Perioperative infection prophylaxis and risk factor impact in colon surgery

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Prophylaxis against perioperative infection in colorectal surgery was examined. Ceftriaxone was compared with other cephalosporins and penicillins. The other cephalosporins used were cefotiam, cefazolin, cefoxitin and cefotoxime. The penicillins used were mezlocillin, amoxicillin-clavulanic acid, ampicillin and miscellaneous.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of patients undergoing elective colon resection. The exclusion criteria were suppurative peritonitis, other pre-existing infections requiring antibiotic therapy, emergency surgery, mechanical ventilation for more than 12 hours, granulocytopenia (fewer than 1,000/mm3) and autoimmune deficiency syndrome.

Setting
The setting was secondary care. The economic analysis was carried out in 114 centres in Germany.

Dates to which data relate
The study was conducted between 1 September 1996 and 30 September 1997. The price year appears to have been 1997.

Source of effectiveness data
The effectiveness data were gathered from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same group of patients as that used in the effectiveness study.

Study sample
No power calculations to determine the sample size were reported. A total of 2,513 patients undergoing elective colon resection were documented.

Study design
This was a prospective cohort study that was conducted in 114 German centres. The patients were risk matched into
pairs using six criteria:

- operation duration (less than or greater than 2 hours);
- blood loss (less than or greater than 3 red cell concentrates);
- colon resection plus rectum resection (yes or no);
- age (less than or greater than 65 years);
- pre-existing diabetes mellitus, hepatic, renal or airway disease (yes or no);
- immunosuppressive therapy (e.g. steroids) or radiation (yes or no).

The design left the choice of dosage to the physician. Ceftriaxone was administrated in 90% of the cases as a single preoperative 2-g dose with an average duration of prophylaxis of 1.48 days. The average duration of prophylaxis with the other beta-lactams was 2 to 3 days, except for amoxicillin-clavulanic acid (1.36 days). Concomitant antibiotic therapies (mainly metronidazole and gentamicin) were given.

Of the 2,513 patients prospectively followed, 32 protocol violators were excluded. In the final analysis, 1,344 patients were assigned to group A (ceftriaxone versus other cephalosporins) and 800 patients to group B (ceftriaxone versus penicillin). No reason was given for this disparity. Groups A and B did not differ in their demographics, preoperative diagnosis, risk factors or type of colon resection.

The length of follow-up was unclear, but it was likely to have been the duration of postoperative hospital stay.

**Analysis of effectiveness**

Only 2,144 patients (1,344 plus 800) were included in the analysis. The main primary health outcomes used in the analysis were the number of local or systemic infections in the first 10 postoperative days and the number of postoperative inpatient deaths. The secondary health outcomes used were the physicians’ impressions, the occurrence of adverse events and microbiology outcomes. There was little difference between the groups in terms of their baseline characteristics.

**Effectiveness results**

The rate of infectious complications in the first 10 postoperative days was 10.0% with ceftriaxone versus 10.9% with other cephalosporins (group A). The corresponding rates in group B were 6.8% with ceftriaxone and 17.8% with penicillin, \( p < 0.001 \).

In group A, there were 0 postoperative inpatient deaths in the ceftriaxone group and 4 in the other cephalosporins group. In group B there was one postoperative inpatient death with ceftriaxone and 2 with penicillin.

The physicians' impressions rated prophylaxis effective in 92.4% with ceftriaxone versus 83.8% with other cephalosporins (group A). In group B, prophylaxis was rated effective in 91.8% with ceftriaxone and in 83.3% with penicillin.

Adverse events occurred in fewer than 5% of the cases. Adverse events were 4.5% with ceftriaxone versus 3.9% with cephalosporins (group A), and 4.3% with ceftriaxone versus 3.0% with penicillin (group B).

Postoperative pathogens were markedly fewer with ceftriaxone in comparison with other antibiotics.

There were also fewer enterococcal and staphylococcal wound infections with ceftriaxone (1 and 4, respectively) than with penicillin (4 and 9, respectively).
Clinical conclusions
Ceftriaxone was more effective than other cephalosporins (non significant) and penicillin (statistically significant).

Measure of benefits used in the economic analysis
The authors did not derive a summary benefit measure. A cost-consequences analysis was therefore performed.

Direct costs
The cost/resource boundary of the analysis was that of the hospital. The direct costs were for postoperative antibiotics, mechanical ventilation, re-operation and days of hospitalisation. The authors used a daily rate of Euro 229.6 for inpatients (general rate plus a 20% departmental rate in the surgical department of the Munich-Grosshadern Hospital, 1997). The costs and the quantities were not reported separately. The price year was unclear, but it was likely to have been 1997. The costs were not discounted since they were incurred in less than one month. Neither the total costs nor the incremental costs were reported. The cost analysis reported the hospitalisation costs averted with ceftriaxone.

Statistical analysis of costs
A statistical analysis of the main postoperative cost factors was carried out using the t-test.

Indirect Costs
No indirect costs were included.

Currency
Euros (Euro).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
Ceftriaxone shortened hospital stay by 0.7 days in group A and by 1.8 days in group B, (p<0.001).

Ceftriaxone saved Euro 160.7 over other cephalosporins and Euro 413.2 over penicillin.

Synthesis of costs and benefits
Not applicable.

Authors' conclusions
Prophylaxis with ceftriaxone was more effective and cheaper (considering all the costs measured) than other beta-lactams used in colon resection.

CRD COMMENTARY - Selection of comparators
The authors seem to have suggested that the prophylaxes compared were in current use at the institution, hence the choice of comparators. You should consider whether these are widely used technologies in your own setting.
Validity of estimate of measure of effectiveness
A prospective cohort study was conducted. The internal validity of the study was high for a cohort study. The study sample was representative of the study population. The patient groups were shown to be comparable at analysis, so confounding should be low for those variables. The patients were risk matched, which should help to reduce selection bias. However, physicians were allowed to choose the dosage, which could well introduce bias. The physicians’ impressions were not discussed in the analysis and do not appear to have been appropriate measures. The details given of the methods used to estimate effectiveness were adequate.

Validity of estimate of measure of benefit
There was no summary measure of benefit. A measure of benefit such as quality-adjusted life-years saved would have been appropriate in this study.

Validity of estimate of costs
The perspective adopted was unclear, but it was likely to have been that of the hospital. Only the unit costs of hospital stay were reported. The cost estimates were likely to have been specific to the Munich-Grosshadern hospital. No sensitivity analyses of the quantities or prices were conducted and this may limit the interpretation of the study findings. Discounting was not undertaken, which was appropriate since the costs were incurred in less than one month. The incremental costs were reported but not the total costs for each option, which would have been helpful.

Other issues
The issue of generalisability to other settings was not addressed. The authors made appropriate comparisons of their findings with those from other studies. The results do not appear to have been presented selectively. The study examined patients undergoing elective colon resection and this was reflected in the authors’ conclusions. The authors reported another limitation of their study, the fact that it did not address the impact of concomitant metronidazole.

Implications of the study
The authors did not stress any implications of the study in relation to ceftriaxone. According to the authors, metronidazole needs to be administrated with all beta-lactams since postoperative infection complications were significantly reduced in each case.

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