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Metronidazole prophylaxis for elective large bowel surgery in children: a prospective trial

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SUMMARY

In a controlled trial in children aged 2 days to 16 years undergoing large bowel surgery a group of 15 patients had preoperative mechanical bowel preparation and oral neomycin while a second group of 15 patients was similarly prepared but also had preoperative and postoperative metronidazole medication.

Five of the 9 postoperative infections in the first group involved Bacteroides spp. but no anaerobe was found in the 3 wound infections in the metronidazole group.

Patients and methods

Thirty patients aged 2 days to 16 years and needing large bowel surgery were randomly allocated to one of two groups. The patients, diagnoses, operations, postoperative infections and bacteriological examinations are summarized in *Tables I* and *II*.

Patients in both groups were prepared for surgery with bowel irrigations, dietary restriction and neomycin. This antibiotic was given orally every 6 h for 3 days in doses of 125 mg (infants of less than 1 year), 250 mg (1–5 years) or 500 mg (more than 5 years). Patients over 5 years of age also had a daily instillation of 500 mg into the distal colon.

Patients in the treatment group also received metronidazole orally every 8 h for 48 h preoperatively in doses of 5 mg/kg (less than 5 years), 100 mg (5–12 years) or 200 mg (more than 12 years). Metronidazole medication was continued postoperatively with suppositories given 8-hourly for 48 h per rectum or via the colostomy in doses of 125 mg (less than 1 year), 250 mg (1–5 years) or 500 mg (more than 5 years).

All patients had routine haematological and biochemical investigations (urea and electrolytes and, in the treatment group, liver function tests) performed on admission and during the postoperative period.

At operation a peritoneal swab was taken as soon as the abdominal cavity was opened. Another swab was taken from the operation site before the peritoneum was closed. Each swab was immediately and separately placed in Stuart's transport medium and sent for culture.

The swabs were cultured aerobically on blood agar, MacConkey's medium and cooked meat broth and also in an anaerobic jar with reinforced clostridium medium plus 10 per cent defibrinated blood. The plates were incubated for 5 days but subcultured on the second day.

Wounds were examined daily for signs of infection, defined according to Ljungqvist's (1964) criteria as indurated and producing pus, swabs of which were sent for bacteriological examination.

Blood samples were taken from all patients in the test group 24 h and 48 h after operation for polarographic determination of the metronidazole concentration by May & Baker Ltd.

Results

Wound infections occurred in 9 patients in the control group and aerobes alone were isolated from 4 of these. Anaerobes did not occur alone in any wound infection and the 5 infections from which both anaerobes and aerobes were isolated were more severe with regard to the temperature and clinical status of the patients than those from which only aerobes were isolated. Nevertheless, even these wound infections responded to simple drainage after 4 days. *Case* 27 developed a pelvic abscess which discharged pus via the perineal wound on the sixth day. Anaerobic infection did not develop in any patient receiving metronidazole and only 3 wound infections were noted in this group from all of which aerobes alone were isolated.

Cultures of peritoneal swabs taken peroperatively were either negative or grew aerobes only.

The white cell count remained normal in 18 patients and in those patients with infection was significantly raised to an average of 15 000. The results of blood urea and electrolyte estimations and liver function tests remained within the normal ranges.

Metronidazole serum concentrations ranged from 7·9 to 46 μg/ml after the first postoperative day and from 8·9 to 76 μg/ml 48 h after operation.

Metronidazole given preoperatively and postoperatively was well tolerated and produced no adverse reaction.

Discussion

More than 96 per cent of the colonic microflora are anaerobic (Drasar et al., 1969; Jawetz et al., 1976) and the commonest pathogenic non-sporing anaerobes are *Bacteroides* spp.; therefore, it is to be expected that such organisms will be the predominant cause of sepsis after colorectal surgery (Leigh, 1975). Long and Swenson (1977) have shown anaerobic organisms to be present within 48 h in the faeces of normally delivered, breast-fed babies.

Metronidazole has been shown to reduce the incidence of anaerobic sepsis after colonic surgery in adults (Goldring et al., 1975; Feathers et al., 1977; Taylor and Cawdery, 1977; Willis et al., 1977; Brass et al., 1978).

In our study of 30 children undergoing elective colonic surgery, there were 5 infections involving non-sporing anaerobic bacteria in the control group and none in the metronidazole group. This difference is significant at $P = 0{\cdot}05$ (Fisher's exact test). These infections were clinically more severe than those involving only aerobes (4 in the control group and 3 in the metronidazole group).

