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ORGINAL ARTICLE

Comparison of The Efficacy and Safety of Penicillins and Cephalosporins In Treatment of Pediatric Patients With Lower Respiratory Tract Infections

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ABSTRACT

The most common Lower respiratory tract infections (LRTI) such as bronchopneumonia, acute bronchiolitis, acute bronchitis. These infections are caused by numerous pathogens, among them virus as well as bacteria are more common. During the period of disease child and the parents also suffer with mental agony in addition to economic loss to the family. This study was conducted to assess and compare the efficacy and safety of penicillins and cephalosporins in treatment of pediatric patients with lower respiratory tract infections (LRTI).This prospective data collection study was conducted in the Department of Pediatrics, Narayana Medical College & Hospital, Nellore. The study was conducted after obtaining permission from Institutional Ethical Committee (IEC) for a period of six months. Fifty hospitalized patients with lower respiratory tract infections were enrolled into the study. Twenty five patients were treated with penicillins and remaining twenty five received cephalosporins. We analyzed the efficacy and safety based on the available data in medical case sheets of patients and also by collecting information from patients or parent of the patients.The mean time for disappearance of cough in the cephalosporin group was significantly lower than penicillin group (p=0.0001). However the time to disappearance of fever and breathlessness was not significantly different between the two groups (p=0.09, p=0.17). The mean time to improvement in all the clinical signs such as wheeze, crepitations and abnormal respiratory rate were in the cephalosporin group was significantly lower than penicillin group (p=0.001,p=0.01,p=0.02). Based on the present study, the clinical cure was observed in all the patients without any residual sequel and no adverse effects were reported. Hence, by our study it can be concluded that both groups of antibiotics were effective and safe.

KEY WORDS : Penicillins, Cephalosporins, Lower Respiratory Tract Infections

Introduction

Lower respiratory tract infections (LRTI) are one of the commonest illness of childhood and infants, which contributes to the morbidity of the child. According to WHO estimates, respiratory infections caused about 987,000 deaths in India, of which 969,000 were due to acute LRTI in 2004. The burden of disease in terms of DALYs (disability-adjusted life years) lost was 25.5 million, of these 24.8 million were due to acute LRTI [1].

Lower respiratory tract infections are caused by numerous pathogens, among them viruses as well as bacteria are more common, (there may be super infection is due to decrease in the immunity of the child). The most common presentations are bronchopneumonia, acute bronchiolitis, and acute bronchitis.

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The presentation of these conditions will depends on age, infecting organism and site of infection. The commonest symptoms at presentation include high fever, cough, and breathlessness [2].

Lower respiratory tract infections place a considerable strain on the health budget and are generally more serious than upper respiratory tract infections. During the period of disease apart from the child, even the parents also suffer mental agony in addition to economic loss to the family. Despite major advances in the prevention and treatment of LRTI in recent years, hospitalization and deaths are increasing every year, thereby causing an increasing economic burden world wide, annually.

Identifying the pathogens in LRTI as well as changing patterns of organism susceptibility to antibiotic continues to make definitive treatment a challenge for physicians. However, LRTI in the community has been extensively studied and guidelines exist that facilitate the prescriber in their choice of antibiotic particularly if an empirical approach is required. Knowledge of prevalent organisms and their current sensitivity is of great help in choosing the antibiotics.

In the department of pediatrics, Narayana Tertiary Care Hospital, Chinthareddy Palem, Nellore, the common ailments seen was of respiratory tract infections of which LRTI are very common, among the LRTI, bronchopneumonia and acute bronchiolitis were common infections. In almost all the cases penicillins and cephalosporins were used as antibiotics to treat these infections. Hence the study was undertaken to compare the efficacy and safety of penicillins and cephalosporins in treatment of pediatric patients with lower respiratory tract infections .

Aims and Objectives

To evaluate the efficacy of antibiotics by analyzing the data collected on time to symptom resolution, time to improvement in clinical sign and time to normalization of lab parameter.

To evaluate the safety by analyzing the available data in case sheets of patients and by collecting information from patients.

Materials and Methods

This prospective data collection study was conducted in the Department of Pediatrics, Narayana Medical College, Chinthareddypalem, Nellore. Fifty hospitalized patients with lower respiratory tract infections were enrolled into the study. Consent was obtained from parent or guardian of all the patients. The study was conducted for the period of 6 months. This study was approved by the Institutional Ethical Committee.

Inclusion criteria:

1) Age less than 12 years
2) Patients with cough, fever, breathlessness.
3) Evidence based diagnosis of lower respiratory tract infections.

Exclusion criteria:

1) Known allergy to the study antibiotics
2) Immuno compromised patients
3) Moderate to severe liver diseases,
4) CNS, CVS diseases
5) Acute and chronic renal failure

Twenty five patients treated with penicillins and twenty five patients treated with cephalosporins were taken as cases for the study. The decision to treat either with penicillin or cephalosporin was at the discretion of the treating physician.

Demographic features such as age, sex, weight, previous medical history and diagnosis was

recorded. Additionally, details pertaining to medications including drug, dosage regimen, route of administration, duration of antibiotic usage, course of disease progression and duration of hospitalization were also recorded. The drugs were given to the pediatric patients as per mg/kg body weight needed to attain a therapeutic dose.

