CORRESPONDENCE

Nitazoxanide as a Broad-Spectrum Antiparasitic Agent

To the Editor—In a randomized, double-blind, placebo-controlled study of nitazoxanide, Rossignol et al. [1] reported excellent therapeutic response in patients with diarrhea caused by *Giardia intestinalis* and *Entamoeba histolytica* and/or *Entamoeba dispar* infection. Earlier open-label clinical investigations of therapeutic response to nitazoxanide in 125 patients with *Fasciola hepatica* infection, with parasitologic examination of stool samples 30 days after initiation of treatment, pointed toward its safety and efficacy [2]. Furthermore, nitazoxanide has been effective during experimental investigations of treatment of antibiotic-induced *Clostridium difficile* intestinal disease in hamsters. Intragastric treatment with nitazoxanide for 6 days, when followed by an inoculation of toxigenic *C. difficile*, resulted in survival of the animals during a 15-day observation period. Necropsy disclosed no signs of toxicity or of *C. difficile* intestinal disease [3].

The encouraging antibacterial and antiparasitic efficacy of nitazoxanide in experimental open-label or placebo-controlled, double-blind investigations [1–3] would be sustained through constant maintenance of its potency and bioavailability. Nitazoxanide formulations would require constant storage under controlled temperatures. Inadvertent exposure to extremes of humidity or temperature would affect drug potency. That was evident recently during field monitoring of the quality of the antiparasitic drug mebendazole. In Nigeria, 5 of the 37 samples being offered to patients did not contain the active drug ingredient, as specified by the British pharmacopeia [4]. An identical scenario with nitazoxanide in the field would almost certainly be associated with frequent therapeutic failures in bacterial and/or parasitic infections. Such cryptic nitazoxanide failures in the field would be best addressed by an on-the-spot evaluation of nitazoxanide quality.

Simple assay formats that could accomplish both qualitative and quantitative analyses of nitazoxanide formulations in clinical settings should be standardized. Recently, a quick and simple test was used to identify counterfeit artesunate in the field without the use of many chemicals or sophisticated equipment [5]. A similar test for nitazoxanide would speedily guide clinicians.

Concurrent intestinal coccidial and protozoan infections would predispose to cholangitis and malabsorption and could alter bioavailability of nitazoxanide, as shown in a 60-year-old immunocompetent patient with chronic biliary isosporiasis who did not respond to nitazoxanide therapy [6]. Prospective tests to quantify nitazoxanide in various body fluids would guide infectious disease practitioners about any linkage of the poor bioavailability with the recorded therapeutic failures of nitazoxanide.

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References


Human Immunodeficiency Virus Protease Inhibitors and *Pneumocystis carinii*

To the Editor—We read with great attention and interest the article by Walzer et al. [1] stating that anti–human immunodeficiency virus (HIV) drugs (mainly HIV protease inhibitors) are ineffective against *Pneumocystis carinii* in vitro and in vivo. The paper presented data that, according to the authors, conflict with our previously published results [2].

In an attempt to better understand these differences, we would like to underline some apparently missed or misunderstood facts:

1. The in vitro system that we used for testing drugs was not the spinner flask (as erroneously mentioned by Walzer et al. in the Discussion section of their article [1, p. 1357]) but, instead, a well-characterized, quantitative, reproducible, and standardized protocol using multiwell plates that was confirmed by several tests of experimental chemotherapy [3–5] followed by clinical use, as was done with clindamycin-primaquine. The spinner flasks...