Comparison of the effects of prophylactic antibiotic therapy and cost-effectiveness between cefazolin (CEZ) and sulbactam/ampicillin (SBT/ABPC) in gastric cancer surgery employing clinical pathway


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 study examined prophylactic antibiotic therapy in gastric cancer surgery employing a clinical pathway (CP). The two antibiotics compared were cefazolin (CEZ) and sulbactam-ampicillin (SBT-ABPC). One gram of CEZ or 1.5 g of SBT-ABPC was scheduled to be administered at the time of surgery (with an extra dose if the operation lasted more than 3 hours), within 6 hours postoperation and twice daily during the following 3 days. Full details of the CP, which lists all drug administered pre- and post-surgery and their doses, were provided in the paper.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients who underwent gastric cancer surgery and were managed by a CP. No further details of the inclusion or exclusion criteria were reported.

Setting
The setting was secondary care. The economic study was conducted at the Nippon Medical School Hospital, Josai University, Nihon University, Japan.

Dates to which data relate
The effectiveness data came from a single study conducted between January 2002 and September 2003. The resource data related to 2002. The price year was not stated.

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

Link between effectiveness and cost data
The cost data for the study were collected retrospectively from the same sample as that used in the effectiveness analysis.

Study sample
Power calculations were not used in the determination of sample size. The study sample comprised 157 hospitalised
patients who had surgery for gastric cancer under a CP. Of these, 62 (38 males and 24 females) were administered CEZ and 95 (69 males and 26 females) were administered SBT-ABPC. The mean age of the CEZ patients was 64.4 years (standard deviation, SD=11) and that of the SBT-ABPC patients was 67.2 years (SD=11). Twenty-nine (46.8%) CEZ patients and 57 (60%) SBT-ABPC patients had complications (e.g. hypertension, diabetes mellitus, ischaemic heart diseases, cardiac arrhythmia, cerebrovascular accident, liver dysfunction, renal dysfunction).

Study design
This was a non-randomised trial that was carried out in a single centre. The period of follow-up was until hospital discharge. No loss to follow-up was reported.

Analysis of effectiveness
The analysis of effectiveness was conducted on an intention to treat basis. The principal outcome assessed was prophylactic effect on infection. Other outcomes assessed were:

- the length of postoperative hospitalisation,
- the number of patients with systemic inflammatory response syndrome (SIRS) at 24 hours after operation,
- changes in body temperature,
- the white blood cell count (WBC),
- C-reactive protein (CRP), and
- clinical outcomes of postoperative care by a nurse during a postoperation period of 7 days.

In terms of baseline characteristics, no significant differences between the groups were observed in the patients' age, composition of genders, number of patients with complications, gastric cancer stage, surgical methods, and operation time and blood loss.

Effectiveness results
The prophylactic effect on infection was 69.4% for the CEZ group and 69.5% for the SBT-ABPC group.

The total length of postoperative hospitalisation was 17.6 days (SD=6.6) for the CEZ group and 19.0 days (SD=9.6) for the SBT-ABPC group.

The number of patients with SIRS positive was 7 (11.1%) in the CEZ group and 17 (17.9%) in the SBT-ABPC group.

No significant differences between the groups were observed in the above figures, or in terms of changes in body temperature, WBC, CRP and clinical outcomes of postoperative care by a nurse during a postoperation period of 7 days.

Clinical conclusions
CEZ and SBT-ABPC have similar effectiveness in terms of preventing postoperative infections.

Modelling
Decision trees were used to compare the cost-effectiveness of CEZ and SBT-ABPC. The model was described in detail by means of a diagram, although the software package used was not stated. The time horizon was to the point of discharge from hospital.
Measure of benefits used in the economic analysis
The measure of benefit used was the prophylactic effects of CEZ and SBT-ABPC.

Direct costs
The direct costs included were the costs of antibiotics. The unit costs and the resource quantities were not reported separately. Discounting was not relevant because of the short period of analysis. The costs were estimated using actual data from the single study. The price year was not stated.

Statistical analysis of costs
The cost data were not treated stochastically.

Indirect Costs
The indirect costs were not included.

Currency
Japanese yen (Y).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
The prophylactic effect on infection was 69.4% for the CEZ group and 69.5% for the SBT-ABPC group.

Cost results
The total anticipated costs for antibiotics were Y15,556 per person in the CEZ group and Y20,402 per person in the SBT-ABPC group.

Synthesis of costs and benefits
The cost-effectiveness (total antibiotic costs divided by prophylactic effect) was Y22,565 per person for the CEZ group and Y29,355 per person for the SBT-ABPC group.

Authors' conclusions
Although the clinical outcomes were similar between the cefazolin (CEZ) and sulbactam-ampicillin (SBT-ABPC) groups, the anticipated costs of antibiotics were higher for the latter (SBT-ABPC). Thus, the authors concluded that the prophylactic effect of CEZ might be more cost-effective. However, they mentioned that when postoperative infection is expected to be serious and long-lasting, SBT-ABPC might be more cost-effective.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clearly described in the paper. CEZ and SBT-ABPC were compared with each other within the context of a CP, which was also clearly described. You should determine if these interventions are relevant to your own setting.

Validity of estimate of measure of effectiveness
The study design (a non-randomised controlled trial) was appropriate for the study question but the lack of
randomisation introduces the risk of bias and confounding. The sample size was quite large but, as no power calculations were reported, it is unclear whether a larger group would be necessary to reveal statistically significant results. However, the authors did demonstrate that the groups were comparable at baseline. The effectiveness results from the study, in addition to cost data, were used to populate a decision tree to integrate the costs and effects. No sensitivity analyses were performed as the data were treated deterministically.

**Validity of estimate of measure of benefit**
The authors utilised the rate of preventing infection as their measure of benefit, which was clearly appropriate for the study question. This measure, unlike the use of utility values such as quality-adjusted life-years, limits comparisons across other health care programmes.

**Validity of estimate of costs**
The cost data were limited to drug costs only. As the authors themselves acknowledged, this was a rather restricted analysis which suggested that future studies should examine a broader economic perspective. The price year was not stated, which limits reflation exercises. No sensitivity analyses were performed on the resource use and costs. The generalisability of the cost results to other settings and countries is, therefore, rather limited.

**Other issues**
The authors did not compare their results with other studies, but this was justified as it was stated that no other studies had examined the cost-effectiveness of these two prophylactic alternatives for the patient domain studied. In terms of generalisability, the authors noted that the use of a single study with a patient sample from the authors' hospital might limit the applicability of the results to other hospitals and settings. The use of effectiveness data from other countries, they argued, would limit the relevance to their institution. In terms of limitations, the authors noted that a meta-analysis of the literature would increase the generalisability of their analysis. In addition, no sensitivity analyses were performed using the decision tree.

**Implications of the study**
In terms of clinical practice, the findings of the study indicated that the clinical outcomes of CEZ and SBT-ABPC are similar, and there is an economic advantage associated with CEZ. However, when postoperative infection is expected to be serious and long-lasting, SBT-ABPC might become more cost-effective. Future research should consider effectiveness data that are derived from a systematic review and meta-analysis, which would enhance the validity and generalisability of the results.

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