

Comparative efficacy of levofloxacin and ceftriaxone in the treatment of community acquired pneumonia in children

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ABSTRACT

Pneumonia is a common cause of mortality and morbidity in under-5 children throughout the world. Globally an estimated 156 million new episodes of pneumonia occur each year in children and 2 million children die from pneumonia each year which is 20 percent of all deaths of children under five years old. Ceftriaxone is a commonly used drug for empiric treatment of community acquired pneumonia (CAP) in children. Levofloxacin may be an adequate option for empiric therapy in treatment of CAP in children because it gives the broad spectrum activity against both bacterial and atypical pathogens causing CAP and studies suggest that it can be safely used in children. This open labeled, randomized, comparative clinical trial was carried out in the Department of Pediatrics, Sylhet MAG Osmani Medical College Hospital, Bangladesh during January, 2011 & December, 2012 to compare the efficacy of levofloxacin and ceftriaxone in the treatment CAP in children. A total 70 cases of CAP were enrolled. 35 cases were allocated to levofloxacin group and another 35 cases to ceftriaxone group. At first the study cases were selected by systematic random sampling. Group allocation to either levofloxacin or ceftriaxone group was done by lottery method. Total duration for receiving study drugs was seven days. Dose of levofloxacin was 10 mg/kg/day children ≥ 5 years, where as it was 10 mg/kg 12 hourly in 6 months to < 5 years age groups. Dose of ceftriaxone was 75 mg/kg/day. Response to treatment was assessed initially after 3 days and also after 7 days by clinical symptoms and signs. Clinical cure rate was determined by disappearance of the clinical signs and symptoms of pneumonia and resolution of radiological findings reported at admission. Clinical responses were categorized as cured and treatment failure. 91.43% cases were cured in levofloxacin

group, whereas cure rate of ceftriaxone group was 68.57% which was statistically significant ($p = 0.0168$). Adverse effects of levofloxacin were found as skin rash in 1 case and vomiting in 2 cases whereas skin rash was found in 1 case in ceftriaxone group. So it can be concluded that levofloxacin is more effective than ceftriaxone in the treatment of CAP in children.

Keywords: Community Acquired Pneumonia; Ceftriaxone; Levofloxacin

1. INTRODUCTION

Pneumonia may be defined as an inflammation of the parenchyma of the lungs [1]. Of the different types, community acquired pneumonia (CAP) is the most common and important from public health point of view. Pneumonia is a substantial cause of morbidity and mortality in children throughout the world, particularly among children < 5 years of age with an estimated 156 million new episodes occur each year and most of these occur in India (43 million), China (21 million), Pakistan (10 million) and Bangladesh, Indonesia and Nigeria (6 million each) [2]. About 2 million children worldwide die from pneumonia each year which is 20 percent of all deaths of children under five years old. These occur mainly (about 75%) in the African and South-East Asian regions [3]. Bangladesh has the fifth-highest rate of pneumonia in the world, with an estimated 6 million cases and 50,000 deaths annually among children under five [3]. The incidence of pneumonia among children age < 5 years who live in the rural area is 0.23 episodes per child-year and urban areas is 0.56 episodes per child-year in Bangladesh [4]. Antibiotics are the mainstay in the treatment of CAP. Empirically used common antibiotics for CAP in children are cotrimoxazole, penicillins, macrolides, aminoglycosides and cephalosporins. Some recent study suggested that fluoroquinolones specially levofloxacin can

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be effectively used in the treatment of CAP in children [5-7].

Due to its unique efficacy and safety ceftriaxone is widely used in the treatment of CAP worldwide. But resistant strain of *Pneumococci* (6%) which is the most common organism causing CAP is noted worldwide [8]. Levofloxacin may be an adequate option for empiric therapy in treatment of CAP in children because it gives the broad spectrum activity against both bacterial and atypical pathogens causing CAP and studies suggest that it can be safely used in children [9]. This study was designed to compare the efficacy of levofloxacin and ceftriaxone in the treatment of CAP in children.

