Campylobacter pylori Therapy: is *in vitro* Disc Testing with Metronidazole Worthwhile?

B.J. Marshall, L.J. Barrett, R.W. McCallum, R.L. Guerrant
University of Virginia, Charlottesville, VA.

C. pylori may be treated with bismuth and metronidazole combinations. The aim of this study was to prospectively evaluate Cp isolates for metronidazole sensitivity using 5 μg discs, and to correlate this with the result of therapy. Date were available from 26 consecutive patients, in whom disc testing had been performed on their *C. pylori* isolates. Patients were then treated with 14 days of bismuth subsalicylate (BSS) 500 mg QID AC and were given metronidazole 1-1.5 mg daily (20 mg/kg/d), between day 4 and day 14. Biopsy was repeated one month after therapy, to confirm eradication of the organism. Antral biopsies were cultured on horse blood agar plates with GCHI supplement (REMEL) for 3 days in a 10% CO_2 incubator. Cp isolates were picked and cultured in the same manner in the presence of a 5 mm diameter 5 microgram metronidazole disc, zone diameters were measured after 3-5 days. Treatment was successful in 19 patients (73%). The mean zone diameter in isolates, from successfully trated patients, was 26.6 mm, SD 14 mm. The mean zone size from patients who failed therapy was 16 mm, SD 14 mm (p=0.1). When the zone diameter was ≥ 15 mm the cure rate was 89%. When the zone size was <15 mm, the cure rate was only 37%. The data suggests that nitroimidazole disc sensitivities can predict the outcome of bismuth/nitroimedazole therapy. We are also comparing methods if sensitivity testing for *C. pylori* which show a correlation of disc and agar dilution techniques.

Introduction

C.pylori may be treated with bismuth and metronidazole combinations with a cure rate of about 75%. About 25% of *C. pylori* isolates are resistant *in vitro* to nitroimidazoles but *in vitro* sensitivity testing has not been proven to be a useful guide to therapy in the United States. The aim of this study was to prospectively evaluate CP isolates for metronidazole susceptibility using 5 μg discs, and to correlate this with the result of therapy.

Subjects and Methods

Patients were diagnosed as having *C.pylori* by rapid urease test (CLO-test) of a gastric mucosal biopsy specimen. If *C.pylori* was present, therapy commenced with bismuth subsalicylate (BSS) 500 mg QID, 30-60 min before meals and at bedtime. After 4-7 days metronidazole was added in a dose of approximately 20 mg/kg/day. BSS and metronidazole were taken concurrently for a further 10 days. Biopsy was repeated, or a ^{14}C-urea breath test was performed, 28 days after completing therapy.

To perform *in vitro* sensitivity testing, antral biopsies were cultured on horse blood agar with GCHI supplement (Regional Media Laboratories, Lanexa, Kansas) for 3 days in a 10% CO_2 incubator. *C. pylori* isolates were picked and grown in the same manner, but in the presence of a 5 μg metronidazole disc (diameter 5 mm). Inhibition zone diameter was measured after 3-5 days.

Results

Follow-up data were available from 34 consecutive patients in whom *C.pylori* had been cultured and disc testing had been performed either on the initial or follow-up isolate. *C.pylori* could not be detected in 19 patients after therapy. The mean zone diameter in isolates from these successfully treated patients was 25.6 mm, s.e.m. 2.5 mm. In contrast, the mean zone diameter of 15 patients in whom *C.pylori* was still present was 7.9 mm, s.e.m. 3.4mm (Table 1).

Note that when the zone diameter was ≥ 15 mm, the cure rate was 94% (16/17). When the zone size was < 15 mm, the cure rate was only 18%. The difference was highly significant (p=0.00001 Fisher's exact test).

Conclusions+

1. Metronidazole disc sensitivities can predict the outcome of BSS/metronidazole therapy.
2. Cure rate approaches 100% when the isolate is sensitive *in vitro*.
3. It is probably useless to give a nitroimidazole when the *C.pylori* isolate is resistant *in vitro*.

Table

ZONE DIAMETER (mm): (disc diam. = 5mm)	FAILED THERAPY	SUCCESSFUL THERAPY
no zone seen	13	2
6-14mm	1	1
15-29 mm	0	7
=30 mm	1	9