Meta-analysis: ertapenem for complicated intra-abdominal infections
Falagas M E, Peppas G, Makris G C, Karageorgopoulos D E, Matthaiou D K

CRD summary
The authors concluded that ertapenem was as effective and safe as other antimicrobials for complicated intra-abdominal infections; evidence was limited to patients with mild-to-moderate infections caused by one or more susceptible pathogens. Apart from the exclusion of two foreign-language studies, the review was generally well-conducted and the conclusions were likely to be reliable.

Authors' objectives
To evaluate the effectiveness and safety of ertapenem in patients with complicated intra-abdominal infections (cIAIs).

Searching
PubMed, Cochrane Central Register of Controlled Trials and Scopus were searched for studies published in English, French, German, Spanish, Italian and Greek. Search terms were reported, but search dates were not. Reference lists of eligible studies were hand-searched.

Study selection
Randomised controlled trials (RCTs) that compared ertapenem with other antimicrobial regimens in patients of any age with cIAIs (intra-abdominal infections extending beyond the site of origin causing peritonitis or abscess formation and requiring surgical intervention) or acute pelvic infections (APIs), were eligible for inclusion. Studies that reported data for relevant subgroups and studies in which 70 per cent of patients had cIAIs were also eligible. Studies had to assess clinical or microbiological success, mortality, adverse events (clinical or laboratory) or withdrawals due to adverse events. The primary review outcomes were clinical success (complete resolution or improvement in the signs and symptoms of cIAIs) assessed at the test-of-cure time point and clinical adverse events (any drug-related adverse event or failing that total adverse events).

Most of the included studies compared 1 g of ertapenem once daily (intravenous or intramuscular) with antipseudomonal penicillins/beta-lactamase inhibitor combinations (piperacillin/tazobactam or ticarcillin/clavulanic acid); other studies used ceftriaxone plus metronidazole as the comparator. The duration of interventions ranged from four to 14 days. Concomitant use of other antimicrobials was permitted in all except one study. Most studies included adults with mild-to-moderate cIAIs; other studies were of children with predominantly cIAIs or women with APIs. Most studies were in patients with one or more pathogens susceptible to the study antibiotics at baseline. Studies assessed cure two to 6 weeks post-treatment.

Two reviewers independently selected studies. Disagreements were resolved by discussion among all review authors.

Assessment of study quality
Study validity was assessed using the Jadad score (use of adequate randomisation, blinding and reporting of withdrawals). The maximum possible score was 5 points. The authors did not state how the validity assessment was performed.

Data extraction
Two reviewers independently extracted outcome data for the modified intention-to-treat population (patients who met disease definition criteria and received allocated treatment). Disagreements were resolved by discussion among all review authors.

Methods of synthesis
Pooled odds ratios (OR) and 95% confidence intervals (CI) were calculated using the fixed-effect Mantel-Haenszel method in the absence of significant heterogeneity. Heterogeneity was assessed using \( \chi^2 \) and \( I^2 \) statistics.

Analyses were conducted for adults with cIAIs, all patients (adults plus children) with cIAIs, adults with APIs and adults...
Results of the review

Seven RCTs were included (n= 5,200). Four RCTs were double-blinded. Four RCTs scored at least 4 points on the Jadad score.

Fixed-effect models were used for all analyses, implying that no significant heterogeneity was found.

For adults with cIAIs, there was no statistically significant difference between ertapenem and other antibiotics in clinical success or clinical adverse for all patients, for other populations of interest or for analyses restricted to double-blind RCTs.

For patients with cIAIs, ertapenem was associated with significantly more laboratory adverse events than other antibiotics; OR 1.73 (95% CI: 1.14, 2.61; four RCTs). None were considered serious. There was no statistically significant difference in laboratory adverse events between ertapenem and other antibiotics for other populations of interest.

There were no significant differences between ertapenem and other antibiotics for secondary outcomes.

Authors' conclusions

Ertapenem is as effective and safe as other antimicrobials for the treatment of complicated intra-abdominal infections. However, evidence was limited to patients with mild-to-moderate infections caused by one or more susceptible pathogens.

CRD commentary

The review question was clearly stated and inclusion criteria were defined. Several relevant sources were searched, but no attempts were made to minimise publication bias. Publications in several languages were eligible, but two potentially relevant studies in non-eligible languages were excluded. Appropriate methods were used to minimise reviewer error and bias during the selection of studies and data extraction, but it was not stated if similar methods were used for the validity assessment. Only RCTs were included and validity was assessed, although only the aggregated score was reported. Appropriate methods were used for the meta-analyses, heterogeneity was assessed and various subgroup analyses conducted. Apart from the exclusion of two foreign-language studies, the review was generally well-conducted and the authors' conclusions were likely to be reliable.

All of the included studies were conducted by the manufacturer of ertapenem.

Implications of the review for practice and research

Practice: the authors stated that in clinical practice the susceptibility of pathogens causing cIAIs to empirically administered ertapenem should be confirmed microbiologically.

Research: the authors did not state any implications for research.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.