
AMPHOTERICIN B EFFICACY IN THE ACUTE PHASE OF PARACOCCIDIOIDOMYCOSIS: LESSONS FROM A MURINE MODEL

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The golden standard drug for the treatment of paracoccidioidomycosis (PCM) still is amphotericin B (AmB), despite the development of newer, effective antifungal compounds. The efficacy of AmB therapy was tested in B10.A mice, susceptible to *Paracoccidioides brasiliensis* infection, using as parameters the dissemination of fungi to various organs and the development of specific cellular immune responses against homologous antigen in the acute phase of PCM. Dosages of 1 or 2mg AmB/kg/day were administered by the i.p. route, every other day, three times a week; therapy began 24 hours before the fungal inoculation. No side effects were observed. At the 7th day after infection, the number of viable fungi, expressed as the log of colony-forming units (log CFU), was not reduced in mice treated with 1mg AmB/kg/day in any of the organs studied, but was significantly diminished in the lungs of animals treated with 2mg AmB/kg/day, when compared with untreated mice. At the 15th day after infection, therapy with 1mg AmB/kg/day led to lower log CFU counts in the spleen and epiplo, while the administration of 2mg AmB/kg/day was able to reduce the fungal load in all organs studied, i.e., spleen, epiplo, liver and lungs. Regarding the development of specific cellular immune responses against homologous *P. brasiliensis* antigen, demonstrated by delayed-type hypersensitivity (DTH) reactions, both untreated and 1mg AmB/kg/day treated mice showed a profile in keeping with that described for the susceptibility pattern, characterized by early and ephemeral DTH responses. These animals presented, at the 7th day after infection, low DTH responses, that increased significantly in the 15th day. On the other hand, therapy with 2mg AmB/kg/day elicited low DTH responses in both time points, in a profile similar to the one developed by mice resistant to PCM infection, whose responses appear later and are sustained. These results suggest that, in our murine model, AmB is efficient in reducing the fungal load during the acute phase of PCM; 2mg AmB/kg/day was the best dosage tested. An interesting parallelism between the severity of infection and the development of antigen-specific cellular immunity could also be noted, once the susceptible pattern of DTH response was accompanied by higher CFU counts, whereas the resistant pattern of DTH response was accompanied by an effective control of the infectious process. Our present data allowed to confirm the efficacy of AmB therapy by real counts of the infectious agent in the animal's tissue. This in vivo observation may help physicians to sustain the indication of AmB for use in humans that for a reason or another cannot be submitted to other therapeutic schedules.

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