A Pilot Study of Single-Dose Azithromycin Versus Three-day Azithromycin or Single-Dose Ceftriaxone for Uncomplicated Acute Otitis Media in Children

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ABSTRACT

Background: The pharmacokinetic profile of azithromycin supports its use as single-dose therapy for uncomplicated acute otitis media (AOM) in children.

Objective: This study was designed to (1) compare the safety of single-dose oral azithromycin, 3 daily doses of oral azithromycin, and a single dose of intramuscular ceftriaxone for the treatment of uncomplicated AOM in children, and (2) provide preliminary efficacy data to support initiation of a larger, comparative trial of single-dose azithromycin for the treatment of uncomplicated acute otitis media in children.

Methods: In this single-center pilot study, children with uncomplicated AOM were randomly assigned to receive single-dose oral azithromycin (30 mg/kg), 3-day oral azithromycin (10 mg/kg once daily), or single-dose intramuscular ceftriaxone (50 mg/kg). Tympanocentesis was performed before administration of the first dose, and clinical response was assessed on days 14–15 and 28–30.

Results: Between September 1995 and May 1997, 198 children (mean age, 2.5 years) were enrolled. All of the patients were evaluable for the safety and clinical intent-to-treat (ITT) analyses, and 98 were evaluable for the microbiologic ITT analysis. On day 14–15, rates of clinical success (cure or improvement) for the 3 treatment groups were: 62/64 (97%) for single-dose azithromycin, 60/63 (95%) for 3-day azithromycin, and 61/62 (98%) for single-dose ceftriaxone. On day 28–30, the corresponding clinical success rates were 61/65 (94%), 61/66 (92%), and 62/64 (97%). For the 98 microbiologically evaluable patients, clinical success rates at day 14–15 were 28/30 (93%) for single-dose azithromycin, 31/35 (89%) for 3-day azithromycin, and 33/33 (100%) for single-dose ceftriaxone. On day 28–30, the corresponding clinical success rates were 27/30 (90%), 30/35 (86%),

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and 32/33 (97%). Treatment-related adverse event rates for single-dose azithromycin, 3-day azithromycin, and single-dose ceftriaxone were 10.6%, 9.1%, and 9.1%, respectively.

Conclusion: In this pilot study comparing single-dose azithromycin, 3-day azithromycin, and single-dose ceftriaxone for the treatment of uncomplicated AOM in children, no differences were detected among the 3 regimens. (*Curr Ther Res Clin Exp.* 2003;64[Suppl A]:A16–A29) Copyright © 2003 Excerpta Medica, Inc.

Key words: acute otitis media, azithromycin, ceftriaxone, *Haemophilus influenzae*, short-course therapy, *Streptococcus pneumoniae*.

INTRODUCTION

Acute otitis media (AOM) is the most common bacterial infection of early childhood and the most common indication for which antibiotics are prescribed.¹ Although a traditional 10-day regimen of amoxicillin is the recommended first-line therapy,² there has been much recent interest in shorter antibiotic regimens for treating AOM. In addition to potential cost savings, shorter courses may improve patient compliance³ and reduce the selective pressure of antibiotics in the community and in the individual patient, depending on the pharmacokinetic characteristics of the agent concerned.^{4,5} A meta-analysis of randomized, controlled trials of shorter-course therapy suggested that a 5-day regimen of short-acting, oral beta-lactam antibiotics is effective treatment for AOM.⁶ However, subgroup sizes in that analysis were too small to reliably predict the risk of treatment failure in children <2 years of age. In addition, other recent publications recommend against the use of abbreviated courses of short-acting antibiotics in children <2 years.^{4,7}

The first single-dose regimen approved by the US Food and Drug Administration (FDA) for the treatment of AOM in children was for intramuscular ceftriaxone. This regimen has been shown to be clinically equivalent to standard therapy with amoxicillin,^{8,9} cefaclor,¹⁰ trimethoprim/sulfamethoxazole,¹¹ amoxicillin/clavulanate,¹² and high-dose amoxicillin/clavulanate.¹³ However, in 1 large, unpublished trial,¹⁴ standard-dose amoxicillin/clavulanate was shown to be more effective than single-dose ceftriaxone. Despite published evidence supporting single-dose ceftriaxone for the treatment of AOM, obvious disadvantages are the pain, inconvenience, and risk of needle-stick injury associated with use of an injectable agent, and the potential selection of bacterial resistance to a group of agents (cephalosporins) commonly used for the treatment of life-threatening diseases in children.

