Prospective randomized trial of single dose cefuroxime against mezlocillin in elective gastric surgery

D. L. Morris, D. Young, D. W. Burdon and M. R. B. Keighley

Department of Surgery and Microbiology, General Hospital, Birmingham

Summary: A prospective randomized control trial was made in 78 patients undergoing elective operations on the stomach where the viscus was opened at operation, and the efficacy of single dose intravenous prophylaxis with cefuroxime 1.5 g or mezlocillin 2 g was compared. The overall rate of sepsis was 10.2 per cent. Infection in the cefuroxime group was significantly lower (2.5 per cent) than in the mezlocillin group (18 per cent) (P < 0.05). Four of the seven patients with infections in the mezlocillin group were due to antibiotic resistant staphylococci. The only infections in the cefuroxime group were due to an antibiotic resistant strain of *Pseudomonas aeruginosa*. One case of pseudomembranous colitis occurred in the cefuroxime group. In view of the high rate of resistant organisms in patients receiving mezlocillin we believe that cefuroxime remains the antibiotic of choice for patients undergoing elective gastric operations.

Introduction

It is not always recognized that elective gastric surgery is associated with a high rate of sepsis, particularly in patients with high gastric juice pH, such as in patients with gastric carcinoma, gastric ulcer, patients on cimetidine and those requiring revisional gastric operations after previous ulcer surgery (Gatehouse et al., 1978). A selective approach to antibiotic prophylaxis based upon gastric juice pH produced an unacceptably high level of sepsis in patients with low gastric juice pH (Keighley et al., 1982). Although cefuroxime has provided good results in our hospital, this antibiotic is not effective against Streptococcus faecalis, an organism commonly found in gastric juice, and the antibiotic is occasionally associated with pseudomembranous colitis. The ureidopenicillins have not been used for prophylaxis in gastric surgery and although they are not always stable to β-lactamase they are effective against Str. faecalis and are rarely associated with pseudomembranous colitis. We therefore designed a prospective randomized control trial to compare single dose pre-operative prophylaxis with 1.5 g cefuroxime compared with 2 g mezlocillin for all patients undergoing elective gastric surgery.

Method

One hundred consecutive patients undergoing elective gastric operations were randomly allocated to receive either cefuroxime 1.5 g iv or mezlocillin 2 g iv after induction of anaesthesia. All patients with a history of penicillin allergy were excluded. Postoperative observation of the wound was by a single clinician (DLM) who did not know which antibiotic had been used for prophylaxis. Any pus discharging from the wound was immediately sent to the microbiology laboratory for identification of organisms and assessment of sensitivity to the antibiotic which had been prescribed. Of the 100 patients entered into this study three were withdrawn; in one, administration of the antibiotic was omitted in error, in a second the colon was damaged during revision gastric surgery and metronidazole prophylaxis was instituted, and in the third, a therapeutic course of antibiotic was considered to be necessary because of the need for prolonged postoperative ventilation.

The types of operation performed in the remaining 97 patients is shown in Table I. Nineteen other patients were subsequently excluded from the analysis because the stomach was not opened at the time of operation, hence there was no potential endogenous bacterial contamination. Statistical analysis was performed using Fisher's exact test.

	Antibiotics		
Operations	Cefuroxime	Mezlocillin	
Proximal gastric vagotomy*	8	8	
Vagotomy and pyloroplasty	11	10	
Partial gastrectomy for GU	12	6	
Gastrectomy for carcinoma	12	14	
Roux Y bile diversion	7	6	
Hiatal hernia repair*	1	2	
Total	51	46	

Table I. Type of operation and treatment groups

Results

None of the three patients withdrawn because of protocol violation developed postoperative sepsis. However, two of the 19 patients excluded because the stomach had not been opened developed wound sepsis (Tables II and III). Of the 40 remaining patients receiving cefuroxime, one developed a wound infection (2·5 per cent) compared with five wound infections in the 38 patients receiving mezlocillin (13 per cent) (Table II). There were four patients who developed a postoperative abscess, one in the cefuroxime group and three in the patients receiving mezlocillin. There was only one patient with an episode of septicaemia after operation, this occurred despite mezlocillin prophylaxis. The total number of patients who were not excluded

^{*} Subsequently excluded from analysis because the stomach was not opened at operation.

Table II. Incidence of infection, other complications and length of stay

	Antibiotic regime		
	51 Cefuroxime	49 Mezlocillin	
Excluded or withdrawn Wound sepsis	11	11 1	
Number remaining Wound sepsis Abscess Septicaemia Fotal with abdominal sepsis	40 1 (2·5%) 1 0 1 (2·5%)	38 5 (13%) 3 1 7 (18%)	NS P<0.05
Overall no. of patients with abdominal sepsis	2 (4%)	8 (17%)	P<0.03
Death: non septic septic Severe chest infection Pseudomembranous colitis	1 0 3 1	2 3 6 0	
Mean hospital stay	8.7	8.0	