These preliminary results encourage us to think that metronidazole may be as useful in paediatric colonic surgery as it is in colonic resections in adults.

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Table I: CONTROL GROUP

Case no./ Sex/Age	Diagnosis	Operation	Peritoneal swab I	Peritoneal swab II	State of bowel	Wound contamination	Postoperative wound infection		
								Aerobes	Anaerobes
1/M/14 wk	Anorectal agenesis	Closure of colostomy	*E. coli*, enterococci, *Staph. epidermidis*	No growth on primary culture, *Staph. epidermidis* on subculture	Empty	+	+	–	–
5/M/5 wk	Anorectal agenesis	Abdominoanal pullthrough	Pus cells and Gram +ve cocci seen but no growth on primary culture	No pus cells or organisms seen, enterococci on culture	Empty	–	–	–	–
6/M/11 yr	Anorectal agenesis	Closure of colostomy	No growth on primary culture, *E. coli* on second	Microscopic examination and primary culture negative	Loaded	+	Pus +	*E. coli*	Bacteroides
8/M/8 yr	Hirschsprung's disease	Swenson pullthrough	No pus cells seen, no growth on culture	*E. coli*, enterococci	Empty	–	Pus +	*E. coli*, proteus	Bacteroides
9/M/12 yr	Hirschsprung's disease	Duhamel pullthrough	Pus cells and Gram –ve cocci, no growth on culture	Pus cells seen and enterococci on culture	Empty	–	Pus + +	Enterococci, *Staph. epidermidis*	–
12/M/14 yr	Anorecta' agenesis	Closure of colostomy	No pus cells seen, no growth on culture	Pus cells seen, *E. coli* on culture	Loaded	+	Pus + +	*E. coli*, klebsiella, *Staph. aureus*	–
13/M/3 wk	Anorectal agenesis	Laparotomy and abdominoanal pullthrough	No pus cells seen, culture –ve	—	Empty	–	Indurated but no pus obtained	–	–
15/M/14 mth	Hirschsprung's disease	Duhamel pullthrough	No pus cells seen culture –ve	As I but *Staph. epidermidis* on subculture	Empty	–	–	–	–
17/M/14 yr	Anorectal agenesis	Laparotomy and colostomy	No pus cells seen culture –ve	—	Empty	–	Erythematous wound on third postop. day discharging pus	Proteus, *Staph. aureus*	Bacteroides
20/M/4 mth	Anorectal agenesis	Closure of colostomy	No pus cells or organisms seen, no growth on culture	No pus cells or organisms seen, no growth on culture	Empty	–	Pus	*E. col*,	–
21/M/2 d	Hirschsprung's disease	Laparotomy, and colostomy with distal mucous fistula	Negative	Negative	Loaded	–	–	–	–
22/F/3 wk	Anorectal agenesis	Abdominoanal pullthrough	No growth on culture	Gram +ve cocci	Empty	+	Pus discharged for 5 d	*E. coli*, proteus	Bacteroides
27/F/14 yr	Ulcerative colitis	Proctectomy	Gram –ve cocci, Gram –ve bacilli, *E. coli* on culture	Gram +ve cocci seen	Empty	+	Dehiscence of wound and discharging pelvic abscess 1 wk postop., total stay in hospital 7 wks	*E. coli*, proteus	Bacteroides
29/F/5 mth	Large bowel stricture after necrotizing enterocolitis	Resection of stricture and double-barrel colostomy	Gram +ve cocci seen, *E. coli*, klebsiella, enterococci on culture	Gram +ve cocci, Gram –ve rods seen, *E. coli*, enterococci, *Staph. epidermidis* on culture	Loaded	–	–	–	–
30/M/4 mth	Anorectal agenesis	Closure colostomy	Negative	Proteus on culture	Empty	+	+	Proteus, klebsiella	–

