Short report

Metronidazole in the treatment of chronic proctitis: a controlled trial

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SUMMARY Twenty-two patients with chronic proctitis were treated with metronidazole for 28 days in a double-blind controlled trial, but they did not appear to benefit from the drug.

Although the cause of proctitis and ulcerative colitis remains unknown, anaerobic bacteria may play a part in the pathogenesis by provoking an immune response (Monteiro *et al.*, 1971), or by secondary invasion of inflamed mucosa. Metronidazole is a bacteriocidal agent which is effective against anaerobes (Tally *et al.*, 1975) and may be of value in proctitis. We first treated 14 patients in an open trial in which all patients were given 800 mg metronidazole orally, while some also had 200 mg twice daily by enema; six responded well, one improved a little, and seven were unchanged.

We then treated 22 patients in a double-blind controlled study. The patients had relatively mild symptoms of increased bowel frequency with loose stools and loss of blood and mucus; the rectal mucosa was abnormal on sigmoidoscopic examination and a previous barium enema was normal. The study was of crossover design in which patients were given metronidazole suppositories (500 mg three times daily) and a placebo in randomised order during two consecutive 28 day periods. During each period patients recorded daily on a diary card the frequency of bowel actions and the occurrence of rectal bleeding. At the end of each period they indicated their clinical progress as excellent, good, fair, bad, or terrible.

A clinical assessment was made initially and at the end of each treatment period; this included sigmoidoscopic examination with a rectal biopsy. The sigmoidoscopic changes were recorded using similar criteria to those described by Baron *et al.* (1964). Grade I was normal; grade II showed hyperaemic mucosa; grade III included spontaneous bleeding and haemorrhages on light contact, and grade IV

referred to severe changes. Rectal biopsies were examined by one pathologist without knowledge of the order of treatments given. The acute inflammatory reaction was graded as normal, moderate, or severe using sections stained with haematoxylin and eosin. This was based on the degree of acute inflammatory infiltrate in the lamina propria, the presence of crypt abscesses, and polymorphs adjacent to epithelial tubules. In addition, sections were stained for eosinophils with carbol chromotrope and the eosinophil counts were made over five high-power fields.

Results

All except four of the 22 patients completed all parts of the trial satisfactorily. Two patients were withdrawn because their symptoms deteriorated, one patient became pregnant, and another patient developed headaches and backache in the first period. The following data are based on the 18 patients who completed the trial.

The patient's general clinical assessment of each treatment period showed that three improved during the metronidazole period, five improved on placebo, whereas 10 patients noticed no difference between the two periods.

The effect of treatment on stool frequency, blood loss, the sigmoidoscopic appearance of rectal mucosa, and histological changes is shown in the Table. There was no significant difference in results from the two periods.

Discussion

Metronidazole, given for 28 days, does not appear

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Table Some clinical and pathological features observed in patients with proctitis, treated for 28 days with metronidazole and placebo

	Treatment period	
	Metronidazole	Placebo
Stool frequency (mean no. in last 10 days of treatment)	35 ± 26	41 ± 28
Blood loss (mean no. of days with blood loss in last 10 days of treatment)	4.8 ± 4.4	4.7 ± 4.2
Sigmoidoscopic appearance (no. of patients)		
Improved	7	8
Deteriorated	2	3
No change	8	6
Histological inflammation in biopsies (no. of patients)		
Improved	1	3
Deteriorated	2	3
No change	10	7
	(From the other five patients at least one biopsy was unsatisfactory)	
Eosinophil count in biopsies (mean/5 hpf after treatment)	40 ± 26	56 ± 33
	(Overall mean was 50 and only two patients had low eosinophil counts <10/5 hpf).	

to benefit patients with proctitis, although our initial observations in an open trial were encouraging. We may have failed to demonstrate an effect for some reason and erratic rectal absorption is one possibility. Although blood levels were not measured, it seems unlikely that impaired absorption played a major part in the outcome, for the drug has been shown to be well absorbed by this route (Willis *et al.*, 1975). The total dose given was greater than in our open study and most patients were able to use three suppositories daily throughout the trial.

There have been several reports of a beneficial effect from metronidazole in Crohn's disease but these have been uncontrolled (Holdstock, 1975; Montgomery, 1975; Ursing, 1976) and need further confirmation by controlled trials.

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