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ORIGINAL ARTICLE

Comparative Evaluation of Immediate Versus Delayed Antibiotic Prescription in Pediatric Acute Otitis Media

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ABSTRACT

Background: Acute otitis media (AOM) is one of the most common pediatric infections and a leading cause of antibiotic prescriptions. As a result of concerns about antibiotic resistance and adverse effects, delayed antibiotic prescribing as an alternative to immediate therapy has been of interest. In this study, immediate versus delayed antibiotic treatment in children with uncomplicated AOM was compared in terms of clinical efficacy, inflammatory response and safety.

Methods: This is a prospective, multicenter study in which, from January 2022 to January 2023, the University Medical College, Islamabad, the Children's Hospital, Taif, and the Children's Hospital, Lahore, enrolled 150 children aged 6 months to 12 years with a clinically diagnosed AOM. We proceeded with nonrandom patient assignment to receive either immediate (n = 75) or delayed (n = 75) antibiotic therapy. Demographics with baseline age, weight, and sex, and inflammatory biomarkers (C-reactive protein [CRP] and white blood cell [WBC] count) were recorded. The primary end point was complete symptom resolution by day 7, and the secondary end points were total antibiotic usage, adverse events, reconsultation rates, and complications.

Results: Groups were similar on baseline characteristics. On day 7, the immediate group was 89.3% and the delayed group was 80.0%, and achieved complete symptom resolution ($p > 0.05$). Thus, the antibiotics were given to all patients in the immediate group, but only 36 percent of the delayed group needed treatment. There were 28% of the immediate group and 14.7% of the delayed group with adverse events. CRP and WBC counts were significantly reduced from baseline in both groups, with no significant between-group difference.

Conclusion: Clinical outcomes of delayed antibiotic prescribing for uncomplicated pediatric AOM are equivalent to immediate therapy and provide reductions in antibiotic exposure and adverse events. This approach facilitates the development of improved antimicrobial stewardship in pediatrics.

Keywords: acute otitis media, pediatric, delayed antibiotic, immediate antibiotic, antimicrobial stewardship, CRP, WBC, antibiotic resistance

INTRODUCTION

Acute otitis media (AOM) is the most frequent cause of physician visits and antibiotic prescription in children, and is a major source of antimicrobial use during early childhood. This condition, which usually occurs in children five years of age or younger, is marked by the sudden onset of signs and symptoms of inflammation of the middle ear following such viral upper respiratory tract infections[1]. Most cases are self-limiting and resolve with no complications, yet clinical practice in many settings continues to recommend immediate antibiotic prescription to decrease symptoms and lessen severe but rare complications like mastoiditis and hearing loss. However, this widespread approach plays a major role in the misuse and, by extension, in the development of antibiotic-resistant pathogens, which is now considered a major global health problem[2, 3].

Alternative prescribing models have been introduced in response to concerns of antimicrobial resistance and adverse drug events. Two of these are the delayed antibiotic prescription strategy, which has attracted attention as a way to reduce unnecessary antibiotic use without sacrificing clinical outcomes[4]. Here, the model instructs caregivers to start antibiotic therapy only after a particular period of observation (usually 48 to 72 hours) and if symptoms do not resolve or worsen. Given the evidence from previous randomized controlled trials and systematic reviews, in selected children with non-severe AOM, delayed prescribing compared to immediate treatment is associated with similar clinical outcomes, less exposure to antibiotics, and lower rates of medication-related adverse effects[5].

However, current guidelines recommend that delayed antibiotic prescribing be based on age, symptom severity, and risk of complications, but this has not been universally implemented across clinical settings[6]. In particular, this is true in low and middle-income countries (LMICs) where follow-up care may not be available or where data regarding the safety and feasibility of delaying prescription are sparse. In addition, most of the current evidence comes from high-income countries and may not generalize well to other healthcare systems and populations with different health-seeking behaviors, availability of antimicrobials, and resistance patterns [7] .

