COMPARISON BETWEEN EFFICACY OF CLARITHROMYCIN VERSUS CEFTRIAXONE IN THE TREATMENT OF COMMUNITY ACQUIRED PNEUMONIA IN CHILDREN

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ABSTRACT

Objective: To compare the clinical effectiveness of clarithromycin and ceftriaxone in the treatment of community acquired pneumonia in pediatric patients.

Methods: This Quasi experimental study was carried out in the Pediatric department of Khyber Teaching Hospital, Peshawar. Duration of the study was 6 months for which a sample size of 140 patients was calculated by WHO software. Patients of both genders and age between 5 to 12 years, meeting the inclusion criteria were enrolled in the study. All the subjects were randomly allocated into two groups (70 in each) where Group A was treated with ceftriaxone while Group B with clarithromycin. Efficacy of the study drugs was determined on the basis of clinical cure i.e. disease resolution after 48 hours of antibiotic therapy, afebrile state without taking antipyretics, respiratory rate <25/min and/or O_2 saturation >96%.

Results: Efficacy in terms of improvement in fever, respiratory rate and O_2 saturation was analyzed and clarithromycin was found to be effective in 90% subjects whereas ceftriaxone in 84% subjects.

Conclusion: Both study drugs are effective in the treatment of community acquired pneumonia in children but clarithromycin showed slightly better results than ceftriaxone.

Key words: Efficacy, Ceftriaxone, Clarithromycin, Community acquired pneumonia

INTRODUCTION

Community acquired pneumonia (CAP) is one of the most common, wide spread and critical respiratory tract infections. It is defined as the presence of clinical features of pneumonia in a previously healthy individual due to an acute infection of duration not more than 14 days, acquired outside the hospital in the community.[1] It usually involves lower respiratory tract and causes cough, tachypnea, and difficulty in breathing or lower chest wall in drawing. There are approximately 120 million cases of pneumonia annually, causing as many as 1.3 million deaths.[2] In 2011, 1.2 million children younger than 5 years lost their lives due to pneumonia.

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According to WHO, every year around 20% of deaths in children occur due to pneumonia of which the majority is observed in the developing countries due to lack of access to health care facilities and interventions.[3][4]

Numerous studies have been performed to evaluate its etiology and treatment.[5-8] While managing a child hospitalized with CAP, a holistic approach like clinical, laboratory and radiographic findings need to be considered. As it is difficult to differentiate bacterial pneumonia from viral pneumonia and because of the frequent presentation of mixed bacterial-viral infections (30-40%), all patients require antibiotics. Ceftriaxone and clarithromycin are two of the most commonly prescribed drugs for the treatment of CAP in children.[9] Several studies have reported these drugs as effective therapeutic agents with variable efficacy. According to Bhavnani SM et al, the clinical efficacy of ceftriaxone is 79.1% in children with CAP.[10] In a comparative study by Lee PI et al, children who received clarithromycin for the treatment of CAP showed efficacy of 94% with superior tolerability.[11] As it is evident that pneumonia is one of the major causes of morbidity and mortality in children in developing countries, so early diagnosis and appropriate treatment can reduce both, which has been the rationale of this study. To the best of our knowledge, no local clinical data is available regarding efficacy of ceftriaxone and clarithromycin in the treatment of community

acquired pneumonia. So, current study was an attempt to evaluate and compare their effectiveness in our local population of children.

MATERIALS AND METHODS

A Quasi experimental study was conducted at the Pediatric department of Khyber Teaching Hospital, Peshawar from Aug 2015 to Jan 2016. A sample size of 140 patients was determined by WHO calculator using 78.2% efficacy of ceftriaxone, 94.9% efficacy of clarithromycin, 95% confidence interval and 90% power of test (Two sided).[12] Patients of both genders and age between 5-12 years, meeting the inclusion criteria i.e. no hospital admission during last one week, fever of >100°F, presence of respiratory signs and symptoms like cough, tachypnea >30/min and/or O_2 saturation <96% with radiological evidence of pneumonia were enrolled in the study. Patients with recurrent cough/wheeze, congenital heart disease, immuno-compromised or malnourished were excluded. The study was conducted after taking ethical approval from the committee and informed consent from parents/guardian of the patients. The recruited subjects were randomly allocated into two groups (70 in each) where Group A was treated with ceftriaxone (50mg/kg/day) while Group B with clarithromycin (15mg/kg/day). All medications were administered in the hospital by trained nursing staff.

