

A systematic review and economic model of switching from non-glycopeptide to glycopeptide antibiotic prophylaxis for surgery

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Executive summary

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Executive summary

Background

Surgical site infections (SSIs) are a major cause of morbidity and mortality in surgical patients. Antibiotic prophylaxis is recommended when the risk of infection is high and/or the consequences of infection are likely to be severe. In recent years, the prevalence of antibiotic-resistant bacteria has increased markedly, methicillin-resistant *Staphylococcus aureus* (MRSA) being a cause of particular concern. Glycopeptide antibiotics (vancomycin and teicoplanin) are active against MRSA, but are normally reserved for the treatment of MRSA infections because of the perceived risk of selecting new resistant strains by increasing glycopeptide use. This project considers the implications of switching from non-glycopeptide to glycopeptide antibiotics for surgical prophylaxis.

Objectives

Our overall objective was to determine whether there is a level of MRSA prevalence at which a switch from non-glycopeptide to glycopeptide antibiotics for routine prophylaxis is indicated in surgical environments with a high risk of MRSA infection. We addressed this question by undertaking:

- a systematic review of the effectiveness of glycopeptide compared with non-glycopeptide antibiotic prophylaxis to determine whether there is evidence to guide antibiotic choice for surgical prophylaxis at different levels of MRSA prevalence
- a systematic review of published economic evaluations, to examine the cost-effectiveness of glycopeptide antibiotics compared with appropriate comparators
- a series of supplementary reviews, to support the modelling work and associated research recommendations
- a modelling approach to estimate the cost-effectiveness of glycopeptide antibiotic prophylaxis relative to appropriate comparators, using orthopaedic surgery as an exemplar.

Methods

Systematic reviews

We searched 11 databases from 1990 to September 2005. Internet searches and searching of the reference lists of included papers were also performed. NHS EED, HEED and IDEAS were also searched for the cost-effectiveness review and modelling.

The effectiveness review included controlled clinical trials, comparing a glycopeptide with an alternative antibiotic regimen in adults undergoing surgical procedures where prophylaxis is recommended, that reported effectiveness and/or adverse events. Controlled observational studies were also included for adverse events. The cost-effectiveness review included economic evaluations comparing glycopeptide prophylaxis with any alternative comparator. Study validity was assessed using standard checklists.

Supplementary reviews

The supplementary economic reviews assessed evaluations of non-glycopeptide antibiotic prophylaxis; evaluations where antibiotic resistance is a problem; methods of modelling resistance in infectious diseases; and developing a conceptual framework.

Economic modelling

An indicative decision analytic model was developed to compare vancomycin with a cephalosporin and with a combination of vancomycin and cephalosporin, using hip arthroplasty as an exemplar. Available data on SSI rates, MRSA rates, effectiveness of the antibiotics in reducing infections and consequences of infection [impact on survival, length of hospital stay, health-related quality of life (HRQoL) and treatment intensity] were incorporated into the model. Costs were estimated from the perspective of the NHS.

Results

Systematic reviews

The effectiveness review included 16 randomised controlled trials, with a further three studies included for adverse events only. There was no

evidence that glycopeptides were more effective than non-glycopeptides in preventing SSIs. Most of the trials did not report either the baseline prevalence of MRSA at the participating surgical units or MRSA infections as an outcome. The cost-effectiveness review included five economic evaluations of glycopeptide prophylaxis. Only one study incorporated HRQoL and undertook a cost-utility analysis. None of the studies was undertaken in the UK, limiting the generalisability of the results to the UK, and none explicitly modelled antibiotic resistance.

Supplementary reviews

The supplementary reviews provided few insights into how to assess cost-effectiveness in the context of resistance. No studies modelled cost-effectiveness alongside epidemiological models of resistance. In addition, there was little information regarding the impact of surgical infections on costs post-discharge and patient quality of life.

Economic modelling

The lack of available clinical evidence limited the development of the cost-effectiveness model and meant that the modelling could only be indicative in nature. Hip arthroplasty was chosen as an exemplar because it is a 'clean' procedure and patients are at high risk of MRSA. The model can be used to show the threshold baseline risk at which the use of vancomycin as prophylaxis might be cost-effective (the model did not include teicoplanin). The indicative model suggests that the baseline risk of MRSA (the average risk of MRSA infection in the population of patients undergoing hip arthroplasty in a given centre) can be fairly modest at below the national average and it would still appear cost-effective to use glycopeptide prophylaxis. However, this conclusion is reached in the absence of any modelling of the effect on resistance caused by increased glycopeptide use. The model indicates

that, at all plausible baseline infection rates, the use of glycopeptides as a form of prophylaxis in addition to a treatment for MRSA infections is unlikely to decrease the total usage and hence reduce the risk of future problems with glycopeptide-resistant bacteria.

Conclusions

Implications for healthcare

There is insufficient evidence to determine whether there is a threshold prevalence of MRSA at which switching from non-glycopeptide to glycopeptide antibiotic prophylaxis might be clinically effective and cost-effective.

Recommendations for research

Future research needs to address the complexities of decision-making relating to the prevention of MRSA and infection control in general. Focusing on MRSA alone is too limited and the prophylactic use of glycopeptides is only one aspect of infection control.

Research including evidence synthesis and decision modelling comparing a full range of interventions for infection control, which extends to other infections, not just MRSA, is needed. A long-term research programme to predict the pattern of drug resistance and its implications for future costs and health is also needed.

Publication

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NIHR Health Technology Assessment Programme

The Health Technology Assessment (HTA) Programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The research findings from the HTA Programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

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First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, the public and consumer groups and professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA Programme then commissions the research by competitive tender.

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Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this issue of the journal was commissioned by the HTA Programme as project number 05/36/01. The contractual start date was in September 2005. The draft report began editorial review in May 2006 and was accepted for publication in April 2007. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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