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ORIGINAL ARTICLE

Comparative Effectiveness of Ceftriaxone Alone and in Combination with Clarithromycin for Paediatric Patients Hospitalized with Community Acquired Pneumonia

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ABSTRACT

Background: Guidelines for treatment of community acquired pneumonia suggests empirical therapy with combination of clarithromycin and ceftriaxone when infection with mycoplasma pneumoniae is considered. But there is limited evidence available.
Aim: To ascertain effectiveness of ceftriaxone alone verses the combination of ceftriaxone and clarithromycin with respect to cure and length-of-stay and total hospital cost.
Methodology: A randomized control trial with 128 patients of age 2 months to 5 years was conducted at Department of Paediatrics, Shaikh Zayed Hospital Lahore from 1st October 2017 to 30th September 2018. Patients selected according to selection criteria through non probability sampling technique and randomly divided into two groups. Antibiotics given according to study objectives, comparative analysis done, and chi square test applied.
Results: The mean age of patients were 27.02±19.28 months in group A and 29.06±18.29 months in group B. In both groups most of the patients were under the age of 40 months. 72% cured in group A while 86% cured in group B. 80% patients stayed in hospital for 3 days in Group A while, 59% patients in group B. 69% patients had cost effectivity in group A while 84% in group B.
Conclusion: The combination of Ceftriaxone and Clarithromycin was more advisable in treating pnemounia verses the use of ceftriaxone alone.
Keywords: Community acquired pneumonia, Ceftriaxone alone, Ceftriaxone and clarithromycin, Mycoplasma pneumonia

INTRODUCTION

All over the world, pneumonia is amongst top most diseases having highest fatality rate in paediatric patients under 5 years of age[1]. The common bacterial pathogens causing pneumonia in school going population are S. pneumoniae followed by mycoplasma pneumonia[2]. It is estimated that about 156 million children suffer from pneumonia every year with figures of 151 million in developing countries and about 35 million in Africa. Among affected 7-13% suffer life threatening episodes requiring hospitalization.[3] Majority of these 75% are from African countries[4]. In Pakistan, pneumonia affects around 10 million children under 5 years of age each year[5].

Pneumonia is difficult to diagnose as results of blood cultures are not reliable due to low sensitivity, difficulty in collecting sputum from very young children and cumbersome staining methods.[6] Little research has been done to decide the adequacy of antibiotic regimens for pneumonia among paediatric patients admitted in hospital.[7] Ceftriaxone is most widely used first line antibiotic worldwide to treat paediatric patients with pneumonia but seems ineffective against mycoplasma pneumonia, which causing pneumonia in 1/3rd of paediatric patients[8,9]. A systematic review published in 2020, studied six articles and concluded that use of macrolide as monotherapy or adjunct therapy to beta-lactam is more effective in treating community acquired pneumonia[10].

The study rationale is the juxtaposition of the effectiveness of Ceftriaxone alone versus its fusion with Clarithromycin in paediatric patient's children with Community Acquired Pneumonia in local setting. Due to its unique efficacy and safety ceftriaxone is comprehensively used in the treatment of pneumonia. Worldwide it is noted that resistant strain of Pneumococci which is the major bacteria causing pneumonia. So, Clarithromycin may be an adequate option for empiric therapy in treatment of pneumonia in children as it widely treats both bacterial and atypical pathogens causing pneumonia and studies suggest that it can be safely used in children.

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MATERIALS AND METHODS

This randomized control trial with sample size of 128 patients was conducted at Department of Paediatrics, Shaikh Zayed Hospital Lahore. The duration of study was one year from 1st October 2020 to 30th November 2021. Children of both genders, aged between 2 months to 5 years and diagnosed with pneumonia on basis of operational definition, visiting Shaikh Zayed Hospital Lahore were included in the study. Children with concurrent diagnosis of bronchiolitis, complex chronic condition, suppurative lung disease, pleural effusion, already on medications i.e. (Ceftriaxone, Clarithromycin) and less than 2 months of age were excluded from the study. After approval from Institutional Review Board Hospital and Ethical committee (IRB No.1505), written informed consent taken from patients. Study population was divided into two groups. Group allocation of the 1st case to combination of ceftriaxone + clarithromycin group was done by lottery method. Then every consecutive patient was allocated to alternate group. Group A was given ceftriaxone alone and group B was given combination therapy of ceftriaxone and clarithromycin. Data was entered and analyzed using SPSS 23.

RESULTS

The mean age of patients were 27.02±19.28 months in group A and 29.06±18.29 months in group B. In both groups most of the patients were under the age of 40 months. There were 38 (59%) male patients and 26(41%) female patients in Group A.

