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Efficacy and safety of cefpodoxime in the treatment of acute otitis media in children

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KEYWORDS

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Abstract *Background:* Acute otitis media (AOM) is a community-acquired respiratory tract infection in childhood frequently encountered by primary-care physicians and can cause a significant morbidity. Increasing bacterial resistance has led to concern about the current options for empirical antibiotic treatment and has prompted a search for effective treatments.
Objectives: To evaluate the clinical efficacy and safety of cefpodoxime proxetil in the treatment of children with acute otitis media.
Patients and methods: A prospective, multicenter study was conducted on 1380 children aged from 1 to 13 years with AOM who were prescribed a 5–10 day course of cefpodoxime proxetil (8 mg/kg/day). Patients were followed-up after 7–14 days from baseline visit. Efficacy was assessed by the percentage of patients with clinical cure, improvement or failure at the follow-up visit. Safety was evaluated by recording the occurrence and severity of any adverse events and by the physicians' and patients' assessment of overall tolerability.
Results: Clinically, 82.5% of patients were cured, 16.4% improved and there was failure of therapy in 1.1% of the patients. The overall combined cure and improvement rate of all related signs and symptoms was 98.9%. Adverse events, diarrhea and skin rash, were reported by only 16 patients (1.2%). The overall tolerability according to the physicians' and patients' assessment was excellent in 93.9% and 88.9%, respectively. Compliance was attained in 99.5% of patients.
Conclusion: Cefpodoxime proxetil is an effective, safe, well-tolerated antimicrobial agent for treatment of acute otitis media in children. It can be considered as an excellent choice for the empirical treatment of bacterial AOM.

Introduction

Acute otitis media (AOM) is one of the most frequent diseases in early infancy and childhood. It is defined as the presence of middle-ear effusion and a rapid onset of signs or symptoms of middle-ear inflammation, such as ear pain, otorrhea or fever.[1] It is estimated that more than two-thirds of children experience

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one or more attacks of AOM by the age of 3 years.[2–4] The peak age of incidence is 6–24 months and decreases with age.[5]

The pathogenesis of AOM is multifactorial, involving the adaptive and native immune system, Eustachian-tube dysfunction, viral and bacterial load, in addition to genetic and environmental factors.[2] Bacteria are believed to play a predominant role in the causation of AOM-related symptoms; therefore antibiotic therapy will accelerate the clinical recovery and may reduce the number of complications related to AOM.[4,6]

Streptococcus pneumoniae has been reported as the predominant pathogen causing AOM for many years, next to *Moraxella catarrhalis* and non-typeable *Haemophilus influenzae*. The implementation of vaccination programs for pneumococcal infection changed the etiology of AOM overtime resulting in *H. influenzae* to be the main pathogen in AOM.[7,8] Moreover, increasing bacterial resistance, particularly beta-lactamase producing strains of *H. influenzae* and *M. catarrhalis* as well as penicillin and macrolide resistance among *S. pneumoniae,* has raised the concern about the current options for empirical antibiotic treatment and has prompted a search for effective treatments.[1,6,9]

Cefpodoxime proxetil is an oral third generation cephalosporin of choice for the treatment of AOM.[1] It exhibits more balanced spectra of activity against the principal bacterial pathogens responsible for outpatient respiratory tract and other infections when compared with other widely used amoxicillin or oral cephalosporin of earlier generations.[10] *In vitro* studies show that it has activity against many common Gram-positive and Gram-negative pathogens associated with common pediatric infections including AOM, making it a useful option for empirical therapy.[1,6,11] Moreover, *in vivo* sensitivity studies assessing the bacteriological efficacy by examining middle-ear fluid before and a few days after the start of treatment and retrospective analyses of treatment failures, have shown a good bacteriological efficacy for cefpodoxime against *H. influenzae* and penicillin-susceptible *S. pneumoniae*.[7,8] It is highly stable to hydrolysis by the most commonly found plasmid-mediated β-lactamases.[10] As well, its concentration within the structures of the middle ear have been shown to achieve the minimum inhibitory concentration (MIC) for the microorganisms responsible for AOM with recommended dosing schedules. Its relatively long half-life and sustained tissue concentrations support twice daily dosing, representing an advantage over many other antibiotics with comparable clinical efficacy and features that may encourage patient compliance.[11]

Non-compliance is a common cause of treatment failure, clinicians should strongly consider factors that will enhance compliance, such as palatability, frequency of administration, adverse events (AEs) and cost. Finally, physicians' familiarity with dosing schedules and potential side effects may reduce prescribing errors.[12]

The aim of the study was to evaluate the clinical efficacy and safety of cefpodoxime proxetil in the treatment of children with acute otitis media.

Patients and methods

Study design

This prospective, multicenter study was conducted in 26 Egyptian medical centers, over a period of one year from January to December 2013. The study was approved by the local Ethics Committee. A written informed parental/guardians' consent was obtained prior to enrollment in the study.

Study population

A total of 1380 children aged 1–13 years, presenting with clinically diagnosed AOM suspected to be of bacterial origin were eligible for the study. Patients were not on any antibiotic therapy when enrolled in the study. The exclusion criteria were restricted to the contraindications to cefpodoxime given in the summary of the product characteristics, i.e. patients with known hypersensitivity to cephalosporin antibiotics.

Methods

Study procedure

The study was conducted in 2 visits, baseline visit at clinical evaluation and treatment initiation, and follow-up visit (day 7–14) following the routine practice of the trained physician.

Baseline visit

All candidates were subjected to comprehensive history-taking and clinical evaluation. The diagnosis of purulent AOM was based on a triad of recent clinical symptoms including otalgia, fever and irritability; tympanic membrane (TM) signs of AOM such as middle ear effusion characterized by bulging, limited or absent mobility of the TM or air-fluid level behind membrane; and otoscopic evidence of TM inflammation indicated by erythema, perforation or otorrhea in at least one ear were eligible for the study.[13] Patients fulfilling the eligibility criteria were prescribed cefpodoxime proxetil 8 mg/kg/day in two divided doses for 5–10 days. Additional medications for symptom relief were prescribed and documented.

Evaluation visit

The physician examined the patient and recorded their adherence to therapy, any drug adverse events and the clinical response to treatment. Symptoms of otalgia, fever and irritability were assessed and recorded. Otoscopy was performed to assess the tympanic membrane for severity of erythema, opacification, loss of light reflex, fullness or bulging, drainage, perforation, mobility and middle ear effusion. Patients were also monitored for any complications. Patients were considered to be compliant with the study medication if at least 80% of the antimicrobial course were taken according to the prescribed regimen; otherwise the patient was considered to be non-compliant.

Study endpoints

Primary and secondary endpoints were the efficacy and safety assessment of cefpodoxime, respectively.

Efficacy assessment

According to the physicians' assessment, efficacy was defined by the percentage of patients with either *clinical cure*: absence of fever, otalgia, irritability, and otoscopic signs of AOM; *clinical improvement*: clinical signs and symptoms including otoscopic findings diminished but did not completely resolve;