CRD summary
The review concluded that tigecycline monotherapy had clinical efficacy and microbiological treatment success rates similar to comparator drugs for various infections, but was associated with higher adverse events, especially of the digestive tract. The authors stated that the findings of the review must be viewed in the context of potential limitations, which seems appropriate.

Authors' objectives
To compare the efficacy and safety of tigecycline (an expanded broad-spectrum glycyclcline antibiotic) with empirical antibiotic regimens in patients with complicated skin and skin structure infections, complicated intra-abdominal infections, community-acquired pneumonia, and other infections caused by methicillin-resistant Staphylococcus aureus or vancomycin-resistant Enterococcus.

Searching
PubMed, the Cochrane Central Register of Controlled Trials (CENTRAL) and EMBASE were searched up to November 2010. Search terms were reported. Reference lists of initially identified articles were handsearched.

Study selection
Randomised controlled trials (RCTs) that compared tigecycline with any other antibiotic used to treat patients with infections caused by Gram-positive, Gram-negative, anaerobic, or atypical bacteria were eligible for inclusion. Trials had to report on the efficacy, safety, or mortality for both regimens.

All included trials evaluated tigecycline in a dosing regimen of 100mg infusion followed by 50mg every 12 hours. Comparators were imipenem-cilastatin (500mg/500mg every six hours), levofloxacin (500mg every 12 to 24 hours), vancomycin (1g over 60 minutes) plus aztreonam (2g twice daily), linezolid (600mg every 12 hours), or ceftriaxone (2g once daily) plus metronidazole (1 to 2g in divided doses). All patients were over 18 years old (where reported). Most included trials were double-blind, but some were open-label.

Two reviewers independently performed study selection.

Assessment of study quality
Trial quality was assessed using modified Jadad criteria. The tool appraised randomisation, allocation concealment, blinding, adherence outcomes, description of withdrawals/drop-outs, and intention to treat to give a maximum score out of 5 points.

The authors did not state how many reviewers performed quality assessment.

Data extraction
Data were extracted on clinical treatment success, microbiological treatment success, mortality and adverse events; these were used to calculate odds ratios (ORs) and 95% confidence intervals (CIs).

Two reviewers independently performed data extraction.

Methods of synthesis
A Mantel-Haenszel fixed-effect meta-analysis was used to calculate pooled odds ratios, together with 95% confidence intervals. Heterogeneity was assessed using $X^2$ and $I^2$. When significant heterogeneity was detected, a DerSimonian and Laird random-effects meta-analysis was conducted.

Subgroup analyses were undertaken on the basis of the different types of infections and intention-to-treat population, the modified intention-to-treat population, the clinically modified intention-to-treat population, the microbiologically
modified intention-to-treat population, the clinically evaluable population, and the microbiologically evaluable population (definitions provided in the review).

Publication bias was assessed via funnel plots.

**Results of the review**

Eight RCTs (over 4,479 patients) were included in the review; trial sample size ranged from 203 to 1,759 patients, where reported. The quality of the included trials was generally good: three trials scored 3 out of 5 points, three trials scored 4 points, and two trials scored the maximum of 5 points.

**Efficacy:** There was no statistically significant difference in treatment success for any of the analyses apart from complicated intra-abdominal infections in the clinically modified intention-to-treat population which favoured control treatment (OR 0.80, 95% CI 0.65 to 0.98; I²=10%; three RCTs). There was no statistically significant difference in total eradication of infection or mortality for any of the analyses.

**Adverse events:** There was a statistically significantly increased risk with tigecycline of adverse events associated with the digestive tract (OR 2.41, 95% CI 1.67 to 3.46; I²=81%; eight RCTs), haemic and lymphatic system (OR 1.24, 95% CI 1.04 to 1.48; I²=50%; seven RCTs), body as a whole (OR 1.17, 95% CI 1.02 to 1.35; I²=0%; seven RCTs), and total adverse events (OR 1.33, 95% CI 1.17 to 1.52; I²=50%; eight RCTs). However, there was a statistically significantly lower risk with tigecycline of developing adverse events associated with the cardiovascular system (OR 0.74, 95% CI 0.61 to 0.90; I²=24%; five RCTs), and skin and appendages (OR 0.58, 95% CI 0.44 to 0.78; I²=42%; five RCTs).

Funnel plots were symmetric.

**Authors’ conclusions**

Tigecycline monotherapy had clinical efficacy and microbiological treatment success rates similar to those of comparator drugs for complicated skin and skin structure infections, complicated intra-abdominal infections, community-acquired pneumonia and infections caused by methicillin-resistant *Staphylococcus aureus*, but it was associated with higher adverse events, especially of the digestive tract.

**CRD commentary**

Inclusion criteria for the review were clearly defined. Several relevant data sources were searched. Publication bias was assessed via funnel plots which were reportedly symmetric, but the validity of assessing publication bias with less than 10 trials was questionable. Attempts were made to reduce reviewer error and bias throughout the study selection and data extraction, but it was unclear if the same methods were used for quality assessment.

Quality assessment was undertaken using a standard checklist, which indicated the generally good quality of the included trials. Trials were combined using appropriate statistical methods; statistical heterogeneity was assessed. There were high levels of statistical heterogeneity in several of the analyses, which the authors acknowledged. Some of the outcomes had a low incidence of occurrence; it was likely that the trials were not powered to detect statistical differences.

The authors stated that the findings of the review must be viewed in the context of potential limitations, which seems appropriate.

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

**Practice:** The authors stated that clinicians should carefully consider the benefits and risks of tigecycline before prescribing. Clinicians should also monitor patients on tigecycline for symptoms of digestive tract adverse events.

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

**Funding**

Not stated.

**Bibliographic details**


PubMedID
21173186

DOI
10.1128/AAC.01402-10

Original Paper URL
http://aac.asm.org/cgi/content/abstract/55/3/1162

Indexing Status
Subject indexing assigned by NLM

MeSH
Anti-Bacterial Agents /therapeutic use; Communicable Diseases /drug therapy /microbiology; Drug Resistance, Bacterial; Enterococcus /drug effects /pathogenicity; Humans; Methicillin-Resistant Staphylococcus aureus /drug effects /pathogenicity; Minocycline /analogs & derivatives /therapeutic use; Skin Diseases, Bacterial /drug therapy /microbiology; Vancomycin /therapeutic use

AccessionNumber
12011002177

Date bibliographic record published
10/08/2011

Date abstract record published
15/02/2012

Record Status
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.