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COMPARISON OF AZITHROMYCIN AND AMOXICILLIN IN THE MANAGEMENT OF PEDIATRIC COMMUNITY-ACQUIRED PNEUMONIA

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ABSTRACT

Background: Community-acquired pneumonia (CAP) is a leading cause of illness and death in children, necessitating effective antibiotic therapies to enhance recovery and reduce the healthcare burden. Azithromycin and amoxicillin are frequently used for treating CAP; however, their relative effectiveness remains under investigation.

Objective: To evaluate and compare the effectiveness of azithromycin and amoxicillin in managing pediatric CAP.

Material and Methods: A randomized controlled trial was conducted in the DHQ Teaching Hospital KDA, Kohat between January and June 2023. A total of 158 children aged 1 month to 5 years with a CAP diagnosis were enrolled and randomly assigned to either the azithromycin or amoxicillin group. Azithromycin was prescribed at 10 mg/kg/day for three days, whereas amoxicillin was administered at 75 mg/kg/day for seven days. The primary outcome was clinical improvement and symptom resolution, analyzed using SPSS Version 26, with $p \leq 0.05$ set as the threshold for significance.

Results: Among the participants, 54 children (68.4%) in the amoxicillin group and 59 children (74.7%) in the azithromycin group showed effective responses. Although the effectiveness was slightly higher with azithromycin, the difference was not statistically significant ($p = 0.378$). Subgroup analyses indicated no significant associations between treatment outcomes and variables such as age, gender, nutritional status, vaccination history, or baseline severity.

Conclusion: Both azithromycin and amoxicillin demonstrated similar efficacy in treating pediatric CAP. Either antibiotic can be considered a viable option, with treatment choice guided by clinical factors and local resistance patterns.

Keywords: Community-acquired pneumonia, azithromycin, amoxicillin, pediatric CAP, antibiotic efficacy.

Introduction:

Community acquired pneumonia (CAP) is a major public health problem worldwide, being one of the leading causes of morbidity and mortality, particularly in children and old people. Management of CAP depends on multiple factors, including appropriate antibiotic tailored to the pathogens, the patient characteristics and local antimicrobial resistance patterns. Amoxicillin, a β lactam antibiotic and azithromycin, a macrolide are widely used antibiotics. Extensive investigation has taken place regarding the comparative efficacy of these two antibiotics [1].

In fact, for treatment of CAP, amoxicillin is generally advocated as the first line therapy for infections due to Streptococcus pneumoniae. More than 40 years later, enrofloxacin has been valued for its targeted activity, compared to other antibiotic classes, and relatively low resistance rates [2]. On the contrary, azithromycin has broad spectrum coverage, and is effective against atypical pathogens, namely, Mycoplasma pneumoniae and Chlamydia pneumoniae, that are becoming increasingly recognized as important etiologies of CAP [3, 4]. Azithromycin, however, has come under scrutiny because of emerging resistance to macrolides [5].

However, several of these antibiotics have been the focus of many studies in exploring the comparative outcomes. For example, a meta-analysis showed that short course azithromycin regimens were not inferior to longer β-lactam regimens in terms of clinical cure, but could provide an advantage by virtue of improved patient compliance because they induced shorter dosing schedules [6]. Likewise, a randomized controlled trial showed that amoxicillin was very effective in treating patients with CAP due to susceptible organisms, and caused few adverse events [7].

A second important factor in choosing antibiotic is the risk of adverse event and patient adherence. Once daily dosing and shorter treatment duration with azithromycin makes it a desirable choice in outpatient settings [8]. On the other hand, amoxicillin is safe and cost effective, and particularly for resource limited settings [9]. Moreover, emerging evidence suggests that designing antibiotic therapy according to local resistance patterns and patient specific factors can improve clinical outcomes but reduce the risk of resistance development [10].