Efficacy of the study drugs was determined based on clinical cure i.e. disease resolution after 48 hours of antibiotic therapy, afebrile state without antipyretics, respiratory rate <25/min and/or oxygen saturation >96%.

Data was recorded in the pre-designed proforma and analyzed in SPSS version 20. Frequencies and percentages were calculated for categorical variables like gender and efficacy. Mean ± SD was calculated for continuous variables like age. Efficacy was stratified among different groups like age and gender to see the effect modifications. Post stratification Chi square test was applied among different groups. P value less than 0.05 was considered significant.

RESULTS

The study was conducted at the Pediatric department where 140 children were observed to compare the efficacy of ceftriaxone and clarithromycin in community acquired pneumonia and the results were analyzed. The distribution of age and gender is demonstrated in **Figure 1,** where in ceftriaxone treated group, 31 (44%) children were in age range of 5-7 years, 24 (34%) in 8-10 years and 15 (22%) in 11-12 years with mean age 8 ± 1.76 years. In clarithromycin treated group, 32 (45%) children were in age range of 5-7 years, 25 (36%) in 8-10 years and 13 (19%) in 11-12 years with mean age 7 ± 1.51 years. There were 44 (63%) male and 26 (37%) female children in ceftriaxone treated group, while 45 (65%) male and 25 (35%) female children in clarithromycin treated group.
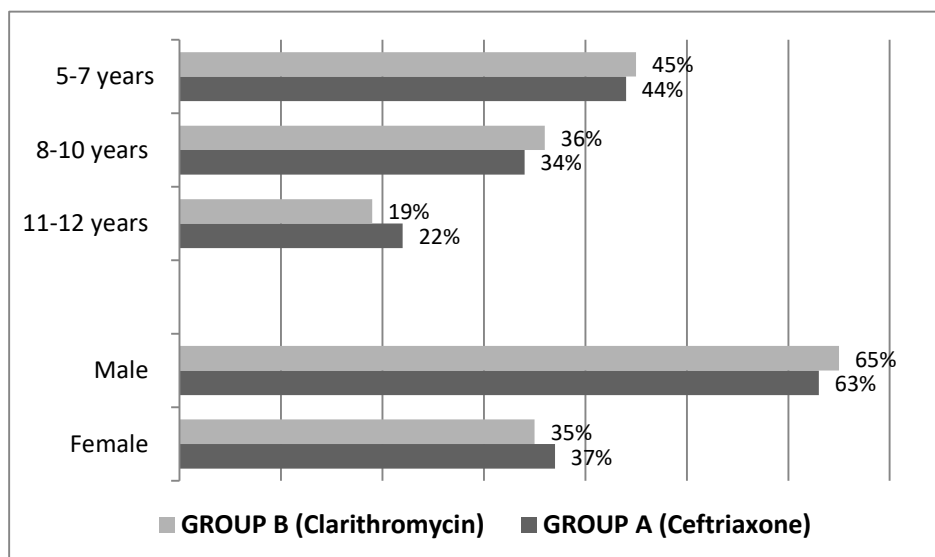