Azithromycin, an azalide antibiotic, has a prolonged half-life of 68 hours, reflecting slow release of drug from tissues into serum after initial rapid distribution.¹⁵ The long half-life allows for once-daily dosing, while sustained high-tissue concentrations for several days after dosing permit shorter-course therapy.¹⁶ Once-daily azithromycin given over 5 days (30 mg/kg total dose) is as effective

as traditional 10-day regimens.¹⁷⁻¹⁹ The same total dose of azithromycin may also be given over 3 days to treat AOM, and several studies have demonstrated clinical equivalence between once-daily azithromycin (10 mg/kg daily) for 3 days and 10-day multidose regimens of amoxicillin, amoxicillin/clavulanate, clarithromycin, and cefaclor.²⁰⁻²⁷ Pukander and Rautanen²⁸ measured total middle-ear fluid concentrations of azithromycin in children with AOM who received a 10-mg/kg dose on day 1 followed by a 5-mg/kg dose on day 2. Total mean azithromycin concentrations at 24 and 48 hours after the initial dose were 8.61 and 9.43 µg/mL, respectively. These concentrations are well above the minimum inhibitory concentrations (MICs) of the majority isolates of the 3 most common otitis pathogens: *Streptococcus pneumoniae* (MIC₅₀, 0.06 µg/mL; MIC₉₀, 16 µg/mL; 72.3% susceptible), *Haemophilus influenzae* (MIC₉₀, 2 µg/mL; 99.5% susceptible), and *Moraxella catarrhalis* (MIC₉₀, ≤0.12 µg/mL; 99.9% susceptible).^{29,30} Dagan et al³¹ also determined middle-ear fluid levels of azithromycin in children with AOM who received the 3-day regimen. They reported a total mean azithromycin concentration of 3.51 µg/mL at 24–48 hours after the last dose.

Amsden and Gray³² recently examined the pharmacokinetics of the standard 1500-mg adult dose of azithromycin administered to adult volunteers, either as a 3-day regimen (500 mg/day) or as a single, large dose. Whereas the area under the serum concentration versus time curve was similar for the 2 regimens, the peak serum concentration after the single dose was significantly higher than that for the 3-day regimen. Whether delivery of the total 30-mg/kg pediatric dose as a single dose achieves higher peak concentrations in the middle ear remains to be determined.

The pharmacokinetics of azithromycin, together with the proven efficacy of the 3-day regimen, led us to consider single-dose azithromycin for the treatment of uncomplicated AOM in children. Given the limited statistical power achievable in small pilot studies, the present trial was designed primarily to evaluate the tolerability of single-dose azithromycin in pediatric patients. A secondary objective was to compare clinical response rates among patients treated with a single, oral dose of azithromycin (30 mg/kg), 3 days of oral azithromycin (10 mg/kg once daily), or a single dose of intramuscular ceftriaxone (50 mg/kg).

PATIENTS AND METHODS

Patients

This single-center trial was conducted between September 1995 and May 1997. The study population consisted of children aged 6 months to 5 years (maximum weight, 20 kg) with AOM. No distinction was made between patients with or without recurrent otitis media; however, patients with a history of antimicrobial therapy within 30 days of enrollment were excluded. Diagnostic criteria included the presence of effusion, as judged by pneumatic otoscopy and/or tympanometry, plus erythema or fullness/bulging of the tympanic membrane, in association

with 1 or more of the following: fever, ear pain or pulling, irritability, or decreased activity. Patients were excluded from the study if they had a history of hypersensitivity to beta-lactams or macrolides, severe underlying disease, or chronic diarrhea or other gastrointestinal condition that might affect drug absorption. Also excluded were patients with a ruptured tympanic membrane. The study was approved by the ethics committee of the National Children's Hospital and the Minister of Health of Costa Rica, and written informed consent was obtained from parents or legal guardians before enrollment. Tympanocentesis was performed before initiation of therapy. A posttreatment tympanocentesis was suggested only for patients considered failures or relapses.

Microbiology

Middle-ear fluid samples were cultured, and AOM pathogens (*S pneumoniae*, *H influenzae*, and *M catarrhalis*) were tested for susceptibility to azithromycin and ceftriaxone by microdilution and disk diffusion.³³ For patients with a resistant baseline pathogen, treatment with study drug was discontinued unless clinical improvement was documented. Laboratory assays were performed by the clinical laboratory of the Hospital Nacional de Niños and Laboratorio Centro de Investigaciones Clínicas, San José, Costa Rica.