Table 1: Comparison of cost effectiveness and signs and symptoms of pneumonia

Variable	Group A		Group B	
	Yes	No	Yes	No
Cost effectiveness	46(69%)	20(31%)	54(84%)	10(16%)
Vomiting	31(48%)	33(52%)	15(23%)	49(77%)
Rash	19(30%)	45(70%)	18(28%)	46(72%)
Arthropathy	2(3%)	62(97%)	5(8%)	59(92%)
Headache	29(45%)	35(55%)	9(14%)	55(86%)
Photosensitivity	2(3%)	62(97%)	4(6%)	60(94%)
Crackle sound	60(94%)	4(6%)	62(97%)	2(3%)
Bronchial breath sound	30(47%)	34(53%)	29(45%)	35(55%)

In Group B, 37(58%) patients were male and 27(42%) were female. Thus, the male to female ratio was 1.46:1 in Group A and 1.37:1 in Group B. Comparison of variables among group A and group B is given in Table 1. Cure rate, improvement on which day, age in months and male to female ratio is given in Table 2.

Table 2: Comparison of cure rate, day of improvement, age in months and male to female ratio

Variable	Group A		Group B	
	No.	%	No.	%
Cured	46	72.0	55	86.0
Not cured	18	28.0	9	14.0
Improvement on which day				
2-4	28	44.0	38	59.0
5-7	21	33.0	32	50.0
8-10	4	6.0	5	8.0
Age (months)				
2-20	28	44.0	25	39.0
21-40	22	34.0	20	31.0
41-60	14	22.0	19	30.0
Mean±SD	27.02±19.28		29.06±18.29	
Gender				
Male	38	59.0	37	58.0
Female	26	41.0	27	42.0
M:F ratio	1.46:1		1.37:1	

DISCUSSION

Worldwide, Pneumonia is the leading cause of pediatric deaths that accounts for 15% of all deaths of children under 5 years old (11). In a study reported by Barberan.[12] Around 85% to 90% of antibiotic are being used in the community, with 80% of this usage goes in the treatment of respiratory tract infections. Once child is diagnosed with pneumonia mortality can be avoided with prompt use of antibiotics.[10] Current study proposed that Macrolides particularly Clarithromycin can successfully be used as a part of the treatment of pneumonia in pediatric patients. Clarithromycin is effective against typical as well as atypical pneumonia causing organisms and studies propose it can be utilized as empiric treatment of pneumonia in pediatric population.[13] Combination therapy kills to birds with one stone as beta-lactams, destroy bacterial cell wall and macrolides prevent of protein synthesis. Macrolides have an add on benefit of being anti-inflammatory.[14]

In the present study, Group A 38(59%) patients were males and 26(41%) patients were female with male to female ratio 1.46:1 while in Group B there were 37(58%) male patients and 27(42%) female patients. A similar study by Tamm reported, that mostly the patients were male in both groups which is comparable with our study.[17] In the current study, 47(73%) patients were cured in Group A while 52(81%) patients in Group B. In the study by Tamm, the symptoms resolution was same for patients treated with ceftriaxone and clarithromycin. In >80% of the clinical patients, cough, dyspnea, rales, and sputum production were still observed at EOS in 23.7%, 22.9%, 16.2% and 19%, respectively and 16.8% of the ceftriaxone plus clarithromycin group. In the study reported by Tamm, the clinical success rate was 82.7% for ceftriaxone plus clarithromycin[17]. A study reported by Leyenaar[15] showed that combination of ceftriaxone and clarithromycin was not much efficacious in pre-school kids and that it is pricier, this is consistent with our result. A systematic review conducted in 2020 included six studies and in treating pnemouina in paediatric patients it compared the efficacy of ß-lactam and Macrolides. Result deducted was, use of macrolides alone or add-on therapy to beta-lactams offers better treatment of community-acquired pneumonia[10].

This study was conducted at tertiary care hospital with small sample size with inclusion criteria of age less than 5 years and diagnosis of pneumonia. Our study showed results that were consistent with many studies done internationally but some limitation included small sample size, limited resources, left against medical advice by some patients and difficulty in diagnosing organisms causing pneumonia due to lack of sensitive diagnostic tests. It should have been conducted at large scale in multiple tertiary care hospitals of Lahore to have more accurate results.

CONCLUSION

The combination therapy is very effective in curing community acquired pneumonia and decreasing hospital stay particularly in school going children infected with mycoplasma pneumonia but was not very cost effective. This can be further improved by formulating a better system to diagnose this disease and effective vaccination.

Conflict of interest: Nil

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