Figure 1: Distribution of age and gender b/w treatment groups

As shown in **Figure 2,** 59 (84%) children in ceftriaxone treated group and 63 (90%) children in clarithromycin treated group become afebrile. 51 (73%) children had

respiratory rate less than 25/min in ceftriaxone treated group and 53 (76%) in clarithromycin treated group. Moreover, 49 (70%) children had O_2 saturation >96% in ceftriaxone treated group and 50 (72%) in clarithromycin treated group. Hence, no significant difference was observed in the post treatment status of fever, respiratory rate and oxygen saturation between two groups with p value 0.313, 0.699 and 0.853, respectively.
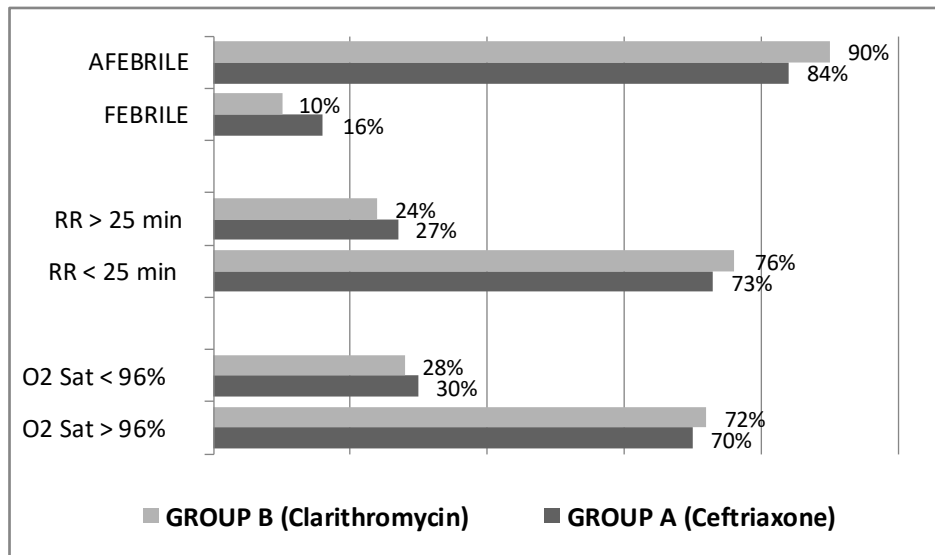

Figure 2: Post treatment status of fever, respiratory rate & O_2 saturation

Comparison between efficacy of study drugs is given in **Figure 3**, displaying the clarithromycin slightly more effective than ceftriaxone i.e. 90% versus 84%, but statistically the difference was not significant with p value 0.313.
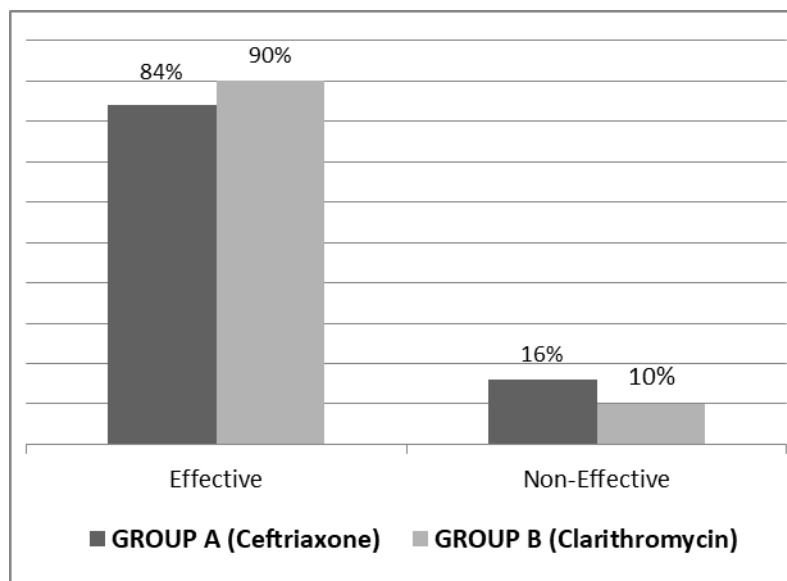

Figure 3: Comparative efficacy of drugs

In **Table 1,** the response of study drugs was also analyzed at different age groups and genders but no significant difference (p value >0.05) was observed upon stratification.

