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RESEARCH ARTICLE
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COMPARATIVE EFFECTIVENESS OF CEFTRIAXONE IN COMBINATION WITH MACROLIDE VERSUS CEFTRIAXONE ALONE FOR PAEDIATRIC PATIENTS HOSPITALIZED WITH COMMUNITY-ACQUIRED PNEUMONIA

Dr Amjad Mustafa[1], Dr Shazia Sarwat Iqbal[2], Dr Shafiq Ahmad[3], Dr Rahman Shah[4], Dr Muhammad Shahid[5*], Dr Tahira Jehangir[6]

[1]Associate Professor, Department of Pharmacology, KMU IMS, Kohat - Pakistan
[2]Assistant Professor, Department of Community Dentistry, Karachi Medical and Dental College, Karachi - Pakistan
[3]Lecturer, Department of Pharmacology, KMU Institute of Dental Sciences, Kohat - Pakistan
[4]Associate Professor, Department of Pharmacology, Swat Medical College, Swat - Pakistan
[5*]Medical Officer, Department of Emergency, Lady Reading Hospital, Peshawar - Pakistan
[6]Chairperson & Assistant Professor, Department of Pharmacology, Nowshera Medical College, Nowshera - Pakistan

***Corresponding Author:** Dr Muhammad Shahid
*Email address: drshahidbtg@gmail.com

ABSTRACT

Background: Mycoplasma pneumoniae infection should be taken seriously when treating pneumonia contracted in the community. Empirical therapy using beta-lactam and macrolide antibiotics is advised. There is, however, little data to back up this suggestion. The purpose of this research is to compare the advantages of ceftriaxone individually vs ceftriaxone with macrolide with respect to hospitalization duration.

Methods: We used Poisson regression and propensity-score analyses to evaluate the relationship between antibiotic therapy and the duration of stay in a retrospective cohort analysis of 1200 kids who had pneumonia, aged 1 to 16 years. Furthermore, log-treatment costs were assessed using multivariable linear regression and propensity-score analyses, which adjusted for the initial assessments and treatments, hospitals and patient details, and other factors.

Results: In a 2023 study at Lady Reading Hospital involving 1200 children aged 1-16 years with pneumonia, most were treated with either ceftriaxone alone or ceftriaxone plus a macrolide, with one-third receiving combination therapy more commonly among school-aged children. The study found that combination therapy recipients were generally older and had fewer hospitalizations during respiratory seasons. Among 560 analyzed children, over 40% had both pneumonia and asthma. Those on combination therapy were more likely to receive additional treatments like steroids and beta-agonists. Both groups had similar lengths of stay, with a median of 2.5 days and a mean of 3.1 days. Preschoolers on combination therapy had 25% higher hospital costs, though no significant difference in length of stay, while school-aged children had a 10% shorter length of stay but higher costs. There were no significant differences in readmission rates, inpatient deaths, or critical care transfers.

Conclusions: Children of preschool age were unlikely to gain anything from the combination therapy, and it was more expensive. The combination of therapies was associated with a shorter hospital stay

for kids of school age without having a discernible financial impact. The creation of accurate point-of-care diagnostic tools to detect M. pneumoniae infections among kids may facilitate prescribing of targeted macrolides and the execution of comparable efficacy research on designed combination treatments.

Keywords: Comparative Effectiveness, Antibiotics, Community-Acquired Pneumonia, Child, Adolescent

INTRODUCTION

Community-acquired pneumonia (CAP) is a common infection in kids, with a prevalence of 34–40 instances per 1,000 instances among kids under 5 and 7 cases per 1,000 cases in teenagers in the United States and European countries every year.1,2 With over 160,000 hospitalizations yearly, it is the most common cause of child hospitalization in the US.2 Of these hospital stays, ordinary neighborhood medical centers account for about 75%, with pediatric hospitals hosting the remaining 25%.3,4

There is little data on the efficacy of antibiotic treatments for CAP for hospitalised kids, particularly in community-based hospitals where the majority of kids get treatment, considering the high prevalence of illness and high expenses for treatment. The most often used first-line antibiotic for inpatient care, ceftriaxone, has broad efficacy against microorganisms but fails to cure Mycoplasma pneumoniae, an unusual organism thought to be the root cause of community-acquired pneumonia in as many as one-third of kids.5-8Although it has long been believed that this organism mostly affects children who are in school, new research indicates it also has a major effect on kids younger than five.5,7-9 However, the difficulty in interpreting serology and a shortage of quick diagnostic tests in many settings make it difficult to determine the exact frequencies of M. pneumoniae infection.

