Clinical efficacy of cefpodoxime in respiratory tract infection

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Acute otitis media (AOM), sinusitis and tonsillopharyngitis are respiratory tract infections frequently encountered by primary-care physicians. Increasing bacterial resistance, particularly in *Streptococcus pneumoniae*, which is one of the most important respiratory tract bacteria implicated in community-acquired respiratory tract infections, has led to concern about the current options for empirical antibiotic treatment and has prompted a search for effective alternative treatments. Data from *in vitro* studies show that cefpodoxime has good activity against the main respiratory tract pathogens, *S. pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis* and *Streptococcus pyogenes*. Clinical studies confirm the efficacy of cefpodoxime in AOM, sinusitis and tonsillopharyngitis. As with all broad-spectrum antibiotics, there is the risk of promotion of bacterial resistance associated with overuse. However, if used with care, cefpodoxime can be considered as an alternative for empirical treatment of bacterial respiratory tract infections encountered in general practice, particularly where penicillins and macrolides have reduced efficacy against the main bacterial pathogens.

Introduction

Community-acquired respiratory tract infections, in particular acute otitis media (AOM), sinusitis and tonsillopharyngitis, are among the most common reasons for general practice consultation, accounting for more than 50% of paediatric consultations and more than 75% of antibiotic prescriptions for out-patients.1

The most important bacterial pathogens in AOM and sinusitis are *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*, and in tonsillopharyngitis, *Streptococcus pyogenes*. As the bacterial aetiology of infection is usually not confirmed prior to initiation of treatment, empirical antibiotic therapy needs to take account of the major causative bacteria. However, increasing bacterial resistance, particularly penicillin and macrolide resistance among *S. pneumoniae* isolates,2 has led to growing concern about current options for empirical therapy and has prompted a search for other effective treatments. This article examines the clinical and bacteriological efficacy of the oral cephalosporin, cefpodoxime, for treatment of bacterial AOM, sinusitis and tonsillopharyngitis.

Acute otitis media

Acute otitis media is particularly distressing for children, and prompt effective treatment is required for symptom relief, as well as for prevention, as far as possible, of long-term sequelae, such as hearing loss and permanent middle-ear damage. Currently, *S. pneumoniae* is regarded as the principal clinically important bacterial cause of AOM, with amoxicillin indicated for first-line therapy.3 The importance of *H. influenzae* as a cause of non-responsive AOM should also be borne in mind.4 It is possible that preventative measures such as the implementation of vaccination programmes for pneumococcal infection may diminish the importance of *S. pneumoniae*, resulting in *H. influenzae* becoming the main pathogen in AOM.5 An antibiotic with a spectrum of antibacterial activity covering both *S. pneumoniae* and *H. influenzae* and effective against penicillin-susceptible and penicillin-intermediate strains of *S. pneumoniae* is necessary to achieve good bacteriological and clinical efficacy and to help prevent the development of resistance.

Data from *in vitro* studies indicate that cefpodoxime, an oral cephalosporin with a broad spectrum of antibacterial activity, may be an appropriate treatment choice in bacterial AOM, as well as in sinusitis, which shares a similar aetiology. Cefpodoxime is active against penicillin-susceptible *S. pneumoniae*, with MIC90 values ranging from <0.06 mg/L to <0.25 mg/L, as well as against penicillin-intermediate strains of *S. pneumoniae* (MIC90 1–2 mg/L).6 It also shows good activity against *H. influenzae* (including β-lactamase-producing strains), with MIC90 values ranging from <0.03 mg/L to 0.13 mg/L.6 In a study conducted in the USA, cefpodoxime
exhibited greater in vitro activity against S. pneumoniae than did cefaclor, cefuroxime, cefprozil, cefixime or loracarbef. Moreover, pharmacodynamic and pharmacokinetic properties of cefpodoxime are favourable, because effective concentrations of cefpodoxime in the middle-ear fluid of paediatric patients are achieved with recommended dosing schedules.