Table III. Postoperative sepsis

Patient	Antibiotic	Type of operation	Sepsis	Organism isolated	Antibiotic sensitivity
1	Cefuroxime	Gastrectomy	W	Ps. aeruginosa	R
		(carcinoma)	Α	Ps. aeruginosa	R
				Staph. albus	RS
				Enterococci	S
2*	Cefuroxime	PGV	W	Staph. aureus, diphtheroids	S/S
1	Mezlocillin	Gastrectomy (carcinoma)	W	Multiple organisms† including Staph. albus	s
2	Mezlocillin		\mathbf{W}	Staph. aureus, Escherichia coli	\mathbf{R}/\mathbf{R}
		(carcinoma)	Se	E. coli	Ŕ
3	Mezlocillin	Gastrectomy	W	Staph. aureus; Klebsiella sp.	R/S
4	Mezlocillin	Gastrectomy (carcinoma)	Α	Multiple organisms† including Staph. albus	S
5	Mezlocillin	Partial	Α	Nil cultured	?
		Gastrectomy (ulcer)			
6	Mezlocillin	Partial	\mathbf{W}	Staph. aureus	R
		Gastrectomy (ulcer)	A	Staph. aureus	R
7	Mezlocillin	Roux en Y	W	Staph. albus,	R
				β-haemolytic streptococci	S
8	Mezlocillin	PGV	\mathbf{W}	Staph. albus	R

^{*}Excluded from analysis.

[†] Multiple organisms: E. coli, Streptococcus viridans, Klebsiella spp. Proteus spp. Diphtheroids. W= wound sepsis; A=abscess; Se=septicaemia; R=resistant; S=sensitive.

or withdrawn developing postoperative sepsis (wound infection, abscess or septicaemia) was eight (10.2 per cent): one receiving cefuroxime (2.5 per cent) compared with seven receiving mezlocillin (18 per cent; P < 0.05). The type of infection and organisms isolated in all patients are shown in Table III. There was one patient with an antibiotic resistant pseudomonas infection in the cefuroxime group. By contrast, seven of the eight patients with postoperative sepsis in the mezlocillin group were associated with staphylococci, of which five were resistant to mezlocillin.

Six patients died postoperatively, five in the mezlocillin group and one after cefuroxime prophylaxis. Of the five deaths in the mezlocillin group, two were from a myocardial infarction but the remaining three were due to sepsis. Of those dying from infection, one was from an intra-abdominal abscess associated with septicaemia from an infarcted gastric remnant, the second was from an anastomotic leak after a total gastrectomy, and the third was a patient who developed a leak and duodenal fistula following a partial gastrectomy. The only death in the cefuroxime group was due to a myocardial infarction. All six deaths were in patients undergoing gastric resection for carcinoma.

Troublesome postoperative diarrhoea occurred in one patient in the cefuroxime group and Clostridium difficile was isolated from the stool. The mean postoperative hospital stay in the two groups excluding patients who died or required re-operation was 8.7 days in the cefuroxime group compared with 8.0 days in the mezlocillin group. Chest infection occurred in three patients in the cefuroxime group compared with six in the mezlocillin group.

Discussion

The overall level of sepsis in this study was 10.3 per cent. In the 37 patients having an operation for peptic ulcer disease only two (5.4 per cent) developed postoperative sepsis, both were relatively minor occurring after proximal gastric vagotomy and due to staphylococci. By contrast, five patients developed severe sepsis in the groups with gastric carcinoma (19.2 per cent). This study has demonstrated that there was a significant difference in the rate of postoperative sepsis between the two antibiotic groups, even though patients were well matched for age, operation and underlying disease. Overall there were only two patients with abdominal sepsis in the cefuroxime group (4 per cent) compared with eight in the patients receiving mezlocillin prophylaxis (17 per cent; P < 0.025). Within the groups not withdrawn or excluded, there was only one patient with sepsis in the cefuroxime group compared with seven in those receiving mezlocillin prophylaxis (P < 0.05). It could be argued, however, that there were three surgical disasters (ischaemic stomach or anastomotic breakdown) in the mezlocillin group, all of which were responsible for abscess compared with only one disaster (anastomotic dehiscence) associated with abscess in the cefuroxime group. On the other hand there is some evidence that anastomotic dehiscence may be reduced by the use of appropriate antibiotic prophylaxis, since a suture line abscess may be the initiating factor in anastomotic breakdown (Hares *et al.*, 1981).

The appearance of a resistant strain of *Ps. aeruginosa* in an abscess from a patient receiving cefuroxime illustrates one of the potential problems with this antibiotic. In the mezlocillin group resistant staphylococci were cultured in five cases. Since *Staphylococcus albus* and *Staph. aureus* are commonly isolated from gastric juice in patients requiring gastric operation, mezlocillin does not appear to be an agent which should be recommended for prophylaxis in elective gastric surgery.

The single case of pseudomembranous colitis in the cefuroxime group illustrates a problem occasionally encountered with the second or third generation cephalosporins, particularly those which are excreted in high concentrations in bile.

We have already reported a low rate of infection using cefuroxime in patients requiring gastric resection for gastric ulcer or gastric carcinoma (Hares et al., 1981). A more recent study has demonstrated that cefuroxime was associated with significantly better results than ticarcillin when used for prophylaxis in gastric surgery (Keighley et al., 1982). In view of the results of this study we believe that cefuroxime remains the antibiotic of choice for prophylaxis in gastro-oesophageal surgery.

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