Abstract

Chemotherapy 1992;38(suppl 1):55

Oral Prophylaxis with Itraconazole of Experimental Aspergillus and Candida Infections

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Key Words

Itraconazole

Aspergillus

Candida

Guinea-pigs

Rats

Abstract

The prophylactic activity of the lipophilic triazole itraconazole was evaluated in systemic aspergillosis and systemic candidosis in guinea-pigs and in vaginal candidosis in rats. Systemic invasive aspergillosis in guinea-pigs was obtained by intravenous inoculation of *Aspergillus fumigatus*, 25,000 CFU/g body weight. The administration of 4 doses of itraconazole, 5 mg/kg, before infection was able to prolong the survival of the animals compared with the excipient-treated group ($p < 0.001$; Mann-Whitney U-test, 2-tailed probability). Systemic and disseminated candidosis in guinea-pigs was obtained by intravenous inoculation of *Candida albicans*, 1,000, 2,000 or 4,000 CFU/g body weight. Oral prophylaxis with itraconazole, 5 or 10 mg/kg, or with the excipient was given for 1, 2, or 3 days. All excipient-treated animals ($n = 38$) showed skin folliculitis and gave positive cultures of the skin and kidneys; the number of CFU/g organ weight was higher with heavier inocula. In the itraconazole-treated animals ($n = 114$), *Candida* folliculitis was absent in 89%, and skin and kidney cultures were negative in 84% and 82%, respectively. In animals given the higher dose of itraconazole and inoculated with 1,000 or 2,000 CFU/g body weight ($n = 60$), however, *Candida* folliculitis was absent in 97%, and skin and kidney cultures were negative in 93% and 88%, respectively. The effectiveness of itraconazole was also related to the number of treatments before inoculation. Oral itraconazole was more effective than parenteral amphotericin B, 1.25 or 2.5 mg/kg, given 24 h and 1 h before inoculation. Female castrated rats maintained in permanent pseudo-oestrus by oestrogen injections were infected intravaginally with *C. albicans* and pre-treated orally with the excipient or with itraconazole, 1.25-40 mg/kg, in various regimens at 1, 24, 48 and 72 h before infection with 1, 2 or 3 doses. The animals were protected against infection at higher doses or when more than 1 dose was administered. No drug-related side-effects were observed. The broad-spectrum therapeutic value of itraconazole is well established. Prophylaxis with this antifungal agent opens new possibilities for the prevention of chronic diseases and for the protection of immunocompromised patients.