

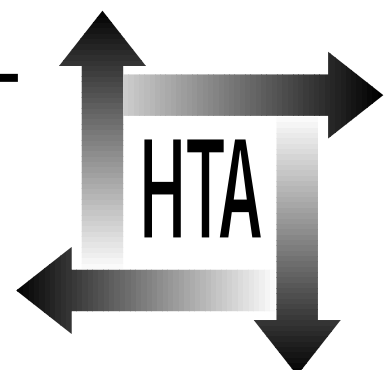
Executive summary

Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomised controlled trials

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Executive summary

Background

Wound infections are the most frequent nosocomial infections among surgical patients and are related to an increase in morbidity and mortality, a prolongation of hospital stay and an increase in the cost of medical care. Colorectal surgery is associated with a high risk of infection due to endogenous contamination by bacteria in the contents of the large bowel.

It is now generally accepted that antimicrobial prophylaxis is one of many important measures that should be taken to prevent postoperative wound infections. To achieve the most cost-effective use of antimicrobial prophylaxis, consideration of the choice, delivery and regimen of antimicrobial agents is necessary.

Objectives

This review evaluates the relative efficacy of antimicrobial prophylaxis in patients undergoing colorectal surgery where there is a high risk of surgical wound infection (SWI).

Methods

Data sources

Literature searches of Medline, Embase and the Cochrane Controlled Trials Register were conducted to identify randomised controlled trials (RCTs) published between 1984 and 1995, which investigated antimicrobial prophylaxis in the prevention of postoperative wound infection in patients who had undergone colorectal surgery. Bibliographies of reviews and all identified trials were examined to locate additional studies. A sample of key journals was also handsearched. All languages were considered.

Validity assessment and data extraction

The identified studies were assessed for both relevance and validity by one reviewer and checked by another. Data extraction was carried out by one reviewer using an electronic data extraction form. This process was again checked by a second reviewer. For articles containing insufficient detail, authors were contacted for clarification. Of all the studies assessed, 147 RCTs, including a total of 23,049 patients, met the review inclusion criteria.

The principal outcome assessed in the review was the incidence of SWI. Where possible, abdominal wound infections were recorded separately from perineal wound infections. Data on other postoperative infections and adverse events were also collected.

Data synthesis

Studies were grouped according to the antibiotic used, route of administration, and number of doses administered (i.e. single versus multiple doses). Where appropriate, formal meta-analysis and investigation of heterogeneity among trials were conducted.

Results

The quality of the RCTs has improved over the last 12 years, though there are still many methodological problems, including inappropriate method of patient allocation, lack of blinding during outcome assessment, and insufficient sample size. The criteria for inclusion and exclusion were described in 87% of the included trials. The exclusion criteria most frequently used were allergy to study drugs, preoperative use of other antibiotics, impaired renal or liver function, children or very old patients, pregnancy or lactation, and certain types of colorectal operations.

More than 70 different antibiotic regimens were tested in 147 trials. The overall rate of SWI across all the included trials of antimicrobials prophylaxis (excluding four non-antibiotic groups) was 11.1% ($n = 22,927$).

The results of this review confirm that the use of antimicrobial prophylaxis is generally effective for the prevention of SWIs in colorectal surgery. Some antimicrobial regimens appear to be less effective than others in this indication. For example, monotherapy with either metronidazole, doxycycline or piperacillin are inadequate for prophylactic treatment in colorectal surgery.

The review found that a single dose or short-term use of an antimicrobial agent is as efficacious as long-term, postoperative use. Pooled results from 17 trials that compared a single-dose regimen with a multiple-dose regimen, showed no significant difference in the rate of SWI (odds ratio = 1.17;

95% confidence interval [CI]: 0.89, 1.54). There is a lack of convincing evidence concerning the importance of a second-dose regimen when surgical procedures are longer than 2 hours.

There is no convincing evidence to suggest that the second- and third-generation cephalosporins are more efficacious than the first-generation cephalosporins in this indication (6% versus 6.4%; odds ratio = 0.93; 95% CI: 0.46, 1.86).

