Analysis of empiric antimicrobial strategies for cellulitis in the era of methicillin-resistant \textit{Staphylococcus aureus}

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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**
The study compared three empiric antimicrobial strategies for cellulitis. The strategies were cephalexin, trimethoprim/sulfamethoxazole (TMP/SMX) and clindamycin.

**Type of intervention**
Treatment.

**Economic study type**
Cost-effectiveness analysis.

**Study population**
The study population comprised a hypothetical population of patients with cellulitis, who were older than 12 years of age. Patients with complicated infections, or who were immunocompromised, were excluded. Only patients whose therapy could be treated on an outpatient basis were included.

**Setting**
The setting for the study was outpatient care. The study was carried out in Virginia, USA.

**Dates to which data relate**
The effectiveness data used to populate the model came from studies published between 1985 and 2006. The price year was 2006.

**Source of effectiveness data**
The clinical and epidemiological data in the model included the probability of infection due to \textit{Staphylococcus aureus} (S. aureus), and the probability of cure for each therapy given the proportion of infection that is susceptible. The proportions of GSA, MRSA and MSSA that are susceptible to each drug were also estimated.

**Modelling**
A decision tree was used to model the three therapies, initial treatment with cephalexin, TMP/SMX or clindamycin, followed by treatment with linezolid in the event of initial treatment failure. The time horizon was not explicitly stated. The model parameters were presented in full in the paper, along with a number of modelling assumptions which were fully justified.

**Sources searched to identify primary studies**
The clinical effectiveness data were derived from a number of clinical trials, while infection and resistance data were
estimated from community studies of the onset of infection. A few of the trials included to inform TMP/SMX efficacy had populations with indications other than skin and soft tissue infections.

**Methods used to judge relevance and validity, and for extracting data**
The authors identified published papers by conducting a literature search using MEDLINE. The keywords used for the search were reported, but not the inclusion criteria. The authors also handsearched literature from listed references. The methods used to synthesise the data were described in the paper.

**Measure of benefits used in the economic analysis**
The summary measure of benefit was the number of cases cured.

**Direct costs**
The costs to the third-party payer were included in the analysis. These were for treatment and physician visits. The costs associated with treatment toxicity were excluded. Resource use, in terms of dosage, was described in the paper and reflects clinical therapy. Antimicrobial costs (cephalexin, TMP/SMX and clindamycin) and physician outpatient costs came from official federal and national sources, while the cost of linezolid represented a mail order retail cost. The price year was 2006. No discounting was required given the short time horizon of the study.

**Statistical analysis of costs**
No statistical analysis of the costs was conducted.

**Indirect Costs**
The productivity costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
The authors undertook one-way and two-way sensitivity analyses. The range of probabilities used generally came from published data, whilst the range of costs was +/- 10% of the base-case value. The univariate analysis individually considered the range of parameters in the model, while the two-way analysis varied the probability of infection due to S. aureus together with the probability of MRSA.

**Estimated benefits used in the economic analysis**
Information on the rate of cure for each intervention was not reported, but cephalexin was reported to be more effective than the other therapies.

**Cost results**
The authors did not report the total cost per patient per treatment. They reported the cost per cure.

Cephalexin monotherapy cost $175 per cure, clindamycin cost $244 per cure and TMP/SMX cost $396 per cure.

**Synthesis of costs and benefits**
The base-case cost-effectiveness analysis found cephalexin to be more effective and less costly than either clindamycin or TMP/SMX (i.e. cephalexin dominated the other interventions).
Authors' conclusions
Cephalexin is a cost-effective treatment for cellulitis given current levels of methicillin-resistant Staphylococcus aureus (MRSA).

CRD COMMENTARY - Selection of comparators
Justifications for the comparators used included popularity, availability, coverage and familiarity. You should decide if cephalexin, TMP/SMX and clindamycin represent widely used empiric therapies for cellulitis in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were obtained from a review of the literature. The literature search was described in part, in terms of the database and keywords, but not the inclusion criteria. However, some assumptions were necessary because of a lack of reliable data, and these were described in the paper. The methods used to synthesise the data were also described. The authors conducted sensitivity analyses to evaluate ranges for these data.

Validity of estimate of measure of benefit
A treatment-specific measure of benefit was adopted. This was the number of cases cured, which was estimated using the decision model. However, the measure of benefit estimates was not reported in the paper. The authors reported the results of the cost-effectiveness analysis.

Validity of estimate of costs
The authors adopted a third-party payer perspective and all the costs relevant to this perspective appear to have been considered. The cost data and the methods used to derive them were adequately reported. The costs were subjected to a sensitivity analysis.

Other issues
The authors made limited comparisons of their findings with those from other studies, partly because this was the first study to model empiric therapies for cellulitis. The authors used a sensitivity analysis to evaluate the impact of varying prevalence data on the economic results. The presentation of the results was limited to the incremental cost-effectiveness ratios, and the cost and effectiveness results were not reported separately. The authors' conclusions appear to have reflected the scope of the analysis. The authors acknowledged some limitations to their analysis, including the lack of reliable data for a number of parameters in their model, and the implicit (rather than explicit) modelling of the impact of adverse effects on treatment costs.

Implications of the study
The authors suggested that further studies of the microbiology of cellulitis, the epidemiology of MRSA, and the clinical effectiveness of clindamycin and TMP/SMX are required. These would better inform future models of the cost-effectiveness of treatment for cellulitis.

Source of funding
None stated.

Bibliographic details

PubMedID
17200425