Study Design

The study design was single-blinded for the 2 azithromycin treatment groups. Because of technical problems with the blinding of ceftriaxone, the ceftriaxone regimen was open label. However, the 2 azithromycin groups were placebo-controlled. Patients were randomly assigned to receive azithromycin oral suspension as a single 30-mg/kg dose followed by 3 doses of placebo, or 10 mg/kg once daily for 3 days plus 1 dose of placebo, or a single, intramuscular dose of ceftriaxone (50 mg/kg). If the patient vomited within the first 30 minutes of ingestion of the suspension, dosing was repeated. Clinical response was evaluated on days 14–15 and 28–30. Each visit included assessment of signs and symptoms of AOM and presence of effusion as determined by tympanometry or pneumatic otoscopy.

Efficacy Evaluation

Efficacy was analyzed separately for the intent-to-treat (ITT) and per-protocol populations. Clinically evaluable ITT patients received at least 1 dose of study drug and had a diagnosis of AOM at baseline. Microbiologically evaluable ITT patients included clinical ITT patients who also had a middle-ear fluid culture that was positive for *S pneumoniae*, *H influenzae*, or *M catarrhalis* at baseline. Clinical per-protocol patients were to have received sufficient study drug (ie, a single 30-mg/kg dose of azithromycin, at least 2 days of azithromycin 10 mg/kg daily, or one 50-mg/kg dose of ceftriaxone) and undergone clinical evaluations at baseline and day 14–15. The microbiologic per-protocol population included

clinical per-protocol patients who also had a baseline pathogen susceptible to the assigned treatment.

The end points for clinical response were days 14–15 and 28–30. Clinical response was based on assessment of clinical signs and symptoms and presence of effusion, as determined by tympanometry or pneumatic otoscopy. The clinical response was classified as: *cure* (complete resolution of all signs and symptoms of AOM), *improvement* (partial resolution of signs and symptom), or *failure* (no change or worsening of signs and symptoms, or a requirement for additional antibiotic therapy for AOM). At both end points, clinical success was defined as clinical cure or improvement.

Assessment of Safety and Compliance

Patients who received at least 1 dose of study drug were included in the safety analysis. Adverse events (all causality and treatment related) were summarized using the investigator's assessment of severity (mild, moderate, severe). Treatment-related adverse events included those judged by the investigator to be related or possibly related to the study drug. Blood and urine were collected at baseline and on day 14–15, and routine hematology, clinical chemistry, and urinalysis determinations were performed. Compliance was assessed by review of diaries and medication containers on day 7–8.

Statistical Methods

The main objective of this study was to assess the safety of the new single-dose regimen. Given the limited statistical power inherent in a small pilot study, the assessment of clinical efficacy was a secondary objective. Accordingly, a sample size of 50 efficacy evaluable patients per treatment group (total of 150) was chosen, which was calculated to be sufficient to detect a difference in clinical efficacy of only 33% to 35%, with a power of at least 0.8 based on a 2-tailed test, at a significance level of 0.05. For the clinical ITT analysis, the chi-square test was used to compare the frequency of cure plus improvement responses versus failures. The normal approximation to the binomial distribution was used to compute 95% CIs. Patients' clinical response stratified by pathogen was assessed; however, a statistical analysis of microbiologic results was not performed.

RESULTS

Population

One hundred ninety-eight children were randomly assigned to treatment groups (66 per group) and received at least 1 dose of study drug; all 198 children were included in the clinical ITT analysis. Eighteen patients (4 azithromycin single-dose, 5 azithromycin 3-day, and 9 ceftriaxone) were excluded from the per-protocol clinical evaluation at day 14–15, and 26 patients (7, 8, and 11, respectively) were excluded from the per-protocol clinical evaluation at day

28–30. The most common reason for exclusion was protocol violation. Ninety-two patients (28 azithromycin single-dose, 32 azithromycin 3-day, and 32 ceftriaxone) were excluded from the microbiologic per-protocol evaluation at day 14–15; and 99 patients (31, 34, and 34, respectively) were excluded from the corresponding evaluation at day 28–30. At both visits, the most common reason for exclusion was absence of a baseline pathogen. Baseline clinical characteristics were similar among the 3 treatment groups (Table I).