2. PATIENTS AND METHODS

2.1. Selection of Patients

This open labeled randomized comparative clinical trial was conducted in the Department of Pediatrics, Sylhet MAG Osmani Medical College Hospital, Bangladesh from January 2011 to December 2012. Children aged 1 - 12 years were included in the study. CAP was diagnosed by the following criteria: 1) Signs and symptoms of pneumonia including at least 2 of the following: (a) fever (axillary or oral temperature $> 100.4^{\circ}\text{F}$); (b) cough for less than 21 days; (c) chest pain; (d) shortness of breath; (e) physical findings of consolidation and (f) white blood cell count $>15000/\text{ul}$ or $<5000/\text{ul}$; 2) Chest x-ray showing evidence of lung infection (pulmonary opacity, pneumatocele). Hospital acquired pneumonia; suppurative lung disease and pleural effusion were excluded from the study. Children with CAP receiving ceftriaxone and levofloxacin before enrollment were also excluded from the study. After diagnosis as CAP children were enrolled in the study by systematic random sampling. Every 2nd case satisfying the inclusion and exclusion criteria were enrolled in the study. A total of 70 cases of CAP were enrolled. 35 cases were allocated to each group. Group allocation of the 1st case to levofloxacin group was done by lottery method. Then every consecutive patient was allocated to alternate group.

2.2. Intervention

Total 35 children received levofloxacin and another 35 received ceftriaxone. Dose of levofloxacin was 10 mg/kg/day children ≥ 5 years, where as it was 10 mg/kg 12 hourly in <5 years age groups [10,11]. Dose of ceftriaxone was 75 mg/kg/day [11]. All the enrolled patients received supportive care for CAP such as oxygen inhalation, maintenance of temperature, oropharyngeal suction and nutrition. Total duration for receiving study drugs were seven days. Regular follow up was given during study period. Response to treatment was assessed initially after 3 days and also after 7 days by clinical symp-

toms and signs (fever, cough, shortness of breath, chest pain, rales on auscultation, dullness to percussion, egophony). Additional chest x-ray was done during assessment at 7th days. Clinical responses were categorized as cured and treatment failure.

If no response occurred after 3 days the respective antibiotic was stopped and another antibiotic suitable for CAP outside the study were started and that case was labeled as treatment failure.

Clinical cure was determined by disappearance of the clinical signs and symptoms of pneumonia and resolution of radiological findings reported at admission. If there was no resolution of clinical signs and symptoms and radiological findings the case was labeled as treatment failure (**Figure 1**).

2.3. Data Collection and Statistical Analysis

Data were collected by a preformed and pretested structured questionnaire. Analysis of age variation was done by unpaired *t* test. Analysis of sex difference and comparison of cure rate between two groups was done by χ^2 test. A p-value of <0.05 were considered as significant. Data were analyzed by using SPSS version 17.

2.4. Ethical Consideration

Informed written consent was taken from parents or legal guardian. Beforehand ethical permission was taken from the ethical committee of Sylhet MAG Osmani Medical College, Sylhet, Bangladesh.

3. RESULT

A total 35 cases were allocated to levofloxacin group and another 35 in ceftriaxone group. The mean age of the patients in both groups was almost identical ($40.7143 \pm$

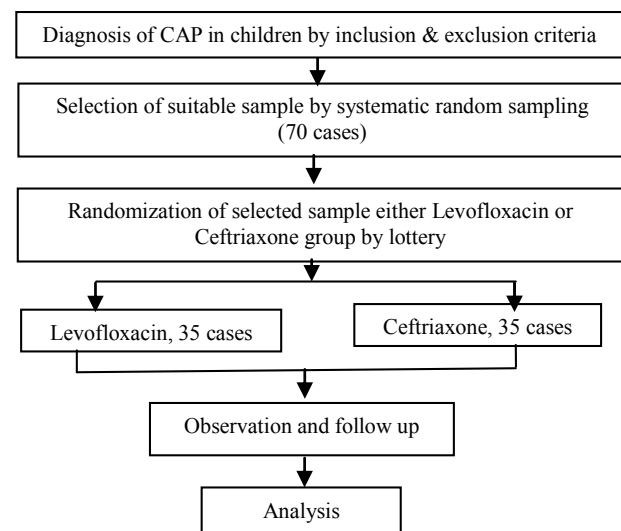


Figure 1. Flow chart of randomization & intervention.

32.73474 months vs. 36.00 ± 33.6181 months, $p = 0.669$). The sex of the patients in levofloxacin group and ceftriaxone group did not show any statistically significant difference ($p = 0.6913$) (Shown in **Table 1**).