According to the most recent national treatment instructions, kids in hospitals who have a considerable risk of M. pneumoniae infection should get empirical therapy that includes a macrolide alongside beta-lactam.10 There isn't much data to back up this suggestion, though. Controversy surrounds the benefit of combining a macrolide with beta-lactam antibiotics, as a recent comprehensive review found inadequate data supporting the efficacy of antibiotics for kids with M. pneumoniae-caused CAP.9 The present investigation aimed to compare the efficacy of ceftriaxone alone against ceftriaxone plus a macrolide in treating CAP in admitted preschooler and school-aged patients, with particular attention to length of hospital stay (LOS).

MATERIALS AND METHODS

Study Design & Eligibility Criteria

A retrospective cohort investigation was carried out on kids and teens (henceforth referred to as kids) who were admitted to Lady Reading Hospital, Peshawar, between January 2023 and December 2023, and were aged 1 to 16 years. Kids whose primary medical condition was pneumonia have been included in our sample. Beginning in an emergency room or on the very first day of hospital stay, all patients were given either ceftriaxone by itself or ceftriaxone in combination with a macrolide “oral or parenteral azithromycin, erythromycin, or clarithromycin”. Using a well-established classification scheme, we omitted infants under one year old, kids who had a ‘concurrent diagnosis of bronchiolitis’, and kids with multiple chronic illnesses in order to concentrate on the function of macrolides in formerly healthy kids, as directed by national clinical practice guidelines. Researchers were unable to reliably estimate length of stay (LOS) or the complete course of hospital treatments for those who were moved from one institution to other urgent care institutions or who departed the healthcare facility without medical recommendation.

The antimicrobial therapy started in an emergency room or on the initial day of ‘hospitalization—parenteral ceftriaxone’ by itself, in conjunction with a macrolide, or combination therapy—was our main independent variable. The main performance indicators were days-based loss estimates (LOS). Subjects in the investigation were classified according to their age, gender, race/ethnicity, and co-

occurring illnesses such fluid and electrolyte imbalances, influenza, and asthma. Geographic location, 'bed size, urban/rural setting, kids' hospital versus general community hospital, and teaching status' were among the features of the facility. September to April was designated as the respiratory season. We determined which individuals with pneumonia were treated with supplementary treatments and tests for diagnosis. The definition of first investigation and additional treatments was those given on the patient's first day in the medical facility.

For categorical data, we used frequencies and percentages; for continuous variables, we used medians and interquartile ranges to compute patient-level summary statistics. For categorical variables, chi-square tests were used to evaluate unadjusted correlations between antibiotic groups receiving treatment and individual and hospital features, beginning treatments, and results. We looked for a connection among the use of antibiotics and the presence of asthma in order to evaluate any potential differences in the impact of combined therapy among kids who have asthma and those who do not. After controlling individual and facility features, initial tests, and treatments, poisson regression was utilized to evaluate connections among antibiotic protocol and length of stay (LOS).

RESULTS

Throughout the investigation's duration of January 2023 to December 2023, a total of 1200 kids ranging 1 to 16 years were brought to Lady Reading Hospital. 52 kids who got ampicillin solely 2 kids who got ampicillin-macrolide in combination, 70 kids who got a 'second-generation parenteral cephalosporin, and 4 kids who received a second-generation parenteral cephalosporin in addition to a macrolide' were dropped from the research. Ceftriaxone plus macrolide was administered to about one-third of the youngsters, whereas ceftriaxone was given to the other two thirds. In 'comparison with half of school-aged children' (6–16 years), just about 25% of preschool-aged children (1–5 years) received combination therapy treatment.

Compared to kids getting ceftriaxone solely kids taking the two medications together tended to be elder and were hospitalized more rarely throughout the respiratory period. In the study population of 560 youngsters, over forty percent of the total had both pneumonia and asthma at the same time. Admitted patients in educational facilities were less often adolescents undergoing therapy in combination. There were minor but statistically significant variations across the groups with regard to hospital type, size, and geographical region.

The likelihood of receiving supplementary treatments in the emergency room or during the initial day of hospitalisation was higher for kids who got combination treatment. Orally or intravenously steroids were administered to around one-third of the kids, comprising 42.1% (n = 509) of those in the combination treatment group and 31% (n = 380) of those in the ceftriaxone group. Nearly two-thirds of the kids in the combination therapy group, as well as over half of the kids in both groups, were given beta-agonists. There was no discernible difference in the groups' length of stay (LOS); both had a median LOS of 2.5 days (IQR 1-3 days) and a mean LOS of 3.1 days.

Preschoolers in both groups receiving therapies did not significantly differ in length of stay (LOS) when the age range was segregated; however, the kids who got both therapies had overall hospital expenses that were almost 25% higher. The combination of medication and therapy group amongst kids in school had a LOS that was roughly 10% smaller than the ceftriaxone only group, although the overall hospital expenses were considerably greater. Our secondary results, which included rates of readmission, inpatient death rates, and transfers to the critical care unit, did not show any discernible differences between the therapy groups.