Microbiologic Evaluation

Of the 198 subjects who received study drug, 98 patients (30 azithromycin single-dose, 35 azithromycin 3-day, and 33 ceftriaxone) had a baseline pathogen isolated from middle-ear fluid and were included in the microbiologic analysis. No patient had >1 pathogen. *S pneumoniae*, the most common pathogen, was recovered from 62 (63%) of 98 culture-positive patients, whereas *H influenzae* and *M catarrhalis* accounted for 34 (35%) of 98 and 2 (2%) of 98 isolates, respectively. All *H influenzae* isolates were susceptible to both azithromycin (MIC ≤ 4 $\mu\text{g/mL}$) and ceftriaxone (MIC ≤ 2 $\mu\text{g/mL}$). Susceptibility data were available for 60 *S pneumoniae* isolates: 58 were azithromycin susceptible (MIC ≤ 0.5 $\mu\text{g/mL}$), and 2 were azithromycin resistant (MIC ≥ 2 $\mu\text{g/mL}$). All 60 *S pneumoniae* isolates were susceptible to ceftriaxone (MIC ≤ 1.0 $\mu\text{g/mL}$).³⁴

Clinical Efficacy

Of 198 children in the ITT population, 189 were evaluable at day 14–15, and 195 at day 28–30. At day 14–15, clinical success rates for clinically evaluable patients were similar for the 3 treatment groups: 62/64 (97%) for single-dose azithromycin, 60/63 (95%) for 3-day azithromycin, and 61/62 (98%) for ceftriaxone ($P = \text{NS}$; 95% CIs: single-dose azithromycin versus ceftriaxone, -8.4% to 5.4% ; 3-day azithromycin versus ceftriaxone, -10.9% to 4.6%). At day 28–30, clinical success rates were also similar for the 3 groups: 61/65 (94%) for single-dose

Table I. Demographic characteristics of patients (intent-to-treat population).

Characteristic	Azithromycin Single-Dose (n = 66)	Azithromycin 3-Day (n = 66)	Ceftriaxone (n = 66)
Age, mean (SD), y	2.5 (1.3)	2.7 (1.5)	2.3 (1.4)
No. (%) of patients <2 y	26 (39.4)	26 (39.4)	35 (53.0)
Sex ratio (M/F)	1.3	1.2	1.0
Body weight, mean (SD), kg	13.2 (3.6)	13.4 (3.6)	12.3 (3.4)
Race			
White	64 (97.0)	63 (95.5)	65 (98.5)
Black	1 (1.5)	1 (1.5)	0 (0.0)
Hispanic	1 (1.5)	2 (3.0)	1 (1.5)

azithromycin, 61/66 for 3-day azithromycin, and 62/64 (97%) for ceftriaxone ($P = \text{NS}$; 95% CIs: single-dose azithromycin versus ceftriaxone, -11.9% to 5.8% ; 3-day azithromycin versus ceftriaxone, -13.7% to 4.8%). For the microbiologically evaluable ITT population (ie, patients from whom a pathogen was isolated at baseline), no statistical analysis was performed. However, at days 14–15 and 28–30, clinical success rates for the 3 groups were similar (93% and 90% for the azithromycin single-dose group, 89% and 86% for the azithromycin 3-day group, and 100% and 97% for the ceftriaxone group, respectively). Results of the clinical response by pathogen analysis also demonstrated similar results among the 3 treatment groups (Table II). Of note, among children in the 3-day azithromycin group with pneumococci at baseline, 3 of 18 did not return for the day 14–15 visit and were recorded as failures; however, 2 of those children did return on day 28–30 and were considered cured at that visit.

The clinical outcome for azithromycin-treated children correlated with susceptibility of the baseline pathogen, except for 5 patients: 1 child in the single-dose group and 2 in the 3-day group with azithromycin-susceptible *H influenzae* were improved at day 14–15 but relapsed at day 28–30. A fourth child with susceptible *H influenzae* failed the 3-day regimen at day 14–15. Azithromycin MICs for these 4 *H influenzae* isolates ranged from 0.5 to 2 $\mu\text{g/mL}$. Because no pathogen was available from these patients at the follow-up visits, it was not possible to determine whether failures were caused by persistence of the baseline pathogen, emergence of a resistant strain, or acquisition of a new pathogen. Of the 2 children with azithromycin-resistant pneumococci at baseline, neither was discontinued from the study. One child in the 3-day group (azithromycin MIC = 256 $\mu\text{g/mL}$) was improved at day 14–15 and cured at day 28–30, whereas the other child, in the ceftriaxone group (azithromycin MIC = 2 $\mu\text{g/mL}$; ceftriaxone MIC = 1 $\mu\text{g/mL}$), was a clinical success at both evaluations. Results from the per-protocol analysis were consistent with those from the ITT analyses and demonstrated similar outcomes among treatment groups (data not shown).

