Original article

An investigation into the sensitivities of translocating bacteria to a prophylactic antibiotic regimen

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Introduction: It is well established that bacterial translocation is associated with a significant increase in septic morbidity. The purpose of this study was to determine the antibiotic sensitivities of translocating bacteria on the basis that this information may influence antibiotic prophylaxis in surgical patients.

Methods: Routine microbiological techniques were used to assess the antibiotic sensitivities of those bacteria cultured from a mesenteric lymph node harvested at laparotomy in a large series of patients.

Results: Culture of the mesenteric lymph nodes yielded growth in 51 out of a total of 447 patients studied (11.4%). The isolates from 40 patients, a total of 60 organisms, were available for sensitivity testing. The most common species grown was *Escherichia coli* (48% of isolates). Thirty-three patients (83%) grew organisms sensitive to the antibiotic prophylaxis used, but there was no significant difference in the incidence of postoperative septic complications between these patients and those in whom resistant bacteria were grown (39% versus 29%, $P = 0.64$ Fisher's Exact test mid P).

Conclusions: The majority of translocating bacteria are sensitive to the prophylactic antibiotics commonly used in patients undergoing laparotomy. However, the occurrence of postoperative septic morbidity is independent of this variable.

Key words: Bacterial translocation – Sepsis – Septic morbidity – Antibiotics

In previous studies, we have reported a significantly increased incidence of postoperative septic morbidity in patients in whom bacterial translocation, defined by culture of viable micro-organisms from a mesenteric lymph node harvested at laparotomy, was identified.^{1,2} We also found that the same bacterial species was cultured from the mesenteric lymph node and from the site of subsequent sepsis in 32% of patients.² This supports the hypothesis that translocating enteric bacteria promote the development of postoperative septic complications. Hence, antibiotic prophylaxis in patients undergoing laparotomy should be influenced by the antibiotic sensitivities of translocating bacteria.

The aim of this study was to determine the sensitivities of those bacteria cultured from mesenteric lymph nodes to routine antibiotic prophylaxis, and to observe whether this had any influence on subsequent septic morbidity.

Patients and Methods

Approval for the study was obtained from the locally organised Ethical Committee. A mesenteric lymph node was harvested in patients undergoing laparotomy over a 5-year period, and sent for culture. The sampling technique and bacteriological methods used, plus the clinical

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Figure 1 Patient diagnoses.

and microbiological results of this study, have been published in detail elsewhere.² All the bacteria isolated from the mesenteric lymph nodes were stored. Antibiotic sensitivities were subsequently assessed using the Stokes Comparative Antibiotic Susceptibility testing method.³ These data have not been reported previously.

Standard antibiotic prophylaxis used throughout the duration of the study comprised intravenous bolus doses of cefuroxime 1.5 g and metronidazole 500 mg given intra-operatively. These were administered only after the mesenteric lymph node had been excised.

All septic complications that occurred in the postoperative period were recorded prospectively for each patient. These complications were defined as the presence of clinical, haematological or radiographic evidence of infection plus a positive bacterial culture from appropriate specimens.

Table 1 Organisms cultured from mesenteric lymph nodes (n = 60)

Bacterial species	No. of cultures
Enterobacteriaceae (n = 45; 75%)	
<i>Escherichia coli</i>	29 (48)
<i>Klebsiella</i> spp.	7 (12)
<i>Enterobacter cloacae</i>	3 (5)
<i>Citrobacter freundii</i>	3 (5)
<i>Proteus mirabilis</i>	2 (3)
<i>Morganella morganii</i>	1 (2)
Other enteric bacteria (n = 9; 15%)	
<i>Pseudomonas aeruginosa</i>	2 (3)
<i>Enterococcus faecalis</i>	3 (5)
<i>Bacteroides fragilis</i>	3 (5)
<i>Clostridium perfringens</i>	1 (2)
Non-enteric bacteria (n = 6; 10%)	
Oral streptococci	3 (5)
<i>Staphylococcus epidermidis</i>	2 (3)
Diphtheroids	1 (2)

Results

A mesenteric lymph node was harvested in a total of 447 patients during the study period. A positive culture was obtained in 51 patients, a point prevalence of bacterial translocation of 11.4%. In 11 cases, samples had either not been preserved or organisms failed to survive, leaving a total of 40 patient samples available for assessment of antibiotic sensitivities. The male:female ratio of these patients was 16:24, and the median age was 73 years (interquartile range, 63–80 years). The indications for surgery are given in Figure 1.

