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Efficacy and Safety of Sarclav in the Treatment of Acute Otitis Media in Children

Abhay Kumar Singh[1], Harsimrat Singh[2], Himani Singh[2]

[1]Assistant Professor, [2]Post Graduate, Department of ENT Saraswathi Institute of Medical Sciences Hapur (U.P)

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 Sarclav (cefpodoxime proxetil) in the treatment of children with acute otitis media.

Patients and Method: 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 Sarclav (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% were 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: Sarclav (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.

Keywords: *Acute otitis media, Sarclav (cefpodoxime) , Children, Efficacy.*

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 one or more attacks of AOM by the age of 3 years.[2, 3, 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.

Streptococcus *pneumoniae* has been reported as the predominant pathogen causing AOM for many years, next to *Moraxella catarrhalis* and non-typeable *Haemophilus*

Corresponding Author:
Dr Abhay Kumar Singh
Assistant Professor, Department of ENT, Saraswathi Institute of Medical Sciences, Hapur (U.P)
E-mail: Abhaysingh2786@gmail.com

influenzae. The implementation of vaccination programs for pneumococcal infection changed the etiology of AOM over time 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]

Sarclav is an oral third generation cephalosporin of choice for the treatment of AOM.[1] *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 Sarclav 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 Sarclav (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] 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]

Finally, physicians' familiarity with dosing schedules and potential side effects may reduce prescribing errors.[12]

Aim

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

Patients and method

Study design

This prospective, multicentre study was conducted in SARASWATHI MEDICAL COLLEGE, Hapur, U.P from May 2017 to December 2018. 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 Sarclav (cefpodoxime) given in the summary of the product characteristics, i.e. patients with known hypersensitivity to cephalosporin antibiotics.

Method

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 Sarclav (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 Sarclav (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; or *failure*: unsatisfactory resolution of tympanic membrane signs or symptoms of AOM, or worsening of the patients' condition.

Safety assessment

Safety was monitored by recording the Sarclav (cefpodoxime) related-adverse events (AEs) during the observational period and by the physicians' and patients' assessment of overall tolerability at the end of the study. The recorded clinical AEs likely to be related to the use of antibiotics are vomiting, diarrhea or rash.4, 14 The severity was assessed by the physicians as mild, moderate or severe. Necessary treatment, outcome at time of report and serious criteria of AEs were recorded. The assessment of the overall tolerability was rated either: excellent, fair or poor.

Statistical analysis

Data were analyzed using Statistical Package for Social Sciences software version 17.0 (SPSS, Inc., Chicago, IL, USA). Numerical data were expressed as mean and standard deviation. Qualitative data were expressed as frequency and percentage. Chi-square test was used to examine the relation between the qualitative variables. *p*-value <0.05 was considered statistically significant.

Results

Two patients out of the enrolled 1380 patients did not show up at the follow-up visit and were excluded. Of the 1378 patients who completed the study, 788 (57.2%) were males and 590 (42.8%) were females, with a mean age of 3.8 ± 2.5 years. Their mean weight and length/height measured at the initial visit were 17.1 ± 7.1 kg and 94.4 ± 19.0 cm respectively.

At baseline visit

The mean temperature was 38.3 ± 0.7 °C. All children had one or more pre-treatment AOM related signs and symptoms; the most frequent were otalgia (93.6%), spontaneous otorrhea (51%), purulent discharge (49.7%), fever (21.6%) and erythematous tympanic membrane (1.7%). In addition, nasal discharge was found in 3.3% of patients, sore throat in 2.4%, cough in 2.2%, and pharyngitis in 1.4% (Fig. 1). The onset of the first symptom occurred at less than 4 days prior to the baseline visit in 87.9% of the patients.

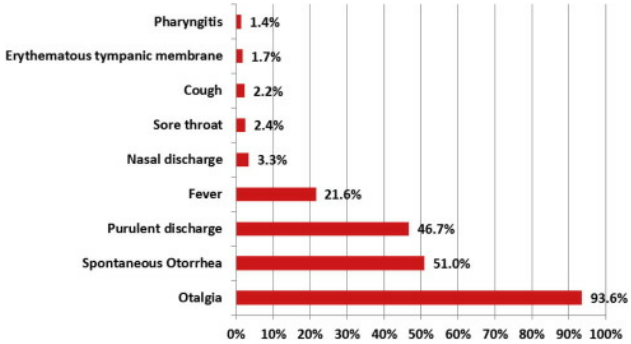

Figure 1. Signs and symptoms of acute otitis media at baseline visit (*n* = 1378).

The most frequently reported prescription durations were five days in 783 (56.8%), seven days in 326 (23.7%) and ten days in 269 (19.5%) of the patients, with a mean duration of 6.5 ± 2.0 days. Other symptomatic medications were prescribed in 66.4% of the patients, ncluding: antipyretics (24.7%), analgesics (22.1%), decongestants (14.6%), cough preparations (2.2%) and anti-inflammatory agents(8.3%).

