Long-acting versus short-acting cephalosporins for preoperative prophylaxis in breast surgery: a randomized double-blind trial involving 1,766 patients


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
The health technologies in the study were two third-generation cephalosporins, perioperative antibiotics used to reduce the incidence of postoperative infections in surgery: ceftazidime and ceftriaxone. Both have a broad spectrum of activity, high serum levels and tissue penetration. However, ceftriaxone is characterised by prolonged half-life: its effect provides a 24-hour antibiotic coverage, while ceftazidime covers the risk of surgical infections for about 2 hours.

Type of intervention
Preoperative antibiotic prophylaxis to prevent postoperative infections.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing breast surgery. Patients with manifest preoperative infections, specific allergies, severe renal or hepatic impairment, or undergoing chemotherapy were not included in the study.

Setting
The setting was secondary care. The economic study was carried out at the National Institute for the Study and Treatment of Cancer, "G. Pascale", Naples, Italy.

Dates to which data relate
The effectiveness evidence and the resource use data were gathered between 1 January 1996, and 31 August 1997. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not performed on the patient sample. All patients aged over 16 years and undergoing breast cancer treatment at the authors’ institution from January 1996 to August 1997 were included in the study. Overall, 1,766 patients were selected and equally distributed between the ceftriaxone (n=883) and ceftazidime (n=883) groups. The mean age was 55.4 years (+/-12.3) in the ceftriaxone group and 55.6 years (+/-12.8) in the ceftazidime group.
Study design
The study was a randomised, double-blind trial, carried out in a single centre (National Institute for the Study and Treatment of Cancer, Naples). Before surgery, patients were assigned to either of two groups using random number tables. Vials of the two drugs were identical in appearance and numbered by use of blocked randomisation tables, and were allocated sequentially following the patients’ enrollment order. Patients were followed for 6 weeks at most. To ensure the blinding method in the outcome assessment, the group assignments were not disclosed to the physicians responsible for clinical evaluation or to the patients until the end of the study.

Analysis of effectiveness
The basis of the effectiveness analysis was not stated, but it appeared that all patients included in the study were accounted for in the analysis. The primary health outcomes used in the analysis were the postoperative infection rate and the number of strains isolated from infected wounds. Statistical analyses were performed to show that the two groups were similar with respect to age, operative procedure, operative time, and time to discharge after operation.

Effectiveness results
The postoperative infection rate was 3.4% (30 infections) in the ceftriaxone group and 7.7% (68 infections) in the ceftazidime group. The difference was statistically significant, (p=0.06, Fisher's exact test). The cases of strains isolated from infected wound were 2 (0.45%) in the ceftriaxone group and 8 (0.91%) in the ceftazidime group.

Clinical conclusions
The study showed that ceftriaxone was more effective than ceftazidime in the surgery prophylaxis.

Measure of benefits used in the economic analysis
No summary benefit measure was used in the economic analysis, therefore a cost-consequence analysis was carried out.

Direct costs
Discounting was not relevant due to the short time horizon of the study (6 weeks). Quantities and costs were not reported separately. The quantity/cost boundary adopted appears to have been that of the hospital, although the authors did not explicitly report this. The costs estimated included prophylaxis antibiotics, intravenous materials and time, hotel expenses, dressing time and materials, and antibiotic treatment of wound infection. The source of the cost data was not reported. Resource use data were gathered between 1 January 1996 and 31 August 1997. The price year was not reported.

Statistical analysis of costs
No statistical analysis was reported.

Indirect Costs
Indirect costs were not included.

Currency
Italian Lira (L). US$1 = L1,700 at the 1998 average exchange rate.

Sensitivity analysis
No sensitivity analysis was carried out.
Estimated benefits used in the economic analysis
See effectiveness results above.

Cost results
In the ceftriaxone group, the total cost was L148,730,30 and the average cost per patient was L168,440.

In the ceftazidime group, the total cost was L298,758,200 and the average cost per patient was L338,345.

The net saving of ceftriaxone versus ceftazidime was L150,027,900, with a saving per patient of L169,905.

Synthesis of costs and benefits
Costs and benefits were not combined.

Authors’ conclusions
The authors concluded that the use of a single dose of antibiotic with a long half-life, ceftriaxone, greatly lessens the risk of any post-operative infection and realises cost savings compared to the short half-life antibiotic, ceftazidime, in patients undergoing breast surgery.

CRD COMMENTARY - Selection of comparators
The two drug therapies selected in the study are common third-generation cephalosporins used for antibiotic prophylaxis in surgery and you should consider whether they represent commonly used technologies in your own setting. It should also be noted, however, that the authors did not justify the exclusion of other antibiotics.

Validity of estimate of measure of effectiveness
The effectiveness evidence was derived from a randomised double blind clinical trial, therefore the internal validity of the study was high. Furthermore, the large study sample was likely to have been representative of the study population, and patient groups were shown to have been comparable at analysis.

Validity of estimate of measure of benefit
Not applicable.

Validity of estimate of costs
The cost estimates were quite specific to the Italian setting and the external validity was limited by the lack of sensitivity analyses. In addition, costs and quantities were not reported separately and neither the price year nor the sources of cost data were mentioned. The perspective of the study was not stated and as a consequence, some costs (relevant to the analysis) could have been omitted or erroneously included. Overall, details and comments on the cost analysis were not reported satisfactorily in the study.

Other issues
The robustness of the results was not tested and the generalisability to other settings was not addressed. The authors made some comparisons of their findings with those of other studies.

Implications of the study
The study results encourage the adoption of long half-life ceftriaxone, given that it is "more cost-effective to administer perioperative prophylaxis than to treat infections that occur in patients who have not received prophylaxis".
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