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The use of metronidazole in the preparation of the bowel for surgery

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SUMMARY

A randomized trial was carried out in 120 patients undergoing colonic surgery mainly for carcinoma. Sixty-one patients received metronidazole and Thalazole and 59 received Thalazole alone. Sepsis occurred in 8 (13·1 per cent) of the 61 patients who received metronidazole, compared with 29 (49·2 per cent) of 59 patients who received only Thalazole. Of the 8 patients with sepsis who received metronidazole, none had infection due to anaerobic organisms.

IT has been known for over a decade that nearly 80 per cent of the faecal flora consists of *Bacteroides* species (van Houte and Gibbons, 1966). It is, however, only recently that attention has been drawn to the use of antibiotics with specific action against these anaerobic organisms in the preparation of the bowel for surgery (Willis et al., 1977). Any major advance to be made in the control of postoperative sepsis following bowel surgery would clearly lie in the choice of an antibiotic effective against anaerobic organisms. With this in mind we designed a trial comparing two groups of patients undergoing colonic resection, in which one group received the antibiotic metronidazole, which is strictly effective against anaerobic organisms. The preliminary results (Taylor and Cawdery, 1977) indicated that a reduction in the wound sepsis rate could be achieved using such an antibiotic. The decision whether to give the control group an antibiotic or not was difficult. Recent observations (*British Medical Journal*, 1976) have suggested that all that is required for adequate bowel preparation is mechanical cleaning. When we planned the study, however, we relied upon the earlier observations of Rosenberg et al. (1971), which indicated that mechanical cleaning alone was inferior to the addition of Thalazole to the regimen. We accordingly used Thalazole to minimize the risk to our patients.

Patients and methods

Patients in whom colonic resection was planned were randomized into two groups by a secretary who selected an appropriately labelled card. Patients in group A received oral Thalazole 2·5 g four times a day for 4 days, while those in group B received oral metronidazole 400 mg three times a day for 4 days in addition to Thalazole in the same dosage, i.e. 2·5 g four times a day. In both groups the bowel was prepared mechanically in an identical way and an oral elemental diet was given during the 4 days of preparation, so that only the antibiotic treatment varied. Antibiotic cover was not extended into the postoperative period. After operation the wound was inspected at intervals determined by the surgical team in charge of the patient and any inflammation or sepsis was recorded using the criteria of Ljungqvist (1964) and a bacteriological swab was taken for aerobic and anaerobic culture. Twenty patients from each group were studied for change in faecal flora by taking a bacteriological swab from the lumen of the specimen after resection and setting it up for aerobic and anaerobic culture.

In all, 126 patients were allocated to the trial. There were 6 exclusions—4 from group A and 2 from group B—for reasons of inoperability or the use of a systemic antibiotic in the early postoperative period. The age range of the group A patients was 26–80 years (mean 60) and that of the group B patients, 34–79 years (mean 57). There were 26 male and 33 female patients in group A and 20 male and 41 female patients in group B.

Statistical analysis was performed using McNemar's test of paired alternatives.

Results

Results of faecal sampling

The results from 40 patients (20 from each group) show that the incidence of anaerobic organisms in group B patients was significantly reduced compared with group A patients. Only 2 patients in group B grew anaerobes from the faecal sample as against all patients from group A. The anaerobes which grew in group B patients were clostridia, which tend to be less sensitive to metronidazole than other anaerobic organisms.

Postoperative sepsis

Of the 120 patients eligible for study, 59 came from group A and 61 from group B. The sepsis rate was 49·2 per cent in group A and 13·1 in group B. This is a significant reduction in sepsis rate ($P = <0·001$). Perineal sepsis occurred more frequently in group A patients (10 out of 15 *v.* 6 out of 19) but the difference was not statistically significant ($P>0·01$). Those patients in group A who had anterior resection of the rectum showed a much higher incidence of wound sepsis than those in group B (*Table I*) (14 out of 30 *v.* 2 out of 31) and the difference is significant ($P<0·001$).

Table I: POSTOPERATIVE SEPSIS IN PATIENTS AFTER COLONIC SURGERY

Operation	Group A	No. with sepsis	Group B	No. with sepsis
Abdominoperineal excision	15	10	19	6
Anterior resection	30	14	31	2
Right hemicolectomy	9	3	8	0
Other, e.g. polypectomy, laparotomy, appendicectomy	5	2	3	0
Exclusions	2		43	
Total	61	29 (49·2%)	65	8 (13·1%)

The organisms cultured from infected wounds in each group are listed in *Table II*. *Bacteroides* spp. were isolated from 17 infected wounds in group A and from no wounds in group B. Patients who had wound infections caused by anaerobic organisms tended to be affected constitutionally by the infection, by way of a rise in temperature and a tachycardia. Those patients with an aerobic wound infection

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Table II: ORGANISMS ISOLATED FROM INFECTED PATIENTS AFTER COLONIC SURGERY

Organism	Group A	Group B
Bacteroides spp.	17	0
Coliforms	20	3
β-haemolytic streptococcus	0	1
Proteus spp.	7	1
Clostridia	5	0
Staphylococcus aureus	7	4
Streptococcus faecalis	0	2

(*Escherichia coli*, *Streptococcus faecalis* and *Staphylococcus aureus*) tended to be less ill and the wound discharge was noted to be less copious and less offensive.

