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Single and multiple dose cotrimoxazole and metronidazole in colorectal surgery

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SUMMARY

Cotrimoxazole and metronidazole were given prophylactically to patients undergoing colorectal surgery as a single peroperative dose or in multiple doses for 5 days. A total of 60 operations randomly divided into two groups showed that the rate of wound infection was low in both groups and there was no statistical difference between them. There were no cases of anastomotic dehiscence in those patients where the anastomosis was carried out from within the abdomen, but 7 out of 9 patients with trans-sphincteric colo-anal anastomoses developed a suture line dehiscence. A greater degree of post-catheterization urinary tract infection was seen in the single dose group (which lacks statistical significance). There were no toxic effects.

COLORECTAL surgery is associated with a high incidence of postoperative sepsis. Even recent reports indicate that wound infection rates as high as 90 per cent may be encountered (1). In a previous study in this hospital (2) the control group of patients had an infection rate of 48 per cent despite attention to preoperative mechanical cleansing of the bowel and careful surgery. It was concluded that antibiotic prophylaxis was necessary in colorectal surgery but the most suitable antibiotic regimen was not clear. After an initial assessment of a combination of cotrimoxazole and metronidazole these drugs were selected for further study.

Patients and methods

Patients

Forty-eight consecutive patients with ages ranging from 22 to 90 years were studied over a 10-month period. They were consecutive patients who underwent 62 emergency and elective, transabdominal operations on the colon and rectum under the care of one of us (A. L.). Patients were not included in the trial if they had received antibiotics in the previous 2 weeks or if they were known to be allergic to sulphonamides. Those patients undergoing elective surgery received castor oil, a fluid diet and rectal or colostomy washouts as described previously (2).

Surgery

All operations were performed under the care of a single consultant (three actual surgeons) and were carried out in a standard manner. An adhesive surgical drape (Steridrape) was applied. All anastomoses were performed using a single layer of interrupted polypropylene (Prolene) sutures and the wounds were closed with continuous Prolene to the rectus sheath and interrupted black silk skin sutures. All wounds were sprayed with povidone-iodine before skin closure. A colostomy was created if conditions at the time of operation were unsatisfactory and all trans-sphincteric colo-anal anastomoses were protected by a transverse colostomy.

Antibiotics

A sealed envelope system of allocation was used. Two regimens of metronidazole and cotrimoxazole were used: metronidazole 500 mg in 100 ml intravenously followed by cotrimoxazole 10 ml in 150 ml physiological saline intravenously administered by the anaesthetist in the first hour of anaesthetic time; or a metronidazole suppository 1 g 8-hourly and cotrimoxazole tablets 2 × 12-hourly or 10 ml in saline intravenously starting on the preoperative day and continuing for 5 days.

Monitoring

Full blood counts were performed before and after surgery and the concomitant antibiotic administration.

Wound assessment

An assessment proforma was completed at 3, 5 and 7 days and subsequent extra comments recorded on a separate sheet. Wounds were assessed by one of us (M. H.) and defined as having (*a*) no infection, (*b*) stitch erythema, (*c*) cellulitis or (*d*) pus present. The patient's general condition, temperature and pulse rate were noted. Bacteriological or other tests were instituted as necessary.

Laboratory methods

These were unchanged from those previously described (2). Urine was despatched for microscopy and culture from all patients on at least two occasions. Appropriate bacteriological samples were obtained for investigation of pyrexia, ill health or when any wound was considered unsatisfactory.

Statistics

The fourfold table test was used as a test of statistical significance in the comparison of patient groups.

Results

Patients in the two groups were well matched for age, sex, operative procedure and disease (*Table I*). Two patients (one procedure each) were withdrawn from the trial. One received a single dose of metronidazole but multiple doses of cotrimoxazole and the other patient underwent a second laparotomy at five days for intestinal obstruction. Neither subsequently became infected. Forty-six patients and 60 procedures remained therefore. In 29 of these procedures a single dose of antibiotics was used and in 31 the multiple dose regimen.

Table I: PATIENTS AND OPERATIONS

	Single dose	Multiple dose
Age range (mean)	25–90 (68·6)	22–86 (64·5)
Male	14	14
Female	15	17
Malignancy	21	24
Closure of colostomy	6	7
Left resection	15	16
Right resection	6	4
Colo-anal anastomoses	3	6
Total	29	31

Wound infection

Wound infections are listed in *Table II*. Seven per cent of wounds became infected after single dosage and 9·6 per cent after multiple dosage. This difference is not statistically significant. The bacteria isolated from wound

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Table II: ABDOMINAL AND PERINEAL WOUND INFECTIONS

	Single dose ($n = 29$)	Multiple dose ($n = 31$)
Extensive pus	0	0
Localized pus	1	1
Cellulitis	0	0
Stitch erythema	1	2
Total infected	2	3

Table III: DETAILS OF INFECTED WOUNDS

Infection	Days postop.	Micro-organisms	Group	Sensitive to PA
Localized pus	11	*E. coli* ±	S	Yes
Stitch erythema	9	*E. coli* ±	S	Yes
Localized pus (perineum)	17	*Proteus mirabilis* *E. coli* Faecal strep.	M	Yes
Stitch erythema	23	*Staph. aureus* ±	M	No
Stitch erythema	22	*E. coli* Faecal strep. *Candida alb.*	M	Yes/No

PA, Prophylactic antibiotics; S, single; M, multiple.

swabs are shown in *Table III*. Anaerobic organisms were not isolated.

