Linezolid versus vancomycin or teicoplanin for nosocomial pneumonia: a systematic review and meta-analysis
Kalil AC, Murthy MH, Hermsen ED, Neto FK, Sun J, Rupp ME

CRD summary
This review concluded that linezolid was not clinically superior to glycopeptides in the treatment of nosocomial pneumonia and that it showed a significance increase in incidence of gastrointestinal events and thrombocytopenia compared to these treatments. The conclusions reflect the results of the review and appear likely to be reliable.

Authors' objectives
To assess whether linezolid was superior to glycopeptides for the treatment of nosocomial pneumonia.

Searching
PubMed, EMBASE and The Cochrane Library were searched from inception to February 2010. Abstracts of four relevant professional meetings were searched for the same period. Websites of clinical trials registries and the US Food and Drug Administration sites were searched. Search terms were reported. No language restrictions were applied.

Study selection
Randomised controlled trials (RCTs) that compared linezolid to vancomycin or teicoplanin for treatment of nosocomial pneumonia were eligible for inclusion. The primary outcome was clinical cure. Microbiological eradication, all-cause mortality and adverse events were assessed (authors' definitions were accepted).

Seven out of nine included studies compared linezolid with vancomycin; two compared it to teicoplanin. Mean ages in most trial arms ranged from 48 to 67 years; one trial enrolled infants with mean ages of 2.2 and 2.9 years. Types of infections in the included trials were pneumonias, methicillin-resistant Staphylococcus aureus (MRSA) infections that included pneumonias, gram-positive infections that included pneumonias and neutropenic fever that included pneumonias.

Two reviewers independently assessed the studies for inclusion in the review; disagreements were resolved through consensus.

Assessment of study quality
Validity was assessed using the Jadad scale (up to 5 points) for criteria of randomisation, blinding and treatment of withdrawals and drop-outs.

The authors did not state how many reviewers performed the validity assessment.

Data extraction
Data were extracted to enable calculation of risk ratios (RRs) with 95% confidence intervals (CI). Clinical cure and microbiological evaluation were defined as being assessed at the relevant evaluation points for the full evaluable population; where these data were unavailable, data from last follow-up were used.

Methods of synthesis
Pooled risk ratios with 95% CI were calculated using the Mantel-Haenszel fixed-effect model and the DerSimonian and Laird random-effects model; results were reported for the fixed-effect model except where significant statistical heterogeneity was detected. Heterogeneity was assessed using Q and I² statistics. Threshold of significance were 0.1 (Q) and 30% (I²). Analyses were adjusted for the comparator employed (vancomycin or teicoplanin). Sensitivity analyses were used to explore the impact of Jadad scores, inclusion of paediatric patients and use of double blinding for the outcomes of clinical cure and microbiological eradication. Egger, Begg and Mazumdar tests were used to assess publication bias.
Results of the review
Nine RCTs (n=2,329 participants) were included in the review. Sample sizes ranged from 50 to 623. Jadad scores were 3 (six trials) and 4 (three trials).

Clinical cure did not differ significantly between linezolid and comparators (RR 1.01, 95% CI 0.93 to 1.10, I²=0%; nine RCTs). There were no statistically significant differences between linezolid and comparators in analyses of microbiological eradication (seven RCTs), including those for patients with MRSA infection only (six RCTs), and in all-cause mortality. Similar results were obtained when the analysis was stratified according to comparator (vancomycin or teicoplanin).

There was a statistically significantly higher rate of gastrointestinal events with linezolid treatment compared to the glycopeptides (RR 2.02, 95% CI 1.10 to 3.70, I² = 62%; six RCTs). There was a statistically significantly higher rate of thrombocytopaenia in the main analysis (RR 1.93, 95% CI 1.30 to 2.87, I²=38%; seven RCTs) and compared to vancomycin only (RR 2.66, 95% CI 1.56 to 4.56, I²=36%; five RCTs). There was no statistically significant difference between treatments in incidence of renal failure (six RCTs).

Results of sensitivity analyses were reported. There was no evidence of publication bias.

Authors' conclusions
This review did not demonstrate clinical superiority of linezolid compared to glycopeptides for the treatment of nosocomial pneumonia. Linezolid showed a significant two-fold increase in incidence of gastrointestinal events and thrombocytopaenia, but no difference in renal dysfunction.

CRD commentary
The review question and inclusion criteria were clear. Several relevant databases and other sources were searched without language restrictions, which reduced the chances of selection biases and omission of relevant studies. The authors reported that they used methods designed to reduce reviewer bias and error during study selection, but not at other stages of the review process. A widely used method was used to assess study validity and the results of this assessment were used to inform the synthesis. However, presentation of summary scores alone as a measure of study quality was not informative. The synthesis used appropriate methods and assessed and explored sources of heterogeneity between studies.

The authors' conclusions reflect the results of the review and appear likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that linezolid should be recognised as an alternative to but not a replacement for vancomycin for treatment of nosocomial pneumonia.

Research: The authors did not state any implications for further research.

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