The symptoms such as cough, fever, breathlessness and the signs like wheeze, crepitations were noted from admission to discharge. At the same time X- ray was taken and ESR was also measured. To evaluate the efficacy of antibiotics, we analyzed the data collected viz on Time to symptom resolution, time to improvement in clinical signs and time to normalization of lab parameters.

To evaluate the safety of the antibiotics we analyzed the available data in medical case sheets of patients and also by collecting information from patients or mother of the patients.

Statistical Analysis

The data were collected from the case record forms. The collected data was then entered into Microsoft office excel. After the data entry, data surfing, data cleaning and data analysis was performed by using the statistical software Graphpad Prism-4 USA. The analyzed data was presented as mean, standard deviation (SD), median, range and percentages. The time to event data such as time to symptom resolution, time to improvement in clinical signs and time to normalization of lab parameters was normally distributed. This data between penicillins like ampiclox, amoxiclav and Cephalosporins like ceftriaxone, cefotaxime was analyzed by using unpaired 't' test to find any difference between the two means. The two tailed probability value of ($P < 0.05$) was considered statistically significant.

Results

In this prospective study a total number of fifty hospitalized pediatric patients with lower respiratory tract infections with the age group 23.4 ± 34.6 months were evaluated. There were 29 male children and 21 were female, 31 suffered from bronchopneumonia and 19 had acute bronchiolits, 12 patients were given Ampiclox, 13 Amoxiclav, 14 Ceftriaxone and 11 Cefotoxime. The decision to treat either with pencillins (ampiclox and amoxiclav) or cephalosporin (ceftriaxone and cefotoxime) was at the discretion of the treating physician. The mean duration of antibiotic usage was 8.1±1.9 days, the mean duration of hospital stay was 7.9±2.8 days. (Table 1).

When we investigated the availability and consistency of data in the case sheets of the patients, we found that documentation concerning symptoms such as cough was in 94% of case sheets, fever 96%, and breathlessness 96%. The availability of clinical signs data as wheeze in 70%, crepitations on 86%, abnormal respiratory rate in 100% and increased ESR in 80%. However only 42% of case sheets had data of abnormal findings X-ray (Table 2). None of the case sheets had data regarding adverse effects. All the patients recovered (50 out of 50) satisfactory.

When we evaluated the presentation and course of disease, the most common symptoms observed were fever, cough and breathlessness. The mean duration for disappearance of symptoms was cough 6.7 ±2.4, Fever 3.9 ±1.6 days, breathlessness 5.4±2.1 days. The mean duration of the improvement of the clinical signs were wheeze 6.1±3.1 days, crepitations 4.9±1.8, days and respiratory rate 5.4±2.1 days. The time taken for normalization of lab parameters such as X- ray was 9.1±2.8 days, and ESR 6.0±1.2 days (Table 2).

Age in Months	23.4±34.6
Body weight (Kg)	7.8±4.8
Male	29
Female	21
Bronchopneumonia	31
Acute bronchiolitis	19
Type of Antibiotic	Ampiclox-12, Amoxiclov-13 Ceftriaxone-14, Cefotaxime-11
Duration of Antibiotic Usage (Days)	8.1±1.9
Change in antibiotic	1(Amoxiclav to Ceftriaxone)
Recovery	50
Adverse Events	0
Length of hospital stay (Days)	7.9±2.8

Table-1 Demographic Characters of all hospitalized patients (n=50)

Time to Event (Days)	Data consistency	Median & Range	Mean ± SD
Disappearance of Symptom			
Cough	47 (94%)	7 (2-13)	6.7±2.4
Fever	48 (96%)	3 (1-10)	3.9±1.6
Breathlessness	48 (96%)	5 (2-11)	5.4±2.1
Improvement in Clinical Sign			
Wheeze	35 (70%)	5 (2-14)	6.1±3.1
Crepititions	43 (86%)	5 (2-10)	4.9±1.8
Respiratory Rate	50 (100%)	5 (2-12)	5.4±2.1
Normalization of Lab Parameters			
X ray	21 (42%)	8 (6-14)	9.1±2.8
ESR	40 (80%)	6 (3-10)	6.0±1.2

Table-2 Descriptive statistics of Time to event data of all hospitalized patients (n=50)

Demographic Characters	Penicillin	Cephal osporin	p Value
Age in Months	23.4±34.6	21±30	0.7
Body weight (Kg)	7.8±4.8	6.9±3.4	0.4
Gender (Male/female)	16/9	13/12	0.5
Clinical Diagnosis Bronchopneumonia / Acute bronchiolitis	14 /11	17/8	0.5
Type of Antibiotic	Ampiclox-12 Amoxiclov -13	Ceftria xone-14 Cefoto xime-11	--
Duration of Antibiotic Usage (Days)	8.1±1.9	6.8±2.5	0.06
Length of Hospital stay (Days)	8.6±2.7	7.0±2.5	0.03