Table II: METRONIDAZOLE GROUP

Case no./ Sex/Age	Diagnosis	Operation	Peritoneal swab I	Peritoneal swab II	State of bowel	Wound contamination	Postoperative wound infection		Metronidazole serum concentration
								Bacteriology	
2/M/9 mth	Hirschsprung's disease	Soave pullthrough	WBC and no organisms seen	No pus cells, no organisms seen	Empty	–	–	–	Day 1 25 μg/ml Day 2 38 μg/ml
3/M/6 mth	Hirschsprung's disease	Duhamel pullthrough	Pus cells, *E. coli* on culture	No cells, *E. coli* and enterococci on culture	Empty	–	+ Wound drained	*E. coli*, enterobacter	Day 1 24 μg/ml Day 2 55 μg/ml
4/M/14 yr	Hirschsprung's disease	Soave pullthrough	No cells seen, no organisms on culture	No cells seen, *Staph. epidermidis* on subculture	Empty	–	–	–	Day 1 37 μg/ml Day 2 76 μg/ml
7/F/2 mth	Colonic stricture after necrotizing enterocolitis	Laparotomy and colostomy	No growth on primary culture, *E. coli* on subculture	Enterococci, *E. coli* on culture	Loaded	–	Pus	Proteus, klebsiella, *Staph. epidermidis*	Day 1 16·7 μg/ml Day 2 34·4 μg/ml
10/M/9 wk	Anorectal agenesis	Abdominoanal pullthrough	No growth on primary culture, micrococcus on subculture	Pus cells, no organisms seen, no growth on culture	Empty	–	–	–	Day 1 9·2 μg/ml Day 2 12·6 μg/ml
11/F/9 yr	Hirschsprung's disease	Soave pullthrough	No pus cells, no growth on culture	Pus cells, no growth on culture	Empty	–	–	–	Day 1 17·9 μg/ml Day 2 22·5 μg/ml
14/M/3 mth	Colonic stricture after necrotizing enterocolitis	Laparotomy and resection and colostomy			Empty	–	–	–	Day 1 9·5 μg/ml Day 2 18·7 μg/ml
16/M/3 mth	Hirschsprung's disease	Soave pullthrough	No pus cells, no growth on primary culture, enterococci and *Staph. epidermidis* on subculture	No pus cells, Gram +ve cocci, enterococci, *Staph. epidermidis* on culture	Loaded	+	–	–	Day 1 13·9 μg/ml Day 2 24·7 μg/ml
18/M/13 mth	Hirschsprung's disease	Duhamel pullthrough	Pus cells, no growth on culture	Pus cells, enterococci and *Staph. epidermidis* on subculture	Empty	–	–	–	Day 1 46·0 μg/ml Day 2 65·0 μg/ml
19/M/4 mth	Hirschsprung's disease	Soave pullthrough	Pus cells, no growth on culture	Pus cells and *Staph. epidermidis* on subculture	Empty	–	–	–	Day 1 45 μg/ml Day 2 59·8 μg/ml
28/M/3½ yr	Hirschsprung's disease	Duhamel pullthrough	Enterococci on primary culture, *E. coli* on subculture	*E. coli* on primary culture, klebsiella and pseudomonas on subculture					Day 1 14·2 μg/ml Day 2 22·4 μg/ml
23/M/9 mth	Anorectal agenesis	Abdominoanal proctoplasty	*E. coli* on subculture	No growth	Empty	–	–	–	Day 1 7·8 μg/ml Day 2 8·9 μg/ml
24/F/6 mth	Hirschsprung's disease	Duhamel pullthrough	Gram +ve cocci seen, no growth on culture	No growth on culture	Empty	–	–	–	Day 1 18·8 μg/ml Day 2 29·6 μg/ml
25/F/16 yr	Hirschsprung's disease	Swenson pullthrough	No growth on culture	*Pseudomonas aeruginosa* on subculture	Empty	–	Pus	Gram −ve bacilli, Gram +ve bacilli, *E. coli*, pseudomonas, enterococci	Day 1 14·7 μg/ml Day 2 19·2 μg/ml
26/M/2 mth	Anorectal agenesis	Closure of colostomy	*E. coli* on culture	No growth	Empty	–	–	–	Day 1 9·8 μg/ml Day 2 12·7 μg/ml

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Notice

The British Journal of Surgery Society Ltd has donated £2500 to the Association of Surgeons to permit the Association to invite a distinguished visitor to their Annual Meeting. The Council of the Association has unanimously agreed to invite Professor Vernon Marshall, Professor of Surgery, Monash University, Melbourne, Australia, to the meeting in Norwich in 1979.

The British Journal of Surgery Society and the Association of Surgeons have agreed that Professor Marshall should be invited to visit the hospitals of some of the Fellows of the Association after the meeting, particularly units not closely associated with academic centres. Fellows who would be interested in extending any invitation to Professor Marshall to visit their hospital should contact Mr Alan Birt, the President of the Association.