In the 40 samples available, 60 organisms were isolated. Species of the *Enterobacteriaceae* group, of which the most frequently isolated was *Escherichia coli*, accounted for 45

Figure 2 Cefuroxime sensitivities of the aerobic bacteria isolated from mesenteric lymph nodes (n = 56).

Figure 3 Postoperative septic morbidity (total of 19 complications in 15 patients).

(75%) of the positive cultures. Other enteric bacteria made up a further 15% of the isolates (Table 1).

Thirty-three patients (83%) grew only organisms that were sensitive to cefuroxime, whilst a cefuroxime-resistant species was cultured in each of the remaining 7 patients. Figure 2 demonstrates the individual cefuroxime sensitivities of the aerobic organisms isolated. Each of the four anaerobic bacteria cultured, *Bacteroides fragilis* in three cases and *Clostridium perfringens* in one, were grown as part of a multi-organism culture. All were sensitive to metronidazole.

A total of 19 postoperative septic complications occurred in 15 of these 40 patients. The incidence of septic morbidity was 13/33 (39%) in the subjects in whom all bacteria were sensitive to the antibiotics used, compared to 2/7 (29%) in those with cefuroxime-resistant isolates (difference 10%; 95% CI, -27.5 to 47.5%; $P = 0.64$, Fisher's Exact test mid P). The nature of the complications and details of the causative organisms are illustrated in Figures 3 and 4, respectively. In 8 cases (42%), the same organism was isolated from both the mesenteric lymph node and the subsequent site of sepsis.

Discussion

The results of this study demonstrate that the majority of bacteria (49/60, 82%) found to translocate through the intestinal wall to mesenteric lymph nodes are sensitive to cefuroxime. In addition, the few anaerobes isolated in the present study were all sensitive to metronidazole. The incidence of postoperative septic morbidity in patients in whom evidence of translocation of cefuroxime-sensitive organisms was identified was not significantly different to that observed in those who grew resistant bacteria.

These findings suggest that the current wide-spread usage of a second-generation cephalosporin such as cefuroxime as prophylaxis in patients undergoing laparotomy is correct. We

Figure 4 Microbiology of postoperative septic morbidity.

would expect this antibiotic, given at the time of induction of anaesthesia, to achieve a therapeutic level in the gut-associated lymphatic tissue for the duration of the operation, and be effective against the majority of bacteria proven to translocate. This concurs with a recent review of antibiotic prophylaxis in colorectal surgery, in which the use of a second-generation cephalosporin (such as cefuroxime together with metronidazole) is recommended.⁴ The present study can be criticised for deferring the administration of antibiotic prophylaxis until after mesenteric lymph node sampling had been performed, as a large prospective trial assessing the timing of prophylaxis in colorectal surgery demonstrated a significant decrease in the incidence of post-operative wound infections in patients given antibiotics 0–2 h pre-operatively when compared to intra-operative administration.⁵ However, the lymph node was excised immediately after opening the peritoneal cavity, with antibiotics administered as soon as this was completed, thus achieving therapeutic tissue levels at the time at which the bowel was opened and any direct contamination likely to occur. It should also be remembered that prophylactic antibiotics can only possibly be effective against bacteria translocating in the peri-operative period. By necessity the sampling techniques employed in the present study provide only a cross-sectional assessment of bacterial translocation at a single point in time. There can be no doubt that this phenomenon occurs in the postoperative period also, although it is at the time of surgery that bacterial translocation is most likely to be of clinical relevance as a consequence of the relative immunosuppression induced by major surgery.

Bacterial translocation is not the only cause of post-operative septic morbidity. Some complications are a consequence of failure of surgical technique, such as direct tissue contamination at the time of operation or failure of

an intestinal anastomosis causing peritonitis. In addition, devices used for therapeutic or monitoring purposes predispose to infection, including endotracheal tubes, urethral catheters and intravascular devices.⁶

Conclusions

This study suggests that although the vast majority of bacteria found to translocate are sensitive to the standard prophylactic antibiotics used in patients undergoing laparotomy, this has no bearing on subsequent septic morbidity. This is probably because the majority of postoperative septic complications occur as a result of mechanisms other than bacterial translocation. However, bacterial translocation occurring in the postoperative period after prophylactic antibiotics have been discontinued may also explain the study findings. Further understanding of the nature of intestinal barrier function is required in order to devise optimal treatment strategies in surgical patients, which may involve the use of agents that manipulate the intestinal

microflora, enhance the integrity of the gut mucosa and stimulate local and systemic immune defences as an adjunct to prophylactic antibiotics.

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