Comparison of cefprozil, cefpodoxime proxetil, loracarbef, cefixime, and ceftibuten
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Authors' objectives
To review the clinical trials of the effectiveness and safety of oral beta-lactams.

Searching
MEDLINE was searched from 1986 to January 1995.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials comparing cefprozil, cefpodoxime proxetil, loracarbef, cefixime, or ceftibuten to conventional therapies were included. Uncontrolled studies were also included where the data were limited for FDA (Food and Drug Administration)-improved indications.

Specific interventions included in the review
Cefprozil, cefpodoxime proxetil, loracarbef, cefixime, and ceftibuten.

Participants included in the review
Patients with community-acquired infections. Infections included are acute otitis media, pharyngitis, sinusitis, bronchitis, pneumonia, uncomplicated gonococcal infection, urinary tract infection, and skin and skin-structure infections. Some trials included both children and adults.

Outcomes assessed in the review
The outcome was clinical response to therapy, as defined in the primary studies, including cure rate and recurrence rate.

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
Differences in validity are discussed in the text of the review. Methodological shortcomings of the studies are highlighted. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

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.

Methods of synthesis
How were the studies combined?
The studies were combined by a narrative review, with some quantitative summaries. Overall clinical response rates are presented, e.g., to summarise the percentage of patients in primary studies who were cured at follow-up.

How were differences between studies investigated?
Reasons for differences between the studies are examined in the text of the review.
Results of the review
Acute otitis media: cefprozil, 5 studies; cefpodoxime, 2 studies; cefixime, 7 studies; loracarbef, 3 studies; and ceftibuten, 2 studies.

Pharyngitis: 13 studies in total.

Sinusitis: 4 studies in total.

Bronchitis: 10 studies.

Pneumonia: 7 studies.

Urinary tract infection: 11 studies.

Skin and skin-structure infections: 4 studies.

No patient numbers are given for the included studies, though the authors state that generally 30 to 50 patients were enrolled per treatment arm.

Acute otitis media: for most studies, clinical response (within 1 to 4 days of completing therapy) was more than 85%. Significant differences between the drug regimens were not found.

Pharyngitis: most studies in paediatric and adult patients demonstrated similar clinical efficacy with no significant differences among the regimens. Response rates of 84 to 100% during the early (less than 10 days post-treatment) and/or late (10 to 50 days post-treatment) evaluation periods were reported. Early bacterial eradication rates of more than 75% were noted for all of the new beta-lactams.

Sinusitis: clinical response within 3 days of treatment was more than 90% and usually not significantly different between the regimens. Presumed or documented bacterial eradication was 80% or more in these studies.

Bronchitis: in patients with acute bacterial bronchitis, loracarbef or cefixime were compared with amoxicillin-clavulanate or cefaclor; clinical response or bacterial eradication were similar for patients enrolled in either treatment arm. One study found a lower response with cefixime and amoxicillin-clavulanate, and this was attributed to the greater age of the patients in this trial. In patients with acute exacerbations of chronic bronchitis, the clinical success rate was 84 to 97% in studies comparing cefpodoxime or cefixime with amoxicillin-clavulanate, cefaclor or cefalexin. Cefprozil or ceftibuten (400 mg once daily) was as efficacious as cefaclor (250 to 500 mg three times daily). Clinical success was achieved in 80 to 96% of patients assigned to either treatment arm, though clinical response was greater with cefprozil than cefuroxime (p=0.032). S. pneumoniae and H. influenzae were isolated frequently in studies enrolling patients with either acute bronchitis or acute exacerbations of chronic bronchitis. Bacterial eradication for these studies was at least 73% and not significantly different between drug regimens.

Pneumonia: in all studies, clinical response was achieved in more than 90% of evaluable patients. When reported, bacterial eradication was at least 70% and was similar for all regimens that were compared.

Uncomplicated gonococcal infection: greater than 95% eradication of N. gonorrhoea was achieved in 2 studies examining ceftriaxone and amoxicillin plus probenecid. A single dose of cefpodoxime (50 to 600mg) was effective for gonococcal urethritis.

Urinary tract infection: no statistically-significant differences could be detected in the clinical or bacterial responses for different beta-lactams. Clinical cure was achieved in at least 75% of patients during early evaluation (5 to 10 days after treatment). Re-evaluation during the late period (4 to 6 weeks after therapy) confirmed clinical resolution in at least 65% of patients. The bacterial response (eradication of e. coli) occurred in a minimum of 70% of patients at the early evaluation period, and was maintained in 65% or more of evaluable patients.

Skin and skin-structure infections: loracarbef, cefprozil and cefpodoxime appear to be as efficacious as amoxicillin-clavulanate or cefaclor. Clinical response and bacterial improvement were favourable in 85 to 100% of patients
evaluated. Overall response (favourable clinical response with concomitant documented or presumed bacterial cure or colonisation) determined 3 to 18 days after completion of therapy was more than 84% for patients treated with loracarbef, cefaclor, cefprozil or amoxicillin-clavulanate, with no significant differences between the regimens.

Safety: in paediatric patients, a significantly higher incidence of diarrhoea or loose stools was noted with amoxicillin-clavulanate than with other antibiotics, while in adults this effect was more common with amoxicillin-clavulanate than with loracarbef (p<0.033) or cefprozil (p<0.05). Four case-reports have described a serum-sickness type reaction following cefprozil therapy.

Authors' conclusions
These newer agents appear to be as clinically effective as conventional therapies for the treatment of common community-acquired infections. They may also have the potential to improve compliance due to their once or twice daily mode of administration.

CRD commentary
A detailed and critical review. Whilst the review appears to be similar in format to a conventional narrative review, there does appear to be an assessment of the validity of the primary studies, and investigation of differences in results between studies does occur where it appears warranted. A wider search, i.e. of databases other than MEDLINE, may have identified a larger number of primary studies for inclusion in the review. In addition, since many different antibiotic regimens are compared, it would have been helpful if details from individual studies were summarised in a table: the numbers of patients in trials is not always presented, and the small sample size in many trials may be related to the non significant differences between regimens.

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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.