Title: Hyperbaric hyperoxia enhances the lethal effects of amphotericin B in Leishmania braziliensis panamensis

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Abstract: Leishmania braziliensis panamensis promastigotes were exposed in vitro to amphotericin B (AmB), menadione, or phenazine methosulfate under normoxic conditions. Promastigotes were also exposed to hyperoxia alone (100% O2 at total pressures of 101.3 or 253.3 kPa), or combined with drugs. After incubation for 24 h at 27 degrees C, viable promastigotes were stained with fluorescein diacetate and counted using epifluorescence microscopy. Hyperbaric hyperoxia alone (PO2 = 229.3 kPa) was as effective as AmB alone (0.2 microM); both reduced the number of viable promastigotes to approximately 13% of the original inoculum. In addition, AmB in a hyperbaric hyperoxic environment killed more promastigotes (97% of the original inoculum) than AmB in normoxic (PO2 = 21.1 kPa) or hyperoxic conditions (PO2 = 91.7 kPa). Finally, AmB in hyperbaric hyperoxia killed significantly more (75%) promastigotes than hyperbaric hyperoxia alone. High oxygen tensions did not significantly alter the lethal effects of either menadione or phenazine methosulfate. In conclusion, the lethal effects of low dose AmB in Leishmania promastigotes were augmented by hyperbaric hyperoxia in vitro, but only at oxygen doses too high to be tolerated by human patients.

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