Out of 35 patients 32 (91.43%) were cured with levofloxacin, 3 patients (8.57%) were not cured. In the ceftriaxone group 24 (68.57%) children were cured and 11 patients (31.43%) were not cured. This difference was statistically significant ($p = 0.0168$) (Shown in **Table 2**).

Both levofloxacin and ceftriaxone showed no major adverse effects. Adverse effects of levofloxacin were found as skin rash in 2 (5.7%) cases and vomiting in 1 (2.85%) case. Skin rashes were transient in nature. No arthropathy was observed in this group. In ceftriaxone group skin rash was found in 1 (2.85%) case. Adverse effects of levofloxacin and ceftriaxone are shown in **Table 3**.

4. DISCUSSION

Pneumonia is a one of the most common cause of childhood morbidity mortality. Effective and resource compatible antimicrobial management is one of the fundamental aspects of the treatment of CAP.

In the present study age and sex characteristics of levofloxacin and ceftriaxone groups were almost identical (40.7143 ± 32.73474 months versus 36.00 ± 33.6181 months, $p = 0.669$ and in case of sex, $p = 0.203$).

The present study revealed that cure rate of levoflox-

acin group was 91.43%, whereas cure rate of ceftriaxone group was 68.57% ($p = 0.03647$). Bradley *et al.* [5] in their comparative study of levofloxacin in the treatment of children with community-acquired pneumonia showed that cure rate of levofloxacin was 94.3% whereas cure rate of comparator group (0.5 to <5 years: amoxicillin/clavulanate or ceftriaxone; > or =5 years: clarithromycin or ceftriaxone with clarithromycin or erythromycin lactobionate) was 94%. File *et al.* [12] in their comparative study of intravenous and/or oral levofloxacin (500 mg once daily) or the comparative agents, parenteral ceftriaxone (1 to 2 g once to twice daily) and/or oral cefuroxime axetil (500 mg twice daily) in treatment of adults with community-acquired pneumonia showed that clinical success rate of levofloxacin (96%) is superior to ceftriaxone and/or cefuroxime axetil (90%) in the management of adult with CAP. Cure rate of levofloxacin in these mentioned studies support the present study. But cure rate of ceftriaxone is much less in the present study. Less cure rate of ceftriaxone in present study may be due to its resistance as a result of indiscriminate use of ceftriaxone at the community level of Bangladesh.

Adverse effect of levofloxacin was found as skin rash in 2 (5.7%) cases and vomiting was found in 1 (2.85%) case. Skin rashes were transient in nature. In ceftriaxone group skin rash was found in 1 case (2.85%). There was no need to discontinue treatment in both groups. In the comparative study of Bradley *et al.* [5], adverse events leading to treatment discontinuation occurred in 2% levofloxacin-treated and 1% comparator-treated children. No single type of treatment-limiting adverse event occurred in more than 1% of children. In the levofloxacin group, the most frequent category of adverse events that were treatment-limiting involved the gastrointestinal system (1%). Levofloxacin was as well tolerated as standard of care antibiotics for the treatment of CAP. Congress report from the 41st inter-science conference on antimicrobial agents and chemotherapy Chicago, IL, USA, states levofloxacin has no serious adverse reaction in children [13].

As the diagnosis of CAP was not confirmed by bacteriological study, microbial cure rate was not determined in the present study.

5. CONCLUSION

Levofloxacin was more effective than ceftriaxone in the treatment of CAP in children. Large scale study may further strengthen its use in the treatment of CAP in children.

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Table 1. Age and sex characteristics of CAP patients.

Demographic character	Levofloxacin group (n = 35)	Ceftriaxone group (n = 35)	p-value
Age in months (Mean \pm SD)	40.7143 \pm 32.73474	36.00 \pm 33.61810	0.669
Sex			
Male	21(60%)	26 (74.28%)	0.6913
Female	14 (40%)	09 (25.71%)	

Table 2. Comparison of levofloxacin and ceftriaxone in the treatment of CAP.

Parameter	Levofloxacin group (n = 35)	Ceftriaxone group (n = 35)	p-value
Cured	32 (91.40%)	24 (68.57)	0.0168
Not cured	03 (8.57%)	11 (31.43%)	

Table 3. Adverse effects of levofloxacin and ceftriaxone.

Adverse effects	Levofloxacin	Ceftriaxone
Vomiting	1 (2.85%)	0
Rash	2 (5.7%)	1 (2.85%)
Arthropathy	0	0
Headache	0	0
Photosensitivity	0	0

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