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


CRD summary
This review concluded that there was insufficient evidence to draw definitive conclusions comparing glycopeptide antibiotics with non-glycopeptide in surgical patients at high risk of methicillin-resistant Staphylococcus aureus (MRSA). There was significant clinical heterogeneity, but this was a generally well-conducted review and the authors’ cautious conclusions were likely to be reliable.

Authors’ objectives
To assess the clinical and cost-effectiveness of glycopeptide compared with non-glycopeptide antibiotic prophylaxis, and determine whether there is a level of methicillin-resistant Staphylococcus aureus (MRSA) prevalence at which a change from non-glycopeptide to glycopeptide antibiotics is indicated in surgical patients.

Searching
MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials, Science Citation Index and BIOSIS Previews were searched between 1990 and September 2005 for articles in any language. Search terms were reported. In addition, six databases were searched for unpublished and ongoing research, two internet searches were conducted and references of retrieved articles were searched manually.

Study selection
Randomised and quasi-randomised controlled clinical trials comparing the use of single or combined pre- or intra-operative glycopeptide antibiotics (vancomycin, teicoplanin, ramoplanin and decaplanin) with other antibiotics for preventative treatment in adults undergoing clean or clean-contaminated surgery were eligible for inclusion. Studies continuing administration of multiple doses of antibiotics after surgery were eligible if the first dose was given prior to or during surgery. Eligible studies were required to report mortality and rates of infection (superficial, deep or organ space) occurring within and after 30 days of surgery as the primary outcomes. Secondary outcomes and adverse events were also reported.

Included studies were conducted in patients undergoing various surgical procedures, including cardiac and orthopaedic procedures, in the UK, USA, Europe and Israel. Follow-up, where reported, ranged from hospital stay to 26 months. The majority of included studies assessing clinical effectiveness compared vancomycin or teicoplanin with a cephalosporin at varying doses and intervals.

Two reviewers independently screened articles for relevance. Disagreements were resolved by consensus or referral to a third reviewer where necessary.

Assessment of study quality
Two reviewers independently assessed methodological quality using the following criteria: randomisation, allocation concealment, comparability of patients at baseline, blinding, intention-to-treat analysis (ITT), sample size calculation, withdrawals and eligibility criteria. Disagreements were resolved by discussion or through referral to a third reviewer.

Data extraction
The number of patients experiencing infection, mortality, and adverse events (dichotomous data) were extracted for each treatment group to calculate relative risk (RR), with 95% confidence intervals (CIs), based on an ITT basis. Secondary outcomes (continuous data) were extracted to calculate the mean difference between treatment groups, with 95% CIs.

One reviewer extracted data, which was checked by a second reviewer. Disagreements were resolved by consensus, or through referral to a third reviewer if necessary.
Methods of synthesis
Due to clinical heterogeneity, pooling of the results was not undertaken. Instead, data were presented as a narrative synthesis, in tables and as forest plots grouped by outcome and surgical speciality.

Results of the review
Nineteen studies (n=11,878): 18 randomised controlled trials and one prospective historical control group were included in the review. Three trials scored well on most quality criteria, with the remaining trials reporting various levels of quality.

Surgical site infection (SSI)
Only one trial reported statistically significant benefit with glycopeptide on SSIs within 30 days of surgery (12 trials). No statistically significant differences were reported between glycopeptide and cephalosporin for preventing SSIs. There was no statistical difference between glycopeptide and cephalosporin prophylaxis in patients reporting SSIs after hospital discharge (five trials).

Results of treatment effects on various types of bacteria causing SSI varied and were reported in the review.

Mortality
The rate of infection-related deaths was generally small and no statistically significant differences were found between patients receiving glycopeptide and patients receiving cephalosporin prophylaxis (six trials).

Secondary outcomes and adverse events were reported in the review.

Cost information
An indicative model addressing the cost-effectiveness of surgical antibiotic prophylaxis suggested that baseline risk of MRSA can be modest (below the national average) and use of glycopeptides remains cost-effective.

Authors’ conclusions
There was insufficient evidence to draw definitive conclusions about whether glycopeptide or non-glycopeptide antibiotics were more effective for preventing surgical infection. Similarly, there was insufficient evidence to draw conclusions about the risk of increasing bacterial resistance to glycopeptides.

CRD commentary
The objectives of the review and the inclusion criteria were detailed and clear. A comprehensive literature search was carried out using various electronic databases and other relevant sources. Validity was assessed using appropriate criteria, although the quality of included studies was generally poor. Appropriate methods were used to minimise the potential for reviewer error and bias and synthesise the data. There was significant clinical heterogeneity, which was acknowledged by the authors. CIs were wide for many of the individual studies, which reduced the reliability of the of the included studies. This was a generally well-conducted review. The authors’ cautious conclusions seemed appropriate and were likely to be reliable.

Implications of the review for practice and research
Practice: the authors stated that it was not possible to determine whether a certain level of MRSA infection required changing from non-glycopeptide to glycopeptide prophylaxis.

Research: the authors stated that future research should investigate the clinical and cost-effectiveness of alternative infection control policies, using both experimental and non-experimental data. A full synthesis and modelling study to inform wider decision-making in infection control was warranted to include a range of interventions and polices for controlling MRSA and other infections. Further long-term research was also required to predict the pattern of drug resistance and its implications for future costs and health.

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