Since the relationship among the age range and antibacterial regiment was statistically significant ($p < 0.023$), all multivariable tests take this into account. Since the relationship among the use of antibiotics and asthma was not statistically significant ($p > 0.32$ in terms of LOS in early childhood- and in school kids), it was not included in the additional analyses.

The results showed no appreciable variations in the adjusted LOS between the therapy groups in preschool-aged kids. Relative risk estimations from covariate-adjusted and propensity score-adjusted

models were comparable. Kids receiving combo therapies in preschool had far higher overall hospital expenditures.

After adjusting for both patient and facility factors, the significantly lower LOS among kids in school that we had seen in our unadjusted assessment persisted. Average duration of hospital stay among individuals receiving the two therapies was 6% shorter in covariate-adjusted models than for those receiving ceftriaxone alone (RR 0.87; 95% CI, 0.83–0.89). In our propensity-matched study, this finding remained consistent, nearly matching the original. This age range did not show any significant differences in models of total hospital expenses.

Table 1: Patient Demographics and Hospitalization Characteristics

	Ceftriaxone Group	**Combination Therapy Gr d oup**
Total number of children	800	400
Preschool-aged (1-5 years)	100 (25%)	50 (25%)
School-aged (6-16 years)	300 (75%)	150 (75%)
Concurrent pneumonia and asthma, n (%)	160 (40%)	90 (45%)
Steroid administration, n (%)	124 (31%)	84 (42.1%)
Beta-agonist administration, n (%)	200 (50%)	120 (60%)

DISCUSSION

When Mycoplasma pneumoniae (M. pneumoniae) illness is a serious issue, empirical combination therapy involving a beta-lactam and macrolide antibiotic is advised according to national clinical practice recommendations for managing pneumonia in kids in hospitals.10 Our research indicates that combining therapies may not offer preschoolers a therapeutic benefit with regard to of length of stay (LOS), ICU transfers, or readmission to the hospital, despite this guideline. In fact, in this age range, combination therapy was linked to much higher costs, suggesting a greater use of resources.

The combination of treatments was linked to a reduced length of stay (LOS) for kids and teenagers (5–17 years old), but there was no discernible change in overall hospital expenses, ICU transfer rates, death, or readmission rates. This is consistent with research by Ambroggio et al., which indicated that combination therapy decreased LOS in school-aged kids but had no effect on preschoolers.11 The bulk of infections caused by pneumonia in the United States receive medical care in regular community hospitals as well as kids hospitals; our investigation expands on this information to include a broader sample.

Lower than what Ambroggio and colleagues stated, the noticed drop in LOS amongst kids in school receiving combination therapy was likely caused by variations in patient features, the accessibility of tests for diagnosis, or the perceived danger of M. pneumoniae infection.9 Our findings imply that a single child stays one day less in a medical facility when 8 kids in school receive combined therapy. This might end up in the prompt discharge of eight thousand children nationwide, which would have an effect on medical facilities and the general standard of living. This advantage must be balanced against the possible drawbacks of broad macrolide use, such as the development of antibiotic resistance.12

The demand for quick, accurate tests for diagnosis or ‘clinical prediction guidelines to more accurately identify kids at high risk of M. pneumoniae infection’ is highlighted by the rise in both usage and resistance of macrolides in the past few years.13 This may make it easier to prescribe more specifically tailored macrolides and to compare the efficacy of focused combination therapy. Additionally, 41% of the kids in our investigation were admitted with both asthma and pneumonia, highlighting the necessity for more research on the treatment of pneumonia in this setting. Although the anti-inflammatory characteristics of macrolides may be beneficial in theory, there was no discernible correlation among the usage of macrolides and asthma. Given the prevalence of beta-agonist and steroid therapy, it is possible that the anti-inflammatory actions of macrolides were lessened by these medications.13

Many restrictions need to be taken into account. We identified pneumonia using ICD-9-CM codes, which may result in misclassification; however, we employed a proven approach and restricted our analysis to first-line antibiotic therapy. Due to administrative data limitations, we were unable to take into account things like the results of a chest x-ray or clinical history. Furthermore, results could still be impacted by unmeasured variables even in cases when propensity-score matching analyses were used. Furthermore, if long-term asthma drugs were misused, our definition of asthma may have overstated its prevalence. Future research ought to examine the best practices for treating pneumonia and asthma at the same time.

Finally, even though recommendations indicate ampicillin for community-acquired pneumonia, we focused on ceftriaxone with or without a macrolide because our group had extremely low levels of ampicillin use.

CONCLUSION

In summary, our research's retrospective observation methodology indicates that while ceftriaxone-macrolide combination treatment might not be beneficial for preschoolers, it may be able to reduce length of stay (LOS) in kids in school without having a substantial financial impact. To assess combination therapy effectiveness and establish clinical recommendations while reducing side effects from nonjudicious macrolide usage, additional research and analytical methods are required.

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