Safety

All patients who received at least 1 dose of study drug were included in the safety analysis. Treatment-related adverse events were reported in 7 (11%) of 66 azithromycin single-dose, 6 (9%) of 66 azithromycin 3-day, and 6 (9%) of 66 ceftriaxone-treated patients. Corresponding rates of diarrhea, the most common adverse event in all 3 groups, were 2 (3%) of 66, 3 (4.5%) of 66, and 4 (6%) of 66, respectively. No cases of diarrhea were judged to be severe. Vomiting, which was judged to be mild, occurred in 3 (4.5%) of 66 azithromycin single-dose patients, and none of the azithromycin 3-day or ceftriaxone-treated patients. Rash occurred in 1 (2%) of 66 azithromycin single-dose, none of 66 azithromycin 3-day, and 4 (6%) of 66 ceftriaxone-treated patients. Three of 4 occurrences of rash in the ceftriaxone group were severe.

Table II. Number (%) of patients with clinical success,* stratified by pathogen (intent-to-treat population).

Pathogen	Day 14–15			Day 28–30		
	Azithromycin Single-Dose	Azithromycin 3-Day	Ceftriaxone	Azithromycin Single-Dose	Azithromycin 3-Day	Ceftriaxone
<i>Streptococcus pneumoniae</i>	20/21 (95)	15/18 (83)	23/23 (100)	20/21 (95)	17/18 (94)	23/23 (100)
<i>Haemophilus influenzae</i>	8/9 (89)	14/15 (93)	10/10 (100)	7/9 (78)	11/15 (73)	9/10 (90)
<i>Moraxella catarrhalis</i>	0/0	2/2 (100)	0/0	0/0	2/2 (100)	0/0

*Cure or improvement.

Sixty-four azithromycin single-dose, 62 azithromycin 3-day, and 63 ceftriaxone-treated patients had at least 1 laboratory assessment and were evaluable for clinically significant laboratory abnormalities. The most common clinically significant laboratory abnormality was neutropenia, defined as an absolute neutrophil count (ANC) of <1500 cells/mm³. Neutropenia was observed in 10 (15.6%), 9 (14.5%), and 8 (12.7%) patients treated with single-dose azithromycin, 3-day azithromycin, or ceftriaxone, respectively. No patient had an ANC of ≤ 500 cells/mm³; in every case, the neutrophil count returned to normal. No serious adverse events occurred during the study, and no patients discontinued treatment because of an adverse event or laboratory abnormality.

DISCUSSION

The equivalent efficacy of shortened versus traditional courses of therapy for AOM has been highlighted in recent reviews.^{3,6,35} We report here the results of a pilot study in which no large differences in efficacy or tolerability were detected among patients with uncomplicated AOM treated with single-dose oral azithromycin, 3 daily doses of azithromycin, or a single intramuscular dose of ceftriaxone. These encouraging findings provided support for a subsequent large, double-blind, double-dummy, nontympanocentesis trial, the results of which have been reported by Block et al.³⁶ In that trial, 350 children with uncomplicated AOM were randomly assigned to receive either single-dose azithromycin (30 mg/kg) or amoxicillin/clavulanate (45 mg/kg administered BID for 10 days). At day 12–16, clinical success rates (cure or improvement) were 86% for azithromycin and 88% for amoxicillin/clavulanate, whereas at day 28–32, clinical success rates were 75% for both treatment groups. Dunne and colleagues³⁷ also assessed the efficacy of single-dose azithromycin in a randomized, noncomparative study in children with uncomplicated AOM. Middle-ear fluid was obtained at baseline, and children were assessed clinically at days 10 and 24–28. Among 124 culture-positive patients, clinical success rates at days 10 and 24–28 were 86% and 81%, respectively.

