Penicillins vs trimethoprim-based regimens for acute bacterial exacerbations of chronic bronchitis: meta-analysis of randomized controlled trials

CRD summary
This review concluded that semisynthetic penicillin and trimethoprim-based regimens seemed to be equivalent for the treatment of acute bacterial exacerbation of chronic bronchitis. The authors' conclusions are reasonable, but they were based on limited evidence and may have limited generalisability to populations with antimicrobial resistance to Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis strains.

Authors' objectives
To compare the effectiveness and safety of semisynthetic penicillins and trimethoprim-based regimens for the treatment of acute bacterial exacerbations of chronic bronchitis.

Searching
MEDLINE, EMBASE, Current Contents and the Cochrane Central Register of Controlled Trials were searched up to July 2006. Only English-language articles were included. Search terms were provided.

Study selection
Randomised controlled trials (RCTs) that compared a penicillin with trimethoprim (alone or in combination) for the treatment of patients with an acute bacterial exacerbation of chronic bronchitis were eligible. The penicillins investigated in the included studies were amoxicillin (most commonly) and pivampicillin and ampicillin. The comparators were trimethoprim alone or in combination with sulfamethoxazole or sulfadiazine. All the antibiotics were administered orally though treatment regimens varied. All except one of the included studies were of hospitalised patients and all were of adults. Treatment success and adverse events were reported. The test of cure visit was between six and 34 days from the onset of the condition. None of the studies were conducted after 1995. Two researchers independently selected studies for inclusion.

Assessment of study quality
Studies were assessed for method of randomisation, allocation concealment, double blinding and reporting of withdrawals using a modified Jadad scale. The maximum possible score was 5 and a study with a score of 3 or more points was defined as high quality. Two researchers independently assessed study quality.

Data extraction
Two researchers independently extracted data. The number of treatment successes and adverse events were extracted for the intervention and comparison groups and the odds ratio and 95% confidence intervals (CI) were calculated. For treatment success, the odds ratio was calculated based on intention to treat data and for clinically evaluable participants. The odds ratio for adverse event data was based on intention to treat only. All-cause mortality was also extracted.

Methods of synthesis
Studies were pooled using a Mantel-Haenszel fixed-effect model when there was no heterogeneity (based on the $I^2$ test); otherwise the DerSimonian-Laird random-effects model was reported. Publication bias was assessed using the Egger test (results not reported).

Results of the review
Five RCTs were included (n=287). Three of the studies were classified as high quality (score ≥3). The quality scores ranged from 0 to 4. Concomitant interventions for the management of acute bacterial exacerbation of chronic bronchitis were not standardised in the trials.

Treatment success: Based on intention to treat data (five RCTs, n=262), there was no statistically significant difference between semisynthetic penicillin and trimethoprim based regimens in treatment success (odds ratio 1.68, 95% CI: 0.91 to 3.09).
Adverse events: Based on intention to treat data from three RCTs (n=186 for adverse events in general and n=179 for withdrawals due to adverse events), there was no statistically significant difference between intervention and comparator for number of adverse events in general (odds ratio 0.37, 95% CI: 0.11 to 1.24) and for withdrawal due to adverse events (odds ratio 0.27, 95% CI: 0.07 to 1.03). In two studies there was no statistically significant difference between the two groups in number of episodes of diarrhoea or skin rash.

Mortality: Based on one trial of 37 patients, there was no statistically significant difference in mortality between amoxicillin (6%) and trimethoprim (11%).

Authors' conclusions
Based on limited evidence, semisynthetic penicillin and trimethoprim-based regimens seemed to be equivalent in terms of effectiveness and toxicity for the treatment of acute bacterial exacerbation of chronic bronchitis.

CRD commentary
There was a clearly stated review question. A number of appropriate databases were searched for studies, although relevant studies may have been missed due to language restriction and limited attempts were made to locate unpublished data; five studies were excluded because they were not written in English. Appropriate methods were used to reduce error and bias in the review processes. Quality was assessed and considered in the interpretation of the findings. The analysis was appropriate, but the cut off for establishing the presence of heterogeneity was not specified. Clinical heterogeneity was present, but based on forest plots statistical heterogeneity did not appear to be a problem. The authors overall conclusions were appropriate, but they raised a number of important caveats in their discussion that need to be kept in mind when interpreting the data. These include the change in antimicrobial resistance since the included studies were undertaken and the possibility that the analysis was underpowered to detect a difference between the two interventions.

Implications of the review for practice and research
Practice: The authors stated that their findings were likely to be of value to clinical practice in countries where there was low antimicrobial resistance among Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhais strains, but not where there were resistance to these pathogens.

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

Funding
Not stated.

Bibliographic details

PubMedID
19155372

Original Paper URL
http://www.cfp.ca/cgi/content/full/55/1/60

Indexing Status
Subject indexing assigned by NLM

MeSH
Acute Disease; Amoxicillin /therapeutic use; Anti-Infective Agents /therapeutic use; Bronchitis, Chronic /drug therapy; Drug Therapy, Combination; Humans; Pivampicillin /therapeutic use; Practice Guidelines as Topic; Randomized Controlled Trials as Topic; Treatment Outcome; Trimethoprim, Sulfamethoxazole Drug Combination /therapeutic use
AccessionNumber
12009103278

Date bibliographic record published
03/06/2009

Date abstract record published
16/09/2009

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.