Specifically, the present study was designed to fill the gaps identified by filling the gaps identified by conducting a comparative evaluation of immediate versus delayed antibiotic prescription in pediatric patients with AOM. The primary aim was to determine the rate of symptom resolution within 7 days in the two groups. Other secondary objectives included comparison of adverse events, parental satisfaction, antibiotic usage rates, reconsultation rates, and the AOM-related complication rates. The data from this study can provide clinically relevant information about the effectiveness and safety of delayed antibiotic prescribing in pediatric AOM and can contribute to evidence-based antibiotic stewardship strategies, especially in settings of increasing antibiotic resistance [8 9].

MATERIALS AND METHODS

Study Design and Setting: This was a 13-month multicenter comparative study from January 2022 to January 2023. The research was done at three tertiary care centers, namely the University Medical College, Islamabad, the Emergency Department, Children's Hospital, Taif, and the ENT Department, Children's Hospital Lahore. The participating institutions are high-volume pediatric referral hospitals with specialized services in otolaryngology and emergency pediatrics that make it an appropriate setting for evaluation of acute otitis media (AOM) management strategies.

Study Population and Sample Size: A total of 150 pediatric patients aged from 6 months to 12 years with symptoms of acute otitis media were enrolled for the study. The diagnosis of AOM was made clinically, as there was both middle ear effusion confirmed by

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pneumatic otoscopy, and signs of acute inflammation such as otalgia, tympanic membrane erythema or bulging, and fever or irritability. A first episode of AOM with symptom onset within 48 hours was considered eligible for children. The exclusion criteria included a history of recurrent AOM (≥3 episodes in the past 6 months or ≥4 in the past 12 months), chronic suppurative otitis media or tympanic membrane perforation, prior antibiotic use within the preceding 72 hours, known immunodeficiency, craniofacial anomalies, or any serious underlying systemic illness. All participants gave informed written consent from the parents or legal guardians.

Study Groups and Intervention Strategy: Seventy-five children were placed into two comparative groups. Children in group A received an immediate antibiotic prescription, and treatment began on the same day of diagnosis. Those who were prescribed antibiotics but were told to wait before starting them unless symptoms worsened or did not improve in 48 to 72 hours were grouped in Group B. Both groups received standardised supportive care, including analgesics such as paracetamol or ibuprofen, antipyretics, and fluid intake counseling. The main antibiotic choice was amoxicillin or amoxicillin-clavulanic acid, and this was determined by local institutional protocols and physician discretion. Caregiver counseling about both approaches resulted in nonrandomized allocation based on shared decision making.

Data Collection and Follow-up: At times of presentation (baseline), and follow-up by in-person visit, or by structured telephone interview, data were collected on days 3, 7, and 14. All centers used a standardized data collection form so that there was consistency. Baseline data included age, sex, weight, symptom duration, tympanic membrane findings, and initial pain score on a visual analog scale of 10. Data regarding treatment-related information, such as type of antibiotic prescribed, adherence, use of analgesics, and timing of antibiotic initiation, were recorded. The clinical outcomes measured during follow-up were symptom resolution (absence of fever and otalgia), incidence of adverse effects (diarrhea, vomiting, rash), need for reconsultation or emergency visits, and AOM-related complications (mastoiditis or persistent effusion). On day 7, parental satisfaction and parental confidence regarding the chosen treatment strategy were assessed on a 5-point Likert scale.

Outcome Measures: The primary outcome of the study was the rate of complete clinical recovery by day 7, defined by resolution of otalgia, fever. Secondary outcomes included the proportion of children from the delayed group who subsequently required antibiotics, the frequency of antibiotic-related adverse events, parental satisfaction scores, the rate of reconsultations in the 14 days, and the incidence of complications secondary to AOM. The relative efficacy and safety of immediate versus delayed antibiotic prescription strategies were compared between the two groups.

Ethical Considerations: All participating centers' IRBs approved the study. All enrolled participants were written informed consent was obtained from the parents or legal participants. The data were anonymized in line with international ethical standards, including the Declaration of Helsinki, and patient confidentiality was maintained at all stages.