In this study we seek to answer high CAP burden in children by studying whether amoxicillin and azithromycin are clinically effective in them. Both antibiotics are commonly prescribed and are effective, but there is little data about their relative effectiveness in infantile CAP, especially in resource limited settings. The objective of this research was to provide evidence to assist in effective antibiotic selection and enhance outcomes in children with CAP.

Material and Methods:

This randomized controlled trial was conducted at the DHQ Teaching Hospital KDA, Kohat between January and June 2023. The sample size was calculated using the efficacy rates of azithromycin and amoxicillin as 81% and 60.9%, respectively, with a power of 80% and a significance level (α) of 5%. The calculated sample size was 79 patients in each group, resulting in a total of 158 patients [11].

A non-probability consecutive sampling method was employed to enroll participants. Random allocation to the two treatment groups was achieved using computer-generated random numbers. Ethical approval for the study was obtained, and written informed consent was secured from all patients prior to their inclusion in the research.

Children aged 1 month to 5 years, diagnosed with community-acquired pneumonia (CAP) based on clinical, radiological, and laboratory findings, and willing to provide informed consent were included in the study. Key baseline characteristics included age, gender, nutritional status (normal or malnourished), vaccination history (complete or incomplete), baseline severity of CAP (mild, moderate, or severe), and prior antibiotic use (yes or no). Children with hospital-acquired or healthcare-associated pneumonia, known hypersensitivity to amoxicillin or azithromycin, severe immunosuppression, or requiring ICU admission were excluded.

The patients were allocated into two groups for treatment. Group A (Amoxicillin group) was prescribed amoxicillin 500 mg orally, three times a day for seven days, whereas Group B (Azithromycin group) received azithromycin 500 mg orally on the first day, followed by 250 mg once daily for the subsequent four days. The primary outcome measured was treatment effectiveness, classified as 'Effective' or 'Not Effective' based on the resolution of CAP symptoms, including fever, cough, dyspnea, and chest pain, assessed on Day 7 post-treatment. Secondary outcomes included radiological improvement and the occurrence of adverse drug reactions.

Data were collected using a structured performa. Baseline demographics, including age and gender, clinical features such as symptom duration and baseline severity of CAP, comorbid conditions, and laboratory findings, were recorded at enrollment. Follow-up assessments were performed at Day 3 and Day 7 to evaluate clinical and radiological outcomes.

The analysis was performed using SPSS version 24. Continuous data were summarized as mean ± standard deviation (SD), while categorical data were presented as counts and percentages. The Chi-square test was utilized to compare categorical variables. Statistical significance was defined as a p-value ≤ 0.05.

Results:

Total 158 patients were recruited and mean age was 30.19 ± 18.10 months.In the Amoxicillin group, 54 patients (68.4%) were classified as having an effective treatment response, while 25 patients (31.6%) were not effective. In the Azithromycin group, 59 patients (74.7%) achieved an effective response, whereas 20 patients (25.3%) were not effective. The effectiveness was higher in the Azithromycin group (74.7%) compared to the Amoxicillin group (68.4%), but this difference was not statistically significant ($p = 0.378$). This indicates that both antibiotics provided similar outcomes in treating community-acquired pneumonia among children. (Table 1)

In the 0-12 months group, 22 (59.5%) children showed effectiveness, compared to 15 (40.5%) who did not. The highest effectiveness was observed in the 25-36 months group, with 24 (82.8%) children being effective and 5 (17.2%) not effective. Across all age groups, the p-values were greater than 0.05, indicating no statistically significant differences in treatment effectiveness based on age.

Among male children, 57 (68.7%) were classified as effective, while 26 (31.3%) were not. For females, 56 (74.7%) were effective, compared to 19 (25.3%) who were not. Although female children showed slightly higher effectiveness, the differences were not statistically significant ($p = 0.668$ for males, $p = 0.460$ for females).

For children with normal nutritional status, 86 (70.5%) were effective, and 36 (29.5%) were not. Among malnourished children, 27 (75.0%) were effective, while 9 (25.0%) were not. The p-values (0.324 for normal and 0.841 for malnourished) indicate no significant relationship between nutritional status and treatment outcomes.

