Cefazolin versus cefazolin plus metronidazole for antibiotic prophylaxis at Cesarean section

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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
Cefazolin and the combination of cefazolin plus metronidazole (CEF-MET) were compared for antibiotic prophylaxis at Cesarean section. Monotherapy comprised 2 g cefazolin, while the combined therapy (CEF-MET) consisted of 1 g cefazolin intravenously (i.v.) plus 500 mg metronidazole i.v.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised women who underwent Cesarean delivery. Women who had received intrapartum antibiotics, or were sensitive to penicillins, cephalosporins or metronidazole were excluded from the study. Also excluded were women who had consumed ethanol within 24 hours of delivery, or who suffered from known liver disease.

Setting
The setting was secondary care. The economic analysis was carried out in the USA.

Dates to which data relate
The effectiveness data were collected between December 1996 and November 1998. Dates for the costs and the price year were not reported.

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

Link between effectiveness and cost data
The costing was carried out retrospectively on the same sample of patients as that used in the effectiveness analysis.

Study sample
Power calculations demonstrated that 62 participants in each group would be required to detect a 10% decrease in postoperative infectious morbidity with a power of 80% at the 0.05 significance level. Women who underwent Cesarean delivery at the Regional Medical Centre and fulfilled the inclusion and exclusion criteria were recruited to the study. The study sample comprised 160 patients, of whom 81 received cefazolin alone and 79 received CEF-MET.
Study design
The analysis was based on a double-blind, single-centre, randomised study. Women were randomly allocated to each group. Randomisation was achieved through the use of computer-generated random numbers. Patients, house staff and attending physicians were blinded to the antibiotic regimen administered. The mean duration of follow-up was not reported.

Analysis of effectiveness
It was not reported whether the analysis was conducted on an intention to treat basis or on treatment completers only. The primary outcomes used were:

- postoperative infectious morbidity,
- the duration of hospitalisation,
- the duration of postoperative hospitalisation,
- the duration of antibiotic therapy,
- the estimated blood loss at surgery, and
- the operation time.

The comparability of the two groups was assessed using a two-tailed Student’s t-test and the chi-squared statistic. The analysis demonstrated that the two groups were comparable in terms of their baseline characteristics.

Effectiveness results
The mean (+/- standard deviation) duration of postoperative hospitalisation was 4.46 (+/- 4.7) days in the cefazolin alone group and 3.12 (+/- 0.8) days in the CEF-MET group. The difference was statistically significant, (p=0.014).

The duration of postoperative antibiotic treatment was also statistically significant between the two groups, 0.4 (+/- 1.04) days in the CEF-MET group versus 1.98 (+/- 5.2) days in the cefazolin alone group.

There was also a significant difference between the two groups in the rates of postoperative infectious morbidity. The rate of postoperative infectious morbidity was 32% in the cefazolin alone group and 14% in the CEF-MET. The difference was statistically significant, (p=0.0064).

Twenty-six patients in the cefazolin alone group versus 11 in the CEF-MET group developed postoperative endometritis. There were no statistically significant differences between these sub-groups in terms of:

- the time from rupture of the membranes until delivery,
- the total operation time,
- the estimated blood loss,
- the total duration of hospitalisation,
- the duration of postoperative hospitalisation, and
- the duration of antibiotic treatment.

Clinical conclusions
The authors concluded that, compared with cefazolin alone, the combined CEF-MET prophylaxis resulted in decreases
in the rates of postoperative infectious morbidity, duration of postoperative hospitalisation and duration of antibiotic treatment.

**Measure of benefits used in the economic analysis**
No summary benefit measure was used in the economic analysis. The study was, in effect, a cost-consequences analysis.

**Direct costs**
The health service costs included in the analysis were those of the drugs. These were derived from actual data (average wholesale drug prices). For the cost of a hospital room for postoperative treatment, charges were used to proxy prices and were based on average rates, although the actual source was not reported. The unit costs were provided, but the costs and quantities were not analysed separately. Discounting was not considered relevant since the costs were incurred during less than 2 years. The dates for the costs and the price year were not reported.

**Statistical analysis of costs**
The costs were treated deterministically (i.e. no statistical analyses of the costs were undertaken).

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analysis was performed.

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

**Cost results**
The costs were reported per patient.

The cost of antibiotic treatment was $26.73 per patient in the cefazolin alone group and $9.12 in the CEF-MET group. The difference resulted in cost-savings of $17.61 per patient.

Hospital charges were estimated to be $1,184.32 per patient in the cefazolin alone group and $828.54 in the CEF-MET group.

The combination antibiotic prophylaxis resulted in cost-savings of $372.39 per patient.

**Synthesis of costs and benefits**
The costs and benefits were not combined.

**Authors' conclusions**
Antibiotic combination prophylaxis would appear to be a better option in terms of effectiveness and lower costs.
CRD COMMENTARY - Selection of comparators
The authors gave a justification for their choice of the comparator. It represented the most common practice in their setting. You should decide if this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a double-blind, single-centre, randomised study which, given the study question, appears to have been appropriate. The study sample was representative of the study population. In addition, the patient groups were shown to be comparable at analysis. The method of randomisation and the length of the study were reported, thus enhancing the internal validity of the study. However, it was unclear whether the analysis was conducted on an intention to treat basis or per protocol. This fact will affect the validity of the results obtained.

Validity of estimate of measure of benefit
The authors did not derive a measure of benefit. The reader is referred to the comments in the "Validity of estimate of measure of effectiveness" field (above).

Validity of estimate of costs
The perspective adopted in the economic analysis was not reported, although it appears to have been that of the hospital. However, some costs that may be considered relevant were omitted from the analysis. In particular, laboratory costs, treatment costs and diagnostic costs were omitted. The omission of these costs might have altered the results obtained. The authors acknowledged that their cost analysis was somewhat elementary. The costs and the quantities were not reported separately, which would make it difficult for the analysis to be reworked for other settings. The quantities were derived from the study, but no statistical analysis of the quantities was performed. This may limit the interpretation of the findings. The costs were derived from published sources and the authors' setting, and hospital charges were used to proxy prices. However, no statistical or sensitivity analyses were performed to assess the robustness of the estimates used. The price year was not reported.

Other issues
The authors compared their findings with those from other studies in terms of the use of cefazolin only, finding consistency in their results. However, no studies had evaluated the use of the combination prophylaxis, thus eliminating the possibility of further comparisons. The issue of generalisability to other settings was not addressed. The study involved women undergoing Caesarean delivery and this was reflected in the authors' conclusions. The authors do not appear to have presented their results selectively.

The authors reported a number of limitations to their study. First, postoperative endomyometritis and postoperative infectious morbidity were diagnosed according to standard criteria or based on the clinical judgement of obstetricians, which may have confounded the results. Second, the authors mentioned that the blinding of the physicians to the treatment option might have been violated, as physicians could have become aware of the treatment regimen through anaesthesia records.

Implications of the study
The authors did not make any explicit recommendations for changes in policy or practice, nor did they identify areas for further research. However, the discussion indicated areas (e.g. the cost analysis) where more information is required.

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