Statistical Analysis: IBM SPSS Statistics version 26.0 was used to enter data and analyze. Demographic and baseline clinical characteristics were summarized by descriptive statistics. Mean ± SD was presented for continuous variables, and frequencies and percentages for categorical variables. The application of the chi-square test or Fisher's exact test was used to compare groups for categorical variables. Independent sample t-test or Mann–Whitney U test was used to compare the continuous variables according to data distribution. All analyses were deemed statistically significant if a p-value was less than 0.05.

RESULTS

A total of 150 pediatric patients with acute otitis media (AOM) were enrolled at random and divided into two groups of 75 each. On top of standard clinical evaluation, huge amounts of demographic data and inflammatory biomarkers were collected at baseline to make the groups comparable. The mean age of patients in the immediate antibiotic group was 4.2 ± 2.0 years, weight was 16.5 ± 4.2 kg, body temperature at presentation was 38.4 ± 0.7 °C, C reactive protein (CRP) at presentation was 12.4 ± 3.6 mg/L, and white blood cell (WBC) count 12,000 ± 2,000/µL. In the delayed antibiotic group, the same values were 4.1 ± 2.1 years, 16.2 ± 3.9 kg, 38.3 ± 0.8 °C, 12.0 ± 3.4 mg/L, and 11,800 ± 1,900/µL. The demographic and baseline biomarker characteristics are summarized in Table 1.

Table 1: Demographic and Baseline Biomarker Characteristics

Characteristic	Immediate Antibiotics (n = 75)	Delayed Antibiotics (n = 75)	p-value
Age (years), mean ± SD	4.2 ± 2.0	4.1 ± 2.1	0.45
Weight (kg), mean ± SD	16.5 ± 4.2	16.2 ± 3.9	0.52
Body Temperature (°C)	38.4 ± 0.7	38.3 ± 0.8	0.60
CRP (mg/L), mean ± SD	12.4 ± 3.6	12.0 ± 3.4	0.48
WBC (×10³/µL), mean ± SD	12.0 ± 2.0	11.8 ± 1.9	0.55

None of these baseline parameters were statistically different between the groups thus assuring that the two populations were well similar before any treatment intervention.

The clinical outcomes and additional biomarkers were then evaluated during follow-up. On day 7, 67/89 of the immediate antibiotic group and 60/80 of the delayed group had complete symptom resolution (absence of fever and otalgia). Additionally, there were great differences in the use of antibiotics among the groups: all the patients in the immediate group received antibiotics, and only 27 patients (36 %) in the delayed group started antibiotics, while 48 patients (64 %) recovered without antibiotics. 21 children (28%) in the immediate group and 11 children (14.7%) in the delayed group had adverse events, mostly mild gastrointestinal disturbances such as diarrhea and vomiting. Reconsultation rates within 14 days were also low and similar between the groups (9.3% for the immediate group, 6.7% for the delayed group), and complications (mastoiditis or persistent middle ear effusion) were rare (2 cases in each group; 2.7%). Table 2 presents these outcome measures.

Table 2: Clinical Outcome Measures

Outcome	Immediate Antibiotics (n = 75)	Delayed Antibiotics (n = 75)	Total (n = 150)
Symptom Resolution by Day 7	67 (89.3%)	60 (80.0%)	127 (84.7%)
Antibiotic Usage	75 (100%)	27 (36%)	102 (68%)
Adverse Events	21 (28%)	11 (14.7%)	32 (21.3%)
Reconsultation within 14 Days	7 (9.3%)	5 (6.7%)	12 (8.0%)
Complications	2 (2.7%)	2 (2.7%)	4 (2.7%)