At the follow-up visit

There was marked improvement of all AOM-related signs and symptoms. Seven patients (0.5%) were non-compliant. Among the remaining 1371 patients – according to physicians' assessment – 1131 patients (82.5%) were cured, 225 (16.4%) improved, and 15 (1.1%) failed to respond to therapy; with one reported worsening of patient's condition. Cure or improvement rate was 100% in all symptoms and signs except spontaneous otorrhea (98.0%), purulent discharge (98.5%) and nasal discharge (93.5%).

Patients that received a 5-day course of Sarclav (cefpodoxime) had a significantly higher cure rate of 84.6% (659/779) compared to those taking Sarclav

(cefpodoxime) for a duration of more than 5 days (472/592, 79.7%) ($\chi^2 = 5.515$, $p = 0.019$).

Adverse events of Sarclav (cefpodoxime) were reported by only 16 patients (1.2%), which included diarrhea (n = 9) and skin rash (n = 7). The nature of AEs were mild to moderate and did not require any dose reduction or discontinuation of the prescribed course; while none of the AEs reported were serious and all resolved without sequelae (Table 1).

Table 1. Sarclav (cefpodoxime) related-adverse events (n = 1371).

Number	Percentage	
Adverse event		
Diarrhea	9	0.7
Skin rash	7	0.5
Severity		
Mild	8	0.6
Moderate	8	0.6
Treatment		
No	8	0.6
Yes	8	0.6
Outcome at time of report		
Resolved	16	1.2
Serious criteria of adverse events		
No	16	1.2
Yes	0	0.0

The overall tolerability of Sarclav (cefpodoxime) according to the physicians' assessment was excellent in 1287 (93.9%) of patients, fair in 73 (5.3%) and poor in 11 (0.8%); while according to the patients' assessment, it was excellent in 1219 (88.9%), fair in 142 (10.4%) and poor in 10 (0.7%) (Fig. 2).

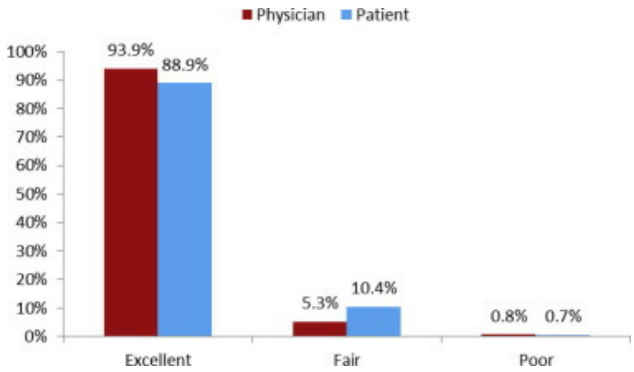

Figure 2. Tolerability assessment from the physicians' and patients' perspectives (n = 1371).

Discussion

Acute otitis media is a community-acquired respiratory tract infection, frequently encountered by primary-care physicians. The selection of the most effective antimicrobial to treat AOM has become more difficult in recent years because of increasing antibiotic resistance among all AOM pathogens to the standard first-line recommended antibiotics.[15,16] . Empirical treatment by cephalosporin with beta lactamase stability should be preferred especially in cases with penicillin allergy. Sarclav (cefpodoxime) is one of three oral third generation cephalosporins recommended for empiric antibiotic treatment of AOM as designated by the AAP guidelines.[1]

Findings of this study indicate that Sarclav (cefpodoxime) is an effective antimicrobial agent for AOM. The 5–10 day treatment course resulted in an excellent response in signs and symptoms. Clinical cure was achieved in 82.5% of patients; and improvement in 16.4%, with an overall combined cure and improvement rate of 98.9%. The clinical efficacy of Sarclav (cefpodoxime) in this study was found to be in line with earlier clinical studies for Sarclav (cefpodoxime) who found that the overall combined cure and improvement rate ranged from 86% to 95%.[19]

The optimal duration of antibiotic therapy for patients with AOM is uncertain.[1] In the present study it was found that Sarclav (cefpodoxime) , in the 5-day treatment regimen, seems to be a suitable drug for AOM in children, with a significantly higher cure rate (84.6%) than an extended treatment course (79.7%) (p = 0.019).

Regarding safety, Sarclav (cefpodoxime) was well tolerated by most patients. It has a tolerability profile similar to that of other oral cephalosporins, with

gastrointestinal related symptoms and skin rash being the most frequently reported AEs.[21] The twice daily regimen was acceptable to the majority of patients and accordingly compliance to treatment regimen was excellent (99.5%). It has been noted that patient compliance is inversely related to the frequency of drug administration and is directly related to the efficacy of the drug.[22] Moreover, the less frequent dosing schedule of Sarclav (cefpodoxime) (BD) compared with either amoxicillin–clavulanate or cefaclor (TDS), would be an added advantage for treatment with Sarclav (cefpodoxime).[21]

As a consequence, the efficacy and safety of Sarclav (cefpodoxime) reported in this multicenter study is likely to be a true reflection of the effectiveness in actual clinical paediatric practice.

Conclusion

Sarclav (Cefpodoxime proxetil) is an effective, safe, well-tolerated antimicrobial agent for treatment of acute otitis media in children. It is an excellent choice for the empirical treatment of bacterial AOM, with a recommended twice-daily regimen for an optimum duration of 5 days.

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