Anastomotic dehiscence

A barium enema study was performed between the eighth and tenth postoperative days on all patients whose anastomosis was beyond palpation by a finger. There were no cases of anastomotic dehiscence. There was, similarly, no patient who developed peritonitis or intraperitoneal abscess.

The results of colo-anal anastomosis were less satisfactory: 3 out of 3 patients in the single dose group and 4 out of 6 in the multiple dose group developed a palpable defect in the suture line with an accompanying local abscess. In 2 instances (1 in each group) these patients became unwell and closure of the colostomy was delayed beyond 3 weeks. One of these patients developed a bacteroides septicaemia (*see* below).

Other infections

Urine: Micro-organisms were isolated in significant numbers from 8 patients, 6 of whom had received a single dose of antibiotics. This difference fails to achieve statistical significance, but may be worthy of note. There were 5 isolations of *Escherichia coli*, 1 *Staphylococcus epidermidis* and 2 *Candida albicans*. All patients had been catheterized, and after removal of the catheter 3 of the patients with *E. coli* had a persistent bacteruria. These patients were treated successfully with the appropriate antibiotic.

Sputum: Three patients had potential pathogens isolated from the sputum, but without clinical or radiological evidence of pneumonia. All had received multiple doses of antibiotics. The organisms were *C. albicans*, *Haemophilus influenzae* and a mixed growth of pneumococcus and *H. influenzae*. None of these patients was treated with antibiotics.

Blood cultures: One blood culture in the study was positive. This derived from a patient (on multiple dose antibiotics) who became pyrexial and ill as a result of an abscess in association with a trans-sphincteric colo-anal anastomosis. The patient required treatment with metronidazole for his bacteroides septicaemia and the abscess subsequently ruptured into the anal canal. The patient made a good recovery and had his colostomy closed 3 months later.

Throat cultures: *C. albicans* was isolated from the throat of one patient. She was treated with nystatin.

Intravenous lines: One cannula produced a growth of *S. epidermidis*. The patient was well and apyrexial.

Other signs: Two patients (1 in each group) had a persistent pyrexia without leucocytosis and were finally found (with histological evidence) to have starch granulomas.

Toxicity

There was no evidence of any toxic effect in any patient. There were no cases of bone-marrow suppression and no patient developed a pseudomembranous colitis. There were 2 postoperative deaths (1 in each trial group). They were due to a cerebrovascular accident and carcinomatosis respectively. The trial drugs did not appear to be related to these deaths.

Discussion

The aim of this study was to determine whether sepsis following colorectal surgery could be controlled by a simple regimen of prophylactic antibiotics. A previous study (2) indicated that antibiotics were effective in reducing the incidence of septic complications and cotrimoxazole and metronidazole seemed appropriate drugs. A multiple dose regimen is costly in terms of both money (approximately £30) and nursing time, is potentially toxic and may encourage resistant organisms or superinfection (3). A low dose antibiotic regimen has been used successfully in general (4, 5), though this has been less successful after colorectal operations using a prophylactic regimen of tobramycin and lincomycin (1). A recent single dose trial of cotrimoxazole in biliary surgery (where coliforms predominate) showed a marked reduction in wound sepsis (6). Results in *Table II* show that there was no difference in wound infection rates between our two groups and suggests, therefore, that a single peroperative dose of cotrimoxazole and metronidazole is as effective a regimen as a 5-day course for wound infection control in colorectal surgery. In neither group was there any anaerobic infection and anaerobes have predominated in serious and life-threatening infections following colorectal surgery in the past (7).

Povidone-iodine was used during wound closure in all the patients in this study. Some doubt has recently been expressed on the efficacy of povidone-iodone in general surgery (8) but this would not affect comparison between our two groups. If effective, it would have played a part in the overall low incidence of wound infection.

Other infections

There was a noticeable difference in the incidence of urinary tract infections between the two groups of patients (who were all catheterized). Twenty-one per cent of the single dose group and 6 per cent of the multiple dose group had positive urine cultures on one or more occasions. The apparent difference between

these two groups fails to achieve statistical significance using the fourfold table test, but this difference may be real and would thus certainly achieve clinical significance. There was no fungal or bacterial superinfection.

Anastomotic infection

The lower in the bowel an anastomosis is performed the more likely it is that anastomotic dehiscence may occur (9). The low trans-sphincteric anastomosis is perhaps most at risk of disruption and our results would certainly support this contention, though the clinical effects need not be devastating. All patients (3) in the single dose group and 4 of 6 in the multiple dose group developed a suture line dehiscence, though this had clinical effects in only 2 patients (1 in each group). It would be unsatisfactory to base any conclusion on a subgroup of 9 patients, but further work in this area may be indicated.

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Verdict on vagotomy

A one-day symposium on vagotomy will be held in Bournemouth on Saturday 29 March 1980, immediately following the joint meeting of the Association of Surgeons and the British Society of Gastroenterology. Members of these Societies have been circulated with details and application forms. Others wishing to come should write to: Dr J. H. Baron, Department of Surgery, Royal Postgraduate Medical School, Hammersmith Hospital, DuCane Road, London W12 0HS.