Linezolid for the treatment of patients with central nervous system infection

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CRD summary
This review assessed the effectiveness of linezolid for the treatment of patients with central nervous system infections. The authors concluded linezolid may be considered for the treatment of these infections where previously administered treatment has failed or where there are limited available options, but that data was limited. Owing to methodological limitations these conclusions may not be reliable.

Authors' objectives
To assess the effectiveness and safety of linezolid for the treatment of patients with central nervous system (CNS) infections.

Searching
PubMed, Current Contents and the Cochrane Library were searched to October 2006. Search terms were reported. The authors also searched the reference lists of included studies for other potentially relevant studies. The authors did not state whether any language restrictions were applied.

Study selection
Randomised controlled trials, prospective studies, retrospective studies, case series and case reports that assessed the effectiveness and safety of linezolid for the treatment of patients with CNS infections were eligible for inclusion in the review. Outcomes of interest were cure of infection, survival and the development of adverse effects.

Most of the patients included in the studies were male and adults (median age 50 years), although the studies also included a few paediatric patients. In some of the included studies patients had undergone neurosurgical operations and/or had prosthetic devices. The most common CNS infection in the included studies was meningitis; other infections included brain abscesses, ventriculitis and ventriculo-peritoneal shunt infection. The most commonly isolated infective pathogens were penicillin-nonsusceptible Streptococcus pneumoniae, vancomycin-resistant enterococci, Nocardia spp., methicillin-resistant Staphylococcus epidermidis and methicillin-resistant Staphylococcus aureus. In most cases linezolid was used when previously administered treatment had failed or caused severe adverse effects. In other cases linezolid was administered after the detection of penicillin-nonsusceptible Streptococcus pneumoniae, or other resistant pathogens, in cerebrospinal fluid. The dosage of linezolid in adults was 600mg twice daily and the mean duration of treatment was 53 days. In the majority of studies linezolid was used in combination with another antibiotic (see paper for further details).

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors extracted data on cure of infection, survival and adverse effects for individual patients included in the studies.

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
Studies were combined in a narrative synthesis. Study details were presented in tables, allowing the reader to assess differences between studies.
Results of the review
Twenty two studies were included in the review (n=42); 4 case series and 18 single case reports. The mean duration of follow-up was 7.2 months, where reported.

Linezolid was associated with cure or clinical improvement of infection in 38/42 (90.5%) patients. Failure of linezolid treatment was seen in only two (4.8%) patients. Seven patients died as a result of co-morbidity, two before completion of linezolid treatment. No studies reported any episodes of recurrence of the central nervous system infection.

Adverse effects were reported in seven patients: four patients suffered from anaemia; one patient suffered from anaemia, thrombocytopenia, lactic acidosis and peripheral neuropathy; one patient suffered from myelosuppression, nausea, vomiting, weight loss, nocturnal myoclonus and reduced visual acuity; one patient suffered from hearing loss. Treatment was discontinued for two patients due to adverse events - one patient because of severe anaemia and the other because of myelosuppression. No adverse event data were available for the other 35 patients.

Authors’ conclusions
The limited data suggest that linezolid may be considered for the treatment of patients with central nervous system infections, where previously administered treatment has failed or where there are limited available options. However, these findings should be interpreted with caution, in view of the limited available evidence.

CRD commentary
The review addressed a clear question and was supported by appropriate inclusion criteria. Three electronic databases were searched, along with reference lists, to identify relevant studies. However, the authors made little attempt to identify unpublished studies and they did not report whether any language restrictions were applied, so the possibility of publication bias and language bias cannot be excluded. The authors did not report the methods used for study selection or data extraction, so there may be reviewer bias and error. The validity of the included studies was not formally assessed. Study details were tabulated with adequate information on participant characteristics and treatment regimen, but the details of study results were limited and adverse events were only described in the text. In view of the nature of the included studies and differences between studies, a narrative synthesis was appropriate. The authors’ cautious conclusions reflect the evidence presented but owing to the lack of reporting of review methods, the potential for publication and language bias and the lack of validity assessment, these conclusions may not be reliable.

Implications of the review for practice and research
Practice: The authors stated that linezolid may be considered for the treatment of patients with meningitis, brain abscess, ventriculitis and other CNS infections when previous treatment has failed or where no other treatment options are available. However, linezolid should be avoided, or used with caution, in patients with underlying myelosuppressive disorders, due to the possibility for development of thrombocytopenia and other myelosuppressant adverse effects. Clinicians should be aware that, among the reported adverse effects, peripheral neuropathy and bone marrow suppression are worrisome. They also stated that drug-drug interactions must always be considered.

Research: The authors stated that the effectiveness of linezolid for the treatment of deep-tissue infections needs to be evaluated further.

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