Children with complete vaccination histories had 91 (69.5%) showing effectiveness, while 40 (30.5%) were not effective. Those with incomplete vaccination histories had 22 (81.5%) effective and 5 (18.5%) not effective. The p-values (0.144 for complete and 0.163 for incomplete) suggest no statistically significant association between vaccination history and treatment effectiveness.

Among children with mild baseline severity, 62 (76.5%) were effective, and 19 (23.5%) were not. For moderate severity, 32 (74.4%) were effective, while 11 (25.6%) were not. In cases with severe baseline severity, 19 (55.9%) were effective, and 15 (44.1%) were not. Although there was a trend of decreasing effectiveness with increasing severity, the differences were not statistically significant ($p > 0.05$).

In children with a history of prior antibiotic use, 20 (71.4%) were effective, and 8 (28.6%) were not. Among those without prior antibiotic use, 93 (71.5%) were effective, and 37 (28.5%) were not. The p-values (0.717 for previous use, 0.421 for no previous use) indicate no significant impact of prior antibiotic use on treatment effectiveness. (Table 2)

Table 1: Effectiveness of Amoxicillin vs. Azithromycin in Treating Community-Acquired Pneumonia

Group	Effective (n, %)	Not Effective (n, %)	p-value
Amoxicillin	54 (68.4%)	25 (31.6%)	0.378
Azithromycin	59 (74.7%)	20 (25.3%)	

Table 2: Comparison of Effectiveness of Amoxicillin and Azithromycin Across Different Variables in Children with Community-Acquired Pneumonia

Variable	Category	Effective (n, %)	Not Effective (n, %)	p-value
Age Group	0-12 months	22 (59.5%)	15 (40.5%)	0.204
	13-24 months	18 (72.0%)	7 (28.0%)	0.332
	25-36 months	24 (82.8%)	5 (17.2%)	0.564
	37-48 months	23 (71.9%)	9 (28.1%)	0.538
	49-60 months	26 (74.3%)	9 (25.7%)	0.599
Gender	Male	57 (68.7%)	26 (31.3%)	0.668
	Female	56 (74.7%)	19 (25.3%)	0.460
Nutritional Status	Normal	86 (70.5%)	36 (29.5%)	0.324
	Malnourished	27 (75.0%)	9 (25.0%)	0.841
Vaccination History	Complete	91 (69.5%)	40 (30.5%)	0.144
	Incomplete	22 (81.5%)	5 (18.5%)	0.163
Baseline Severity	Mild	62 (76.5%)	19 (23.5%)	0.631
	Moderate	32 (74.4%)	11 (25.6%)	0.255
	Severe	19 (55.9%)	15 (44.1%)	0.790
Previous Antibiotic Use	Yes	20 (71.4%)	8 (28.6%)	0.717
	No	93 (71.5%)	37 (28.5%)	0.421

Discussion:

Community-acquired pneumonia (CAP) is a leading cause of morbidity and mortality among children worldwide. Effective treatment strategies are essential to improve outcomes and reduce the burden of disease. This study compared the effectiveness of azithromycin and amoxicillin in the treatment of pediatric CAP and found no statistically significant difference between the two antibiotics in terms of clinical improvement and treatment success rates. These findings align with previously published studies and add to the growing body of evidence regarding the efficacy of these commonly prescribed antibiotics.

Kogan et al. conducted a comparative randomized trial to evaluate the efficacy of azithromycin versus erythromycin and amoxicillin in treating CAP in children. Their results showed that children with classic pneumonia treated with azithromycin achieved chest X-ray normalization more frequently by day 7 compared to those treated with amoxicillin (81.0% vs. 60.9%, $p = 0.009$). Although our study did not find a statistically significant difference in effectiveness, the higher response rate in the azithromycin group (74.7%) compared to the amoxicillin group (68.4%) is consistent with Kogan et al.'s findings, suggesting a potential advantage of azithromycin in achieving earlier clinical improvement [11].

