Linezolid versus vancomycin for the treatment of Gram-positive bacterial infections: meta-analysis of randomised controlled trials


CRD summary
This review found that linezolid was as effective as vancomycin in patients with Gram-positive infections; there was superior clinical and microbiological outcome with linezolid in complicated skin and skin-structure infections caused by Staphylococcus aureus. As language and publication bias was possible in the review process, the reliability of the authors' conclusions is unclear.

Authors' objectives
To evaluate the effectiveness and safety of linezolid and vancomycin for the treatment of Gram-positive bacterial infections.

Searching
PubMed (to June 2009), Current Contents and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for papers written in English; search terms were reported. References of retrieved articles and relevant review papers were scanned. Conference abstracts were excluded.

Study selection
Blinded or unblinded randomised controlled trials (RCTs) that compared linezolid with vancomycin in the treatment of infections caused by Gram-positive cocci were eligible for inclusion. Trials had to assess the effectiveness, toxicity or mortality of both regimens. Additional antimicrobial agents could also be included. RCTs primarily conducted in cancer or neutropenic patients were excluded.

The primary outcome measures were treatment success, all-cause mortality and adverse events. Secondary outcomes were microbiological assessment and eradication of Gram-positive cocci.

Most of the included trials were conducted in patients 18 years or older; one trial included patients 12 years or younger, and two trials included patients 13 years or older. Most trials used an intravenous or oral 600mg dose of linezolid every 12 hours; in some trials this could be followed by oral linezolid; one trial was of intravenous 10mg/kg linezolid every 12 hours, followed by the same dose orally every eight hours. The dose of vancomycin used was 1g every 12 hours intravenously. Patients presumed to have concomitant Gram-negative or mixed infections were treated with appropriate regimens. Additional antibiotics were administered to some patients in the vancomycin groups of three trials.

Two reviewers independently selected studies for inclusion.

Assessment of study quality
A modified Jadad scale was used to give a quality score out of 5 points (3 or more points indicated high quality). Methodological quality was assessed on randomisation, double-blinding, withdrawals and allocation concealment.

The number of reviewers that performed quality assessment was not reported.

Data extraction
Two reviewers independently extracted data to calculate odds ratios (ORs) and 95% confidence intervals (CIs). Data were extracted for the clinically assessed population (who fulfilled all inclusion criteria) and the microbiologically assessed population (a subset of the clinical population who also had microbiologically documented infections), along with intention-to-treat data.

Methods of synthesis
Odds ratios and 95% confidence intervals were pooled using a fixed-effect or random-effects model (results from the random-effects model were presented unless there was significant heterogeneity, in which case the fixed-effect model was reported). Heterogeneity was assessed using the $\chi^2$ test.

Analyses were stratified in the following groups: patients with skin and skin-structure infections, bacteraemia and pneumonia; patients in clinically assessed populations (adults and children). The microbiologically evaluable population was assessed separately; eradication (documented or presumed) of Gram-positive cocci was analysed separately.

**Results of the review**

Nine RCTs were included in the review (n=4,192 patients; range 144 to 1,200). Three trials were double blinded, one trial was single blinded and five trials were non-blinded. The mean quality score was 2.6 (range 2 to 4).

There was no significant difference between linezolid and vancomycin groups for treatment success in clinically evaluable patients. Subgroup analyses showed similar results, except for in treatment of patients with skin and skin-structure infections where linezolid was associated with significantly better treatment success than vancomycin (OR 1.40, 95% CI 1.01 to 1.95; six RCTs).

Linezolid was associated with better treatment success than vancomycin in microbiologically evaluable patients (OR 1.33, 95% CI: 1.03 to 2.06; nine RCTs). Results were similar for *Staphylococcus aureus*, but were not significant for methicillin-resistant *Staphylococcus aureus* (MRSA) strains (associated with significant heterogeneity, $I^2$=51%), enterococci species and streptococci species.

There was no significant difference in mortality with linezolid compared with vancomycin.

There was no significant difference in adverse events possibly or probably related to the drugs between treatments; most were mild to moderate and reversible.

**Authors’ conclusions**

Linezolid was as effective as vancomycin in patients with Gram-positive infections. There was superior clinical and microbiological outcome with linezolid in treating complicated skin and skin-structure infections caused by *Staphylococcus aureus*.

**CRD commentary**

The research question was supported by clear inclusion criteria. Only English language papers were sought and no attempts were described to identify unpublished literature, so language and publication bias may have been possible. Two reviewers selected studies and extracted data, but it was unclear whether similar steps were taken for validity assessment.

Trial quality was assessed; blinding was taken into consideration in the analyses. The meta-analysis appeared appropriate and heterogeneity was assessed.

As language and publication bias were possible in the review process, the reliability of the authors’ conclusions is unclear.

**Implications of the review for practice and research**

The authors did not state any implications for practice or research.

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