Clinical data show that cefpodoxime is an effective treatment for bacterial AOM in children. Table 1 shows the results of five multicentre, randomized trials comparing the clinical efficacy of cefpodoxime with co-amoxiclav, cefixime or cefaclor in a total of 1202 paediatric patients. The duration of treatment with cefpodoxime ranged from 5 to 10 days. In three of these trials, cefpodoxime was clinically at least as effective as the treatment used for comparison. In the other two trials, treatment with cefpodoxime demonstrated significantly greater clinical efficacy and cure rates than either cefixime or co-amoxiclav, respectively.

Clinical trials often fail to show a difference in clinical efficacy between antibiotic treatments, and there are currently no definitive trials of bacteriological efficacy in childhood AOM. Alternative methods of assessing antibiotics, such as the ‘in vivo sensitivity test’ to assess bacteriological efficacy by examining fluid acquired by a tympanocentesis before and a few days after the start of treatment, and retrospective analyses of treatment failures, have therefore been investigated. Such analyses show good bacteriological efficacy for cefpodoxime against H. influenzae and penicillin-susceptible S. pneumoniae (Figure 1). Moreover, the less frequent dosing schedule of cefpodoxime (bd) compared with either co-amoxiclav or cefaclor (tds), would be an added advantage for treatment with cefpodoxime.

Table 1. Summary of comparative clinical studies in paediatric patients with acute otitis media using cefpodoxime

<table>
<thead>
<tr>
<th>Study (no. of patients)</th>
<th>Treatment regimen</th>
<th>Mean age (years)</th>
<th>Clinical endpoint</th>
<th>Clinical efficacy at end of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mendelman et al. (1992)⁷ (n = 229)</td>
<td>cefpodoxime 10 mg/kg/day, 10 days</td>
<td>3.4</td>
<td>cure + improvement</td>
<td>90/98 (92)</td>
</tr>
<tr>
<td></td>
<td>co-amoxiclav 40/10 mg/kg/day, 10 days</td>
<td>3.4</td>
<td>cure + improvement</td>
<td>42/48 (88)</td>
</tr>
<tr>
<td>Cohen et al. (1994)⁸ (n = 146)</td>
<td>cefpodoxime 8 mg/kg/day, 8 days</td>
<td>1.9</td>
<td>cure + improvement</td>
<td>61/69 (88)⁶</td>
</tr>
<tr>
<td>Gehanno et al. (1994)⁹ (n = 262)</td>
<td>cefpodoxime 8 mg/kg/day, 8 days</td>
<td>2.1</td>
<td>cure + improvement</td>
<td>52/71 (73)</td>
</tr>
<tr>
<td></td>
<td>co-amoxiclav 40/10 mg/kg/day, 8 days</td>
<td>2.8</td>
<td>cure + improvement</td>
<td>112/118 (95)</td>
</tr>
<tr>
<td>Cohen et al. (1997)¹¹ (n = 167)</td>
<td>cefpodoxime 8 mg/kg/day, 5 days</td>
<td>3.6</td>
<td>cure + improvement</td>
<td>76/83 (92)</td>
</tr>
<tr>
<td></td>
<td>cefixime 8 mg/kg/day, 5 days</td>
<td>3.6</td>
<td>cure + improvement</td>
<td>100/105 (95)</td>
</tr>
<tr>
<td></td>
<td>co-amoxiclav 40/10 mg/kg/day, 8 days</td>
<td>1.6</td>
<td>cure + improvement</td>
<td>153/184 (83)</td>
</tr>
</tbody>
</table>

²Cefpodoxime versus cefixime, P < 0.05 ; ³cefepin versus AMC, P < 0.005 (χ² or Fisher’s exact tests; 95% confidence intervals).

![Figure 1](https://example.com/figure1.png)

Figure 1. Comparison of eradication rates for (a) H. influenzae and (b) penicillin-susceptible S. pneumoniae in acute otitis media using data from the ‘in vivo sensitivity test’ to assess bacteriological efficacy and retrospective analyses of treatment failures. Filled bars, bacteriological failure; open bars, eradication. Data from Klein¹⁷ except for: *Klein¹⁷ and Dagan et al.¹⁸; †Dagan et al.¹⁹,²⁰.
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Acute sinusitis

The treatment of acute sinusitis is complicated by a difficulty in establishing the causative bacteria. In AOM, sampling of ear fluid using tympanocentesis is a routine procedure in some countries, whereas in sinusitis, sampling of infected fluid using sinus puncture is a painful and rare procedure. Consequently, empirical treatment of acute sinusitis of suspected bacteriological aetiology is the approach usually adopted. Selection of appropriate antibiotic therapy should take account of the most likely causative bacteria, local patterns of bacterial resistance and the pharmacokinetic profile of the antibiotic.