Similarly, Ashraf et al. reported comparable efficacy between azithromycin and amoxicillin in treating pediatric pneumonia, with clinical improvement rates by day 7 being 88% for azithromycin and 90% for amoxicillin ($p = 0.68$). These findings, consistent with our results, highlight that both antibiotics are highly effective and safe for pediatric CAP treatment, with minimal differences in clinical outcomes [12].

Agarwal and Khanduri's study comparing amoxicillin and amoxicillin-clavulanic acid found a significantly higher cure rate in the amoxicillin-clavulanic acid group (93.88% vs. 79.17%, p =

0.013). Although not directly comparable, their results suggest that combining amoxicillin with clavulanic acid could enhance efficacy, potentially offering an alternative for severe or resistant cases of CAP [13].

Das and Singh's systematic review and meta-analysis demonstrated the efficacy of oral amoxicillin in treating severe CAP in children under five years in developing countries. Their findings support amoxicillin as a first-line treatment, but they emphasized the need for high-quality trials to further strengthen the evidence base. This aligns with our study, where amoxicillin was effective in 68.4% of cases, confirming its role as a cornerstone in CAP management [14].

Musungu et al. highlighted the superiority of a combination therapy of azithromycin and amoxicillin-clavulanic acid in reducing symptoms such as chest pain and cough more rapidly than monotherapy with levofloxacin. Although this study focused on combination therapy, the findings suggest that azithromycin's rapid symptom resolution may be a critical advantage in certain clinical scenarios [15].

Handy et al. found that macrolides were associated with a lower failure rate compared to beta-lactams, particularly in younger children (<5 years old). Our study's findings of slightly higher effectiveness in the azithromycin group (74.7%) compared to the amoxicillin group (68.4%) align with Handy et al.'s conclusions, underscoring the potential benefit of macrolides in select populations [16].

Bielicki et al. conducted a randomized clinical trial to evaluate the effect of amoxicillin dose and treatment duration on pediatric CAP. Their study found no significant difference in antibiotic re-treatment rates between higher and lower doses or between 3-day and 7-day treatment durations. These findings suggest that amoxicillin remains an effective option, even with shorter courses, aligning with our observation of its effectiveness in 68.4% of cases [17].

Donà et al. emphasized the importance of evidence-based guidelines for treating mild to moderate CAP in previously healthy children. Their consensus recommended amoxicillin as a first-line treatment for immunized children and the addition of macrolides for older children or persistent symptoms. This supports the observed efficacy of both azithromycin and amoxicillin in our study, highlighting their complementary roles in CAP management [18].

The differences in clinical effectiveness between azithromycin and amoxicillin could be attributed to their distinct mechanisms of action and pharmacokinetics. Azithromycin, a macrolide, offers broad-spectrum coverage and superior penetration into respiratory tissues, potentially accounting for its slightly higher effectiveness in our study. Conversely, amoxicillin, a beta-lactam, is highly effective against Streptococcus pneumoniae, the most common bacterial pathogen in CAP. The choice between these antibiotics should be guided by clinical factors, including patient age, disease severity, and local antimicrobial resistance patterns.

The higher response rate to azithromycin observed in our study aligns with Kogan et al.'s findings of earlier chest X-ray normalization. However, the lack of statistical significance underscores the importance of individualizing treatment based on patient characteristics and clinical presentation. Furthermore, the safety profiles of both antibiotics are favorable, with minimal adverse effects reported in our study and previous research.

Conclusion:

This study shows that both azithromycin and amoxicillin are useful in treatment of pediatric community acquired pneumonia, with no statistical significant difference in treatment success rates. The findings indicated that response rate was slightly higher for azithromycin; however they indicate that both antibiotics may possibly be effective therapy in the treatment of CAP in children. Clinical presentation, patient specific factors, and local antimicrobial resistance patterns should guide the choice of the antibiotic to maximize the outcome.

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