In Vitro Susceptibilities of 40 Campylobacter fetus subsp. jejuni Strains to Niridazole and Metronidazole

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The activities of niridazole and metronidazole were compared by an agar dilution method against 40 strains of Campylobacter fetus subsp. jejuni of human origin. Niridazole had a markedly higher activity than metronidazole.

Metronidazole, a nitroimidazole, is known principally for its trichomonacidal and bactericidal action on anaerobes. Susceptibility of Campylobacter fetus subsp. jejuni is highly variable (3, 6, 8). Niridazole, a nitrothiazole of analogous chemical structure, has the same antiparasitic properties. A very high susceptibility of Campylobacter spp. was initially pointed out by Hof et al. (3). We have determined the minimal inhibitory concentrations of these drugs on 40 strains of human origin.

Niridazole (batch 106; activity, 100.3%) obtained from Ciba-Geigy Corp. was dissolved in dimethyl sulfoxide (Merck r 802912) to obtain a solution at 1,000 µg/ml. Metronidazole (batch 2240135; activity, 100.1%) obtained from Specia was dissolved in ethanol-water (1:1, vol/vol) to obtain a solution at 1,000 µg/ml. Stock solutions were kept at -20°C for up to 1 month. They were further diluted in distilled water and mixed with Mueller-Hinton agar (bioMérieux) to obtain graded concentrations from 0.06 to 64 µg/ml for metronidazole and from 0.001 to 8 µg/ml for niridazole.

Forty strains of Campylobacter fetus subsp. jejuni were tested: 1 reference strain (ATCC 29428) and 39 recent clinical isolates. These 39 strains were isolated from diarrheal stool specimens of hospitalized children on Skirrow medium (4) and were identified according to the criteria of Veron and Chatelain (7) and Smibert (5).

Minimal inhibitory concentrations were determined with serial dilutions in Mueller-Hinton agar. All strains were subcultured overnight at 42°C on Mueller-Hinton agar plates under an microaerophilic atmosphere by the method of Butzler and Skirrow (1). These bacteria were suspended in a solution containing per liter: sodium chloride, 2.25 g; potassium chloride, 0.105 g; calcium chloride, 0.045 g; and sodium hydrogen carbonate (Merck Ringer-tabletten r 10113), 0.05 g. Suspensions were adjusted with a spectrophotometer (Jouan) to an optical density of 12 to 14 at 580 nm (corresponding to an 0.5 McFarland standard). Colony counts established that these suspensions contained between 0.5 × 10^2 and 2 × 10^6 CFU/ml (mean, 10^5 CFU/ml). A further 1/100 dilution of these suspensions gave the final inoculum (10^8 CFU/ml). Ten-microliters (10^5 CFU) portions of these last dilutions were spotted on the plates with a multipoint inoculator.

Control plates without antibiotics were always incubated in the same conditions: microaerophilic atmosphere, 37°C, 48 h. Microaerophilic atmosphere was verified by the inclusion in each jar of control plates seeded with Pseudomonas aeruginosa and Clostridium perfringens (2). The minimal inhibitory concentration was taken as the lowest concentration of the antibacterial agent which did not allow visible growth.

Our results are given in Fig. 1. As can be seen, antimicrobial activity of niridazole was substantially higher than that of metronidazole. A general correlation was observed (correlation coefficient, 0.9 with P < 0.01). These results were in perfect agreement with those of Hof et al. (3), suggesting a possible clinical use.

The break point of niridazole may tentatively be fixed between 4 and 8 µg/ml of active drug (unmetabolized), well below the usual concentration in stool specimens with conventional dosage.

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LITERATURE CITED