Establishing the efficacy of different routes of administration of antibiotic prophylaxis was complicated by the use of different antibiotics or use of extra antibiotics. No additional benefit was observed in six trials that compared parenteral alone, with parenteral plus topical use of antibiotic prophylaxis. Several trials, showing extra benefit of oral antibiotics, used inadequate parenteral antibiotics such as metronidazole alone, or piperacillin alone. Oral or topical application of antibiotics in addition to the parenteral administration of appropriate antibiotics seem to be of limited value in most cases.

In general, the estimates of efficacy of many of the different regimens included are similar and it is very difficult, if not impossible, to identify the best one. However, the Type-II error or lack of statistical power cannot be ruled out as a potential reason for statistically non-significant findings in many small trials.

A total of 74 of the 134 trials published in English reported adverse events following antibiotic prophylaxis in colorectal surgery. Skin rash, diarrhoea, and nausea were commonly mentioned adverse events that may be attributable to the use of some antibiotic treatments. No serious toxicity or adverse events were reported except in one trial that reported postoperative bleeding in some patients treated with latamoxef.

The costs associated with SWI are high in terms of both antibiotic treatment and prolonged hospitalisation with some studies reporting an additional 12 days in hospital as a result of SWI. Three trials that included cost data in comparisons of monotherapy and combination therapy showed that monotherapy was as effective as the combination regimens but less expensive. The overall cost data available from the RCTs suggest that drug acquisition costs need to be viewed in terms of their efficacy, as a reduction in infection rates is associated with a shorter hospital stay, the 'hotel' costs of which account for the highest proportion of overall cost during treatment.

Conclusions

The use of antimicrobial prophylaxis is efficacious in the prevention of SWI in colorectal surgery. With the exception of a few inadequate regimens, there is no significant difference in the rate of SWI between many regimens. The use of a multiple-dose regimen may be unnecessary for the prevention of SWI, as single-dose regimens have been demonstrated to be as efficacious as multiple dosing and in addition, may be associated with less toxicity, fewer adverse events, less risk of developing bacterial resistance and lower costs. Similarly, no convincing evidence supports the idea that the new-generation cephalosporins are more efficacious than first-generation cephalosporins in preventing SWI in colorectal surgery.

Implications for policy

Two principles are important to follow when selecting an antimicrobial prophylactic regimen in colorectal surgery:

- antibiotics or antibiotic combinations should be active against both aerobic and anaerobic bacteria;
- the administration of antibiotics should be timed to ensure that the tissue concentration of antibiotics around the wound area is sufficiently high when bacterial contamination occurs.

Universal acceptance and use of a regimen should be avoided in order to minimise the development of antibiotic-resistant bacteria. Based on the research evidence, guidelines should be developed locally in order to achieve a more cost-effective use of antimicrobial prophylaxis in colorectal surgery.

Recommendations for research

Further studies of efficacy may be of little value and would require large numbers of patients in order to demonstrate a statistically significant difference. Future research should focus on the understanding of the practical use of antimicrobial prophylaxis in colorectal surgery in the UK and the cost-effectiveness of different regimens of antibiotic prophylaxis.

Publication

Song F, Glenny AM. Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomised controlled trials. *Health Technol Assessment* 1998;2(7).

NHS R&D HTA Programme

The overall aim of the NHS R&D Health Technology Assessment (HTA) programme is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and work in the NHS. Research is undertaken in those areas where the evidence will lead to the greatest benefits to patients, either through improved patient outcomes or the most efficient use of NHS resources.

The Standing Group on Health Technology advises on national priorities for health technology assessment. Six advisory panels assist the Standing Group in identifying and prioritising projects. These priorities are then considered by the HTA Commissioning Board supported by the National Coordinating Centre for HTA (NCCHTA).

This report is one of a series covering acute care, diagnostics and imaging, methodology, pharmaceuticals, population screening, and primary and community care. It was identified as a priority by the Pharmaceutical Panel.

The views expressed in this publication are those of the authors and not necessarily those of the Standing Group, the Commissioning Board, the Panel members or the Department of Health. The editors wish to emphasise that funding and publication of this research by the NHS should not be taken as implicit support for the recommendations for policy contained herein. In particular, policy options in the area of screening will, in England, be considered by the National Screening Committee. This Committee, chaired by the Chief Medical Officer, will take into account the views expressed here, further available evidence and other relevant considerations.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

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