Table 3: Changes in Inflammatory Biomarkers from Baseline to Day 7

Biomarker	Immediate Antibiotics (Baseline)	Immediate Antibiotics (Day 7)	Delayed Antibiotics (Baseline)	Delayed Antibiotics (Day 7)	p-value (Day 7)
CRP (mg/L)	12.4 ± 3.6	4.8 ± 2.0	12.0 ± 3.4	5.2 ± 2.3	0.35
WBC (×10³/µL)	12,000 ± 2,000	9,000 ± 1,500	11,800 ± 1,900	9,100 ± 1,400	0.40

In addition, inflammatory biomarkers were measured from baseline to day 7 for changes. CRP levels decreased from 12.4 ± 3.6 mg/L to 4.8 ± 2.0 mg/L in the immediate group, and the WBC counts fell from 12,000 ± 2,000/µL to 9,000 ± 1,500/µL. As was the

case in the delayed group, in the early group, CRP levels fell from 12.0 ± 3.4 mg/L to 5.2 ± 2.3 mg/L, and WBC counts fell from 11,800 ± 1,900/µL to 9,100 ± 1,400/µL. As shown in Table 3, there were similar reductions in inflammatory markers between the two groups on Day 7.

Within each group, CRP and WBC counts were significantly reduced ($p < 0.01$ for both), but the difference between the groups at day 7 was not statistically significant. Thus, together, both treatment strategies result in a similar resolution of the inflammatory process driving AOM.

Overall, the study findings show that although immediate antibiotic therapy is associated with a slightly higher rate of symptom resolution by day 7, this difference is not statistically significant compared to delayed antibiotic prescription. Importantly, the delayed strategy reduced overall antibiotic use, adverse events, and similar reconsultation and complication rates. Changes in key inflammatory biomarkers were also comparable between the two groups, providing support that delayed antibiotic prescribing is an effective and safe alternative to the management of uncomplicated AOM in children who can be safely deferred from antibiotics while reducing the amount of unnecessary antibiotic exposure.

DISCUSSION

Through a multicenter, prospective, comparative design, this study presents important information for the management of pediatric acute otitis media (AOM) based on immediate and delayed antibiotic prescription. While children in the immediate group seemed to have a slightly higher rate of complete symptom resolution by day 7, this difference was not statistically significant from those in the delayed group [10 11]. And importantly, the delayed antibiotic strategy led to a much less overall use of antibiotics in the children, since only 36 percent of the children needed antibiotics compared to 100 percent in the immediate group. The finding highlights the possibility of delayed prescribing being able to significantly reduce unnecessary antibiotic exposure, a key strategy in the battle against antimicrobial resistance[12].

This also adds to evidence that the underlying inflammatory process resolves similarly whether antibiotics are initiated early or later. Furthermore, the lower rate of adverse events in the delayed group may also represent a safety advantage from reduced exposure to antibiotics and their associated side effects[13]. The low and similar rates of reconsultation and complications in both groups imply that the delayed strategy does not jeopardize the clinical outcome and does not increase the risk of treatment failure in children with uncomplicated AOM[14].

However, there are some limitations to be acknowledged despite these promising results. Given that these findings are based on a non-randomised design and a small sample size, the generalizability of these findings may be limited[15]. In addition, although inflammatory biomarkers objectively demonstrated disease resolution, they need to be further investigated as predictors of outcome in AOM. These results need to be validated with future studies in larger, randomized cohorts with longer follow-up periods to determine the broader effects of delayed antibiotic prescribing on antimicrobial resistance patterns and patient outcomes[16, 17].

CONCLUSION

We conclude that there is clinical effectiveness and safety of a delayed antibiotic prescribing strategy in the management of uncomplicated pediatric AOM. Despite the potential for a slightly higher rate of early symptom resolution, delaying prescribing antibiotic therapy confers several advantages, including reducing overall antibiotic use and side effects without affecting the patient and not increasing complication rates. Finally, the results encourage the adoption of delayed antibiotic strategies into clinical practice as a viable means for improving antimicrobial stewardship in pediatric care. Future research should investigate larger, randomized studies to further delineate the long-term benefits and perhaps limitations of this approach in a variety of clinical settings.

Conflict of Interest: The authors declare that no conflicts of interest exist.

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