A meta-analysis of clinical studies of imipenem-cilastatin for empirically treating febrile neutropenic patients

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Authors' objectives
To evaluate the relative efficacy of imipenem-cilastatin (combined) for the empirical therapy of fever in neutropenic patients undergoing chemotherapy for malignancy.

Searching
EMBASE, MEDLINE and the Central Internal Product Information Database of Merck Sharp and Dohme were searched from 1985 onwards.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials were included.

Specific interventions included in the review
Imipenem-cilastatin was compared with other antibiotic regimens.

Participants included in the review
Febrile neutropenic patients undergoing chemotherapy for malignancy were included.

Outcomes assessed in the review
Treatment failure, assessed at the end of the treatment.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
There was no systematic assessment of validity.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction. Letters were sent to authors of the primary studies for missing information.

Methods of synthesis
How were the studies combined?
Peto's method is used to estimate overall odds ratio (OR) across studies, based on assumptions of both fixed-effect and random-effects models.

How were differences between studies investigated?
Homogeneity in the OR across studies was statistically tested. Separate analyses were undertaken for comparison groups with and without aminoglycosides.

Results of the review
Nineteen studies (3,201 patients in total) were included.
The failure rate in patients treated with imipenem-cilastatin was on average lower than that in patients treated with a regimen containing an aminoglycoside: 26 versus 31% (overall OR 0.77, 95% confidence interval, CI: 0.61, 0.98). Compared with a regimen that did not include an aminoglycoside, imipenem-cilastatin was also associated with a lower failure rate: on average 27 versus 33% (overall OR 0.67, 95% CI: 0.54, 0.84). Statistical analysis did not find significant heterogeneity across studies (p=0.56 for studies with comparison regimens containing aminoglycosides, and p=0.119 for those that did not).

**Authors' conclusions**
The results indicate that imipenem-cilastatin was beneficial, compared with beta-lactam-based regimens, for empirical treatment of febrile neutropenic patients. However, firmer conclusions are not possible because of methodological limitations such as subjective assessment of the outcome without proper blinding.

**CRD commentary**
The results of this meta-analysis should be interpreted with great caution. The authors mention some of the methodological limitations, e.g. the definition of clinical failure is not consistent across studies and its diagnosis may depend largely on subjective judgement. None of the trials measured clinical outcome blindly and very few analysed the results on an intention-to-treat basis. The search was restricted to computerised databases and it is unclear whether non-English publications were considered or not. The validity of the included studies was not systematically assessed.

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