Two patients from each group sustained deep pelvic infection following anterior resection of the rectum with discharge of pus from the drain site and per rectum. All had associated infection of the abdominal wound. Two group A patients had septicaemic episodes in the postoperative period. In one a *Bacteroides* sp. was grown on blood culture and treatment with metronidazole was effective. The infection appeared to arise from coexistent pelvic and wound infections.

Discussion

There is evidence that the addition of metronidazole to a standard bowel preparation reduces the rate of wound sepsis after operation. It is also evident that the drug is effective in eliminating infection due to anaerobic organisms. (*Table II.*) In group A there were 17 instances of infection due to *Bacteroides* spp. and none in group B patients ($P<0{\cdot}001$). It also seems that prophylaxis with the drug is only required during the preoperative preparation of the patient for the elimination of infection due to anaerobic organisms. Its use therefore need not be extended into the postoperative period. Metronidazole is entirely selective in its effects on anaerobic organisms and is completely inactive against aerobic bacteria (Willis et al., 1977). It appears to be non-toxic when used for short periods and at low total dosage. The results obtained in our series suggest that in some way anaerobic organisms work in synergism with aerobic organisms to produce their effects in the wound. Removal of the anaerobes alone may be all that is required to reduce sepsis and it may be unnecessary to add another antibiotic effective against Gram-negative bacteria (Goldring et al., 1975). Recent information supporting this hypothesis comes from Ingham et al. (1977), who provide evidence that *Bacteroides melaninogenicus* and *B. fragilis* interfere with the phagocytosis and killing of *P. mirabilis* and other aerobic bacteria *in vitro*, thus rendering them pathogenic. This could explain why agents such as Thalazole used alone, as in our control group, are relatively ineffective in reducing wound sepsis after colon surgery.

There is therefore good evidence that wound sepsis can be reduced significantly by the preoperative use of metronidazole, and that the patients who do become infected with aerobic organisms do not fare as badly as those infected with anaerobes. It was noted that of those of our patients who developed perineal sepsis following abdominoperineal excision of the rectum, it was those infected with anaerobes who had the most protracted and morbid postoperative course. It is also of note that in group B patients it was the perineal wound which became infected and not the abdominal incision, whereas those patients in group A who developed perineal wound infection also had infected abdominal wounds.

These results are an improvement on those of other quoted series in which lincomycin was given (Downing et al., 1977). The use of improved methods of cleansing the bowel by mechanical means is now well established (Crapp et al., 1975). This, in conjunction with meticulous surgical technique and the elimination of anaerobic organisms from the resected colon, serves to improve the sepsis rate after colonic surgery.

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References

BRITISH MEDICAL JOURNAL (1976) **2**, 773.

CRAPP A. R., POWIS S. J. A., TILLOTSON P. et al. (1975) Preparation of the bowel by whole-gut irrigation. *Lancet* **2**, 1239–1240.

DOWNING R., MCLEISH A. R., BUROON D. W. et al. (1977) Duration of systemic prophylactic antibiotic cover against anaerobic sepsis in intestinal surgery. *Dis. Colon Rectum* **20**, 401–404.

GOLDRING J., SCOTT A., MCNAUGHT W. et al. (1975) Prophylactic oral antimicrobial agents in elective colonic surgery. *Lancet* **2**, 997–999.

INGHAM H. R., SISSON P. R., THARAGONNET D. et al. (1977) Inhibition of phagocytosis *in vitro by* obligate anaerobes. *Lancet* **2**, 1252–1254.

LJUNGQVIST U. (1964) Wound sepsis after clean operations. *Lancet* **1**, 1095–1097.

ROSENBERG I. L., GRAHAM N. G., DE DOMBAL F. T. et al. (1971) Preparation of the intestine in patients undergoing major large-bowel surgery, mainly for neoplasms of the colon and rectum. *Br. J. Surg.* **58**, 266–269.

TAYLOR S. A. and CAWDERY H. M. (1977) The use of metronidazole in the preparation of the bowel for surgery. *Proc. R. Soc. Med.* **70**, 481–482.

VAN HOUTE J. and GIBBONS R. J. (1966) Studies of the cultivable flora of normal human faeces. *Antonie van Leeuwenhoek* **32**, 212–222.

WILLIS A. T., FERGUSON I. R., JONES P. H. et al. (1977) Metronidazole in prevention and treatment of *Bacteroides* infections in elective colonic surgery. *Br. Med. J.* **1**, 607–610.

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