Table 1: Stratification of drug efficacy with age and gender distribution

AGE		GROUP A (Ceftriaxone)	GROUP B (Clarithromycin)	P value
5-7 years	Effective	26	29	0.421
	Not Effective	5	3	
Total		31	32	

		GROUP A (Ceftriaxone)	GROUP B (Clarithromycin)	P value
8-10 years	Effective	20	23	0.355
	Not Effective	4	2	
	Total	24	25	
11-12 years	Effective	13	11	0.877
	Not Effective	2	2	
	Total	15	13	
GENDER		**GROUP A (Ceftriaxone)**	**GROUP B (Clarithromycin)**	**P value**
Male	Effective	38	41	0.478
	Not Effective	6	4	
	Total	44	45	
Female	Effective	21	22	0.478
	Not Effective	5	3	
	Total	26	25	

DISCUSSION

Since many years, different guidelines for the treatment of community acquired pneumonia have been developed.[13, 14] Despite of this high pace advancement in the field of medicine and therapeutic strategies, considerable cases of pneumonia have been associated with high mortality rate, especially in developing countries like Pakistan. Very limited studies have been conducted to evaluate the treatment protocols including the use of recommended antibiotics and practice of empirical antimicrobial therapy for community acquired pneumonia, especially in children.[15-17]

This study was conducted on 140 pediatric patients to compare two most commonly prescribed antibiotics in the treatment of CAP. Clinical efficacy in terms of cure in fever, respiratory rate and oxygen saturation was analyzed and found clarithromycin effective in 90% children whereas ceftriaxone in 84% children, indicating both agents useful and comparable in the therapeutic armamentarium. But risk of development of super infections like clostridium difficile associated diarrhoea (CDAD) and MRSA remain a challenge with cephalosporins. So, it is prudent not to encourage its use and would be counter intuitive to recommend even as second-line therapy. Many hospitals in the UK have moved away from cephalosporins for the treatment of CAP in an attempt to reduce these unwanted consequences. Moreover, there is no high quality evidence that cephalosporins are more clinically or cost-effective in respiratory infections as compared to clarithromycin and other macrolides. Rather, there is emerging evidence that narrow-spectrum prescribing is as effective as broad-spectrum prescribing.

For severe pneumonia, many studies and guidelines recommend combination therapy. In an Australian prospective study on CAP treatment, the authors call a combination of macrolide with beta lactam antibiotic like ceftriaxone to be the first-line treatment for severe disease.[18] The BTS guidelines recommend combination of clarithromycin plus co-amoxiclav as first-line therapy and a combination of clarithromycin plus cephalosporin as alternative regimen for treating severe CAP.[19] Findings supporting our results were observed in some studies done in the past where ceftriaxone efficacy in terms of clinical cure rate in clinically evaluable population and modified intent to treat population was 78.2% and 77.2%, respectively.[20] Similarly, English ML et al conducted a trial where the respective clinical cure rate of clarithromycin in intent to treat population and per protocol clinical population was 81.8% and 93.8% in focus 1 while 88.5% and 95.9% in focus 2.[12]

This local statistics about comparative efficacy of common antibiotics would enable the healthcare professionals to select best possible antimicrobial agent for quick recovery of children hospitalized with CAP. Moreover, these results could be projected to various health care institutions to improve current treatment protocols and decrease morbidity and mortality rate in the region.

CONCLUSION

It is concluded that both study drugs are effective in the treatment of community acquired pneumonia in children but clarithromycin showed relatively more promising results than ceftriaxone.

AUTHORS CONTRIBUTION

The study was planned and designed by Waqar hayat. Arshad khan and Iqbal hussain executed the study and collected all relevant clinical data. Muhammad saleh faisal has written the manuscript while Arif jamal and

Waheed iqbal helped in statistical analysis, bibliography and critical review.

CONFLICT OF INTEREST
Authors declare no conflict of interest

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