Co-amoxiclav is currently regarded as first-line therapy for acute bacterial sinusitis. However, the increasing prevalence of resistant strains among the main pathogens of acute sinusitis does suggest the need for effective treatment alternatives. As the bacterial aetiology of acute sinusitis is similar to that observed with AOM, cefpodoxime, which shows good in vitro activity against both S. pneumoniae and H. influenzae, may be an appropriate alternative. Data from clinical trials show that treatment with cefpodoxime is clinically at least as effective as amoxicillin or co-amoxiclav in both adults and children. Moreover, clinical cure rates in adults with acute sinusitis are significantly better after a 10 day treatment course with cefpodoxime than with cefaclor (Table 2).

Tonsillopharyngitis

Acute tonsillopharyngitis is one of the most common reasons for consultation in general practice. In most countries, antibiotic treatment is definitely indicated for treatment of group A β-haemolytic streptococci (GABHS), the most common bacterial cause of acute tonsillopharyngitis, to prevent suppurative complications and serious sequelae such as acute rheumatic fever or glomerulonephritis. Clinical diagnosis of GABHS infection is, however, difficult, because many of the signs and symptoms of GABHS tonsillopharyngitis are non-specific and are indistinguishable from viral infections, even for experienced clinicians. Diagnosis of GABHS requires confirmation by either rapid antigen test or culture prior to initiation of antibiotic therapy.

Traditionally, oral penicillin therapy for 10 days has been regarded as the treatment of choice for GABHS tonsillopharyngitis because of its proven efficacy, narrow spectrum of antibacterial activity and tolerability. Although effective in most patients, the treatment failure rates with penicillin are typically in the region of 10–30%, while the causative pathogen remains susceptible to β-lactam therapy. Possible reasons for this observed failure rate include poor compliance and co-pathogen colonization with, for example, Staphylococcus aureus, H. influenzae or M. catarrhalis, which produce β-lactamase, thereby inactivating penicillin before it can exert any effect. Therefore, antibiotics that have high potency against GABHS are β-lactamase stable, and are effective in a shorter regimen, are preferred. Macrolide therapy is a possible alternative treatment. The increased prevalence of macrolide resistance, particularly in Italy and Spain, should, however, be considered.

Cefpodoxime has good in vitro activity against S. pyogenes, with an MIC₉₀ of <0.06 mg/L. Clinical studies show that treatment with cefpodoxime 200 mg daily for 5–10 days is at least as effective as eradicating GABHS as a standard 10-day treatment course of penicillin in both adult and paediatric patients. In studies in paediatric patients (Table 3), the rate of bacterial eradication following a 5 day or 10 day course of cefpodoxime was significantly higher than that observed following treatment with penicillin V for 10 days.

Table 2. Summary of comparative clinical trials in adult and paediatric patients with acute sinusitis