In the present study, the single-blind study design, with open-label dosing for ceftriaxone, is one of the limitations that should be considered when interpreting the data. However, the potential for bias would likely be greater in the open-label ceftriaxone group, in which parents or physicians might assume better efficacy for a parenteral versus an oral agent. Another important observation is that this trial was conducted between 1995 and 1997 in a population with low macrolide resistance rates. Thus, the results would not be applicable to geographic areas with high rates of penicillin- or macrolide-resistant *S pneumoniae*. Finally given the small sample size, this pilot study was not powered to detect clinically important efficacy differences. Nevertheless, the purpose of the study was to provide sufficient preliminary data to support initiation of a larger, well-controlled trial of the efficacy and safety of single-dose azithromycin for treating uncomplicated AOM.

In this study, recurrence rates among microbiologically evaluable patients at day 28–30 tended to be lower than those noted in the single-dose azithromycin trials by Block et al.³⁶ and Dunne et al.³⁷ This may be explained by the low frequency of day-care and preschool attendance in Costa Rica at the time of the study,³⁸ and the low rates of resistance among pneumococcal isolates in our trial and throughout Costa Rica during the study period.³⁹ Since then, a recent analysis of middle-ear fluid isolates obtained from Costa Rican patients between years 1999 and 2001 has shown that *S pneumoniae* penicillin resistance rates have increased, whereas the susceptibility patterns of macrolides and cephalosporins have remained unaltered.⁴⁰ It is important to note that expert opinion regarding the validity of the day 28–30 efficacy end point has changed in recent years.⁴¹ Nevertheless, the design of the present study is consistent with the 1998 FDA Guidance for acute otitis media trials.⁴²

The efficacy of single-dose azithromycin for the treatment of high-risk children with AOM has not been studied formally. Recent expert opinion indicates that 5-day regimens of short-acting, oral beta-lactam antibiotics may not be appropriate for children younger than 2 years or those with recurrent AOM, underlying medical conditions, or tympanic-membrane perforation.^{5,43} It should be noted that the mean age of our patients was 2.5 years, and only 39% were aged ≤ 2 years. In addition, children with a perforated tympanic membrane, recent antibiotic exposure, or serious underlying illness were excluded from the study. Thus, our patients would be considered at low risk for recurrent episodes of AOM and infection due to resistant pneumococci.⁷ Among children aged ≤ 2 years, Block and associates³⁶ reported comparable efficacy at day 12–16 for single-dose azithromycin and amoxicillin/clavulanate. However, as expected, clinical success rates among these younger children were 15% (azithromycin) and 12% (amoxicillin/clavulanate) lower than for children > 2 years. In their noncomparative single-dose azithromycin study, Dunne et al.³⁷ also reported a lower success rate at day 10 among children ≤ 2 years compared with those > 2 years (84% vs 91%, respectively). Similarly, at day 24–28, children in the ≤ 2 -year age group and those > 2 years had clinical success rates of 77% and 89%, respectively. These results suggested that a higher dose of azithromycin may be more appropriate for children at risk for recurrent or persistent AOM. Accordingly, a new, high-dose azithromycin regimen (20 mg/kg daily for 3 days) was recently compared with high-dose amoxicillin/clavulanate (45 mg/kg administered BID) for the treatment of recurrent or persistent AOM in children.⁴⁴ In this high-risk population, 3-day high-dose azithromycin demonstrated clinical efficacy comparable to that of 10-day, high-dose amoxicillin/clavulanate for the treatment of bacteriologically confirmed AOM.

The benefits of short-course therapy, when used appropriately, are considerable. Longer courses of therapy may not only increase the risk of side effects, but also reduce compliance.³⁵ Compliance, in turn, is influenced by palatability, side effects, dosing frequency, and duration of exposure. Azithromycin oral suspension has received high ratings for palatability when compared with other

antibiotics frequently prescribed for the treatment of AOM.⁴⁵ In addition, the tolerability of azithromycin has been well documented over nearly a decade of use in pediatric patients.^{46,47}

Another compliance-related advantage of single-dose azithromycin is its potential for use as directly observed therapy. This approach may be particularly valuable in settings such as the emergency department or clinic, where poor compliance is suspected or social barriers to filling prescriptions may exist. In the treatment of tuberculosis, directly observed therapy has been shown to improve clinical success and decrease the potential for resistance emergence.⁴⁸

CONCLUSIONS

In this pilot study comparing the efficacy and tolerability of single-dose oral azithromycin with either 3-day azithromycin or single-dose intramuscular ceftriaxone for the treatment of uncomplicated AOM, no differences were detected among the 3 regimens. These data provided the rationale for 2 larger clinical trials, the results of which further document the efficacy and tolerability of single-dose oral azithromycin therapy for uncomplicated AOM in children.

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