Universidade Federal de Pelotas, RS, Brazil.

Amphotericin B (AmpB) has been well-successfully used to treat *Leishmania* infection, although high toxicity has been observed in the patients. In the present study, this drug was administered in *Leishmania infantum*-infected BALB/c mice by three different systems, aiming to compare their efficacy against infection, as well as their side effects in a known murine visceral leishmaniasis (VL) model. Amphotericin B was administered associated to a Poloxamer P407 (Pluronic® F127)-based polymeric micelle system (Amp/M), as a lipid formulation, Ambisome® (Lip-Amp), and in a free format (free Amp). Glucantime® was used as a comparative drug. Aiming to evaluate different endpoints, the efficacy of the therapeutics was investigated one and 15-days after the end of the treatments, by determination of the parasite load, when a limiting dilution and quantitative PCR (*q*PCR) were performed, as well as the immune response generated in the treated and infected animals. The occurrence of toxicity in these animals was also investigated. In the results, Amp/M or Lip-Amp-treated animals were those that presented better results, since significant reductions in the parasite load in all evaluated organs, as well as a parasite-specific Th1 immune response and no hepatic or renal damage were observed. However, free AmpB or Glucantime®-treated mice presented organic toxicity, a lower Th1 response and side effects such as ataxia and weight loss. Comparatively, Amp/M was the most effective drug tested in our experimental murine model, and results showed that this AmpB-carrying system could be considered as an alternative for future studies for a safer treatment against VL.

Keywords: Amphotericin B; poloxamer 407; liposome; toxicity; visceral leishmaniasis; treatment.

Financial Support: Programa de Pós-Graduação em Ciências da Saúde: Infectologia e Medicina Tropical, Faculdade de Medicina, UFMG. FAPEMIG. CAPES. CNPq.