<table>
<thead>
<tr>
<th>Study (no. of patients)</th>
<th>Treatment regimen</th>
<th>Mean age (years)</th>
<th>Clinical endpoint</th>
<th>Clinical efficacy at end of treatment [n/total cases (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gehanno et al. (1990)²⁵</td>
<td>cefpodoxime 400 mg/day, 10 days</td>
<td>41.3</td>
<td>cure + improvement</td>
<td>116/122 (95)</td>
</tr>
<tr>
<td>(n = 267)</td>
<td>cefaclor 1500 mg/day, 10 days</td>
<td>42.1</td>
<td>cure + improvement</td>
<td>102/122 (84)²⁶</td>
</tr>
<tr>
<td>Von Sydow et al. (1995)²²</td>
<td>cefpodoxime 400 mg/day, 10 days</td>
<td>33.0</td>
<td>cure + improvement</td>
<td>106/114 (93)</td>
</tr>
<tr>
<td>(n = 286)</td>
<td>amoxicillin 1500 mg, 10 days</td>
<td>33.0</td>
<td>cure + improvement</td>
<td>77/114 (68)</td>
</tr>
<tr>
<td>Autret et al. (1994)²³</td>
<td>cefpodoxime 8 mg/kg/day, 10 days</td>
<td>6.9</td>
<td>cure + improvement</td>
<td>112/117 (96)</td>
</tr>
<tr>
<td>(n = 116)</td>
<td>co-amoxiclav 40/10 mg/kg/day, 10 days</td>
<td>6.9</td>
<td>cure + improvement</td>
<td>103/113 (91)</td>
</tr>
<tr>
<td>Sabater et al. (1995)²⁴</td>
<td>cefpodoxime 400 mg/day, 5 days</td>
<td>35.5</td>
<td>cure + improvement</td>
<td>42/44 (95)</td>
</tr>
<tr>
<td>(n = 66)</td>
<td>co-amoxiclav 1500/375 mg/day, 8 days</td>
<td>36.6</td>
<td>cure + improvement</td>
<td>23/28 (82)</td>
</tr>
</tbody>
</table>

*Cefpodoxime versus cefaclor, P < 0.05.
Given the fact that poor compliance is an important contributing factor to bacteriological treatment failure in GABHS tonsillopharyngitis, cefpodoxime, given over a 5–10 day period, may be a suitable treatment option.

Discussion

Cefpodoxime has good in vitro activity against the bacterial pathogens that are responsible for common respiratory tract infections such as AOM, acute sinusitis and tonsillopharyngitis. Clinical studies show that cefpodoxime is at least as effective as standard first-line antibiotic therapy for each of these indications. As with all broad-spectrum antibiotics, there is the risk of increased resistance if they are overused or used inappropriately. However, if used with care, cefpodoxime can be considered as an appropriate choice for the empirical treatment of community-acquired respiratory tract infection caused by bacteria, particularly where there is emerging resistance to traditional antimicrobial chemotherapy.

References


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Table 3. Summary of comparative clinical trials in adult and paediatric patients with group A β-haemolytic streptococcal tonsillopharyngitis

<table>
<thead>
<tr>
<th>Study (no. of patients)</th>
<th>Treatment regimen</th>
<th>Mean age (years)</th>
<th>Bacteriological efficacy [eradication/total cases (% eradication)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown <em>et al.</em> (1991)29&lt;br&gt;(n = 93)</td>
<td>cefpodoxime 200 mg/day, 10 days&lt;br&gt;penicillin V 1 g/day, 10 days</td>
<td>31.4&lt;br&gt;29.4</td>
<td>29/30 (97)&lt;br&gt;30/33 (91)</td>
</tr>
<tr>
<td>Dajani <em>et al.</em> (1993)30&lt;br&gt;(n = 578)</td>
<td>cefpodoxime 10 mg/kg/day, 10 days&lt;br&gt;penicillin V 40 mg/kg/day, 10 days</td>
<td>8.4&lt;br&gt;8.3</td>
<td>256/275 (93)c&lt;br&gt;112/138 (81)</td>
</tr>
<tr>
<td>Portier <em>et al.</em> (1994)31&lt;br&gt;(n = 220)</td>
<td>cefpodoxime 200 mg/day, 5 days&lt;br&gt;penicillin V 1800 mg/day, 10 days</td>
<td>30.4&lt;br&gt;28.6</td>
<td>79/82 (96)&lt;br&gt;64/68 (94)</td>
</tr>
<tr>
<td>Pichichero <em>et al.</em> (1994)32&lt;br&gt;(n = 484)</td>
<td>cefpodoxime 10 mg/kg/day, 5 days&lt;br&gt;penicillin V 40 mg/kg/day, 10 days</td>
<td>8.1&lt;br&gt;7.4&lt;br&gt;8.0</td>
<td>113/125 (90)e&lt;br&gt;112/118 (95)b&lt;br&gt;101/129 (78)</td>
</tr>
</tbody>
</table>

χ² Or Fisher’s exact test: aCefpodoxime 5 days versus penicillin V, P <0.05; bcefpodoxime 10 days versus penicillin V, P <0.005; ccefepodoxime versus penicillin V, P <0.01.
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