Table-3 Demographic Characters of hospitalized patients receiving antibiotics

Time to Event	Penicillin (n=25)			Cephalosporin (n=25)			Signi ficance
Days	Data	Median & Range	Mean ± SD	Data	Median & Range	Mean ± SD	p Value
Disappearance in Patient Symptoms							
Cough	24 (96%)	7.5 (5-13)	7.8 ± 2.2	23 (92%)	6 (2-10)	5.3 ± 1.9	0.0001
Fever	25 100%	4.0 (2-10)	4.2 ± 1.7	23 (92%)	3 (1-6)	3.4 ± 1.5	0.09
Breathlessness	25 100%	6.0 (2-10)	5.84 ± 2.1	23 (92%)	5 (3-11)	5.0 ± 1.9	0.17
Improvement in Clinical signs							
Wheeze	20 (80%)	6.5 (3-14)	7.4 ± 3.3	15 (60%)	4 (2-7)	4.2 ± 1.3	0.001
Crepitations	19 (16%)	5.0 (3-10)	5.5 ± 1.9	24 (96%)	4 (2-9)	4.4 ± 1.6	0.01
Respiratory Rate	25 100%	6.0 (2-10)	6.1 ± 1.9	25 (100%)	4 (2-12)	4.7 ± 2.0	0.02
Normalization of Lab Parameters							
X ray	13 52%	10.0 (6-14)	9.8 ± 2.7	8 (32%)	7 (7-14)	7.8 ± 2.4	0.1
ESR	18 72%	7.0 (4-8)	6.2 ± 1.1	22 (88%)	6 (3-10)	5.7 ± 1.3	0.2

Table-4 Comparison of time to event data among the patients receiving antibiotics

Discussion

Respiratory syncytial virus (RSV) is the primary cause of hospitalization for acute respiratory tract illness in general and specifically for bronchiolitis in young children, and it may be responsible for 40–90% of cases of bronchiolitis, for 5–40% of cases of pneumonia [3]. Numerous studies have shown that the occurrence of a secondary or concurrent bacterial infection in hospitalized children with RSV lower respiratory tract disease (LRTD) is <1% [4]. Despite this, nearly half of all hospitalized infants with RSV LRTI were treated with antibiotics [5]. However, In our study all the patients suffering with acute bronchiolitis were prescribed antibiotics.

In the present study, we observed that all the cases of hospitalized patients with lower respiratory tract infections received antibiotics. The commonly prescribed antibiotics in children were, either penicillins like ampiclox, amoxiclav, or cephalosporins like ceftriaxone and cefotaxime regardless of diagnosis. One of the opinions of physicians was an immediate antibiotic usage strategy would most likely provide the best clinical outcomes in patients with lower respiratory tract infections than delayed antibiotic use. Delaying antibiotics may reduce antibiotic use for acute infections. However, the delay also reduced patent satisfaction compared to immediate antibiotic use. The early use of antibiotics may fasten recovery and decrease the complications of disease.

A planned subgroup analysis was performed between pediatric patients receiving penicillins (ampiclox, amoxiclav) and cephalosporins (ceftriaxone, cefotaxime). The mean duration of antibiotics used in the Penicillin group was 8.1 ±1.9 days, whereas it was 6.8 ±2.5 days in cephalosporin group. The observed difference in the duration of antibiotics use in the penicillin group was statistically significant different from the cephalosporin group. The mean time for disappearance of symptoms such as cough, fever, breathlessness in penicillin group was 7.8±2.2, 4.2±1.7, 5.8 ±2.1 days respectively; whereas in cephalosporin group it was 5.3±1.9, 3.9±1.5, and 5.0±1.9 days respectively. The mean time for disappearance of cough in the cephalosporin group was lower than in penicillin group. This observed difference was statistically significant (Table 4). However the time for disappearance of fever and breathlessness was not significantly different between the two groups. The mean time for improvement of clinical signs such as wheeze, crepitations and respiratory rate in penicillin group was 7.4±3.3, 5.5±1.9 and 6.1±1.9 days respectively, where as it was 4.2±1.3, 4.4±1.6, and 4.6±2.0 days in cephalosporin group. The mean time for improvement in all the clinical signs was significantly lower in the cephalosporin group than penicillin group (Table 4). This observed difference was statistically significant. The mean time for normalization of lab parameters such as X-ray and ESR was 9.8±2.7 and 6.2 ±1.1 days respectively in penicillin group whereas it were 7.8±2.4 and 5.7 ±1.3 days in Cephalosporin group. The mean time for normalization of lab parameters in cephalosporin group was lower compared to the penicillin group. But the observed difference was not statistically not significant (Table 4).

A study by Pareek A et al, [6] reported that the clinical success rate was statistically superior in adults with lower respiratory tract infections treated with Cefuroxime-Sulbactam (100%) compared with patients treated with amoxiclav (88%), with no significant difference between treatments. Both treatments were safe and well tolerated. But in the present study clinical success rate was similar with both group of drugs (100%) such as Cefotaxime and Amoxiclav in the treatment of lower respiratory tract infections. But time to symptom and signs resolution was faster in Cefotaxime group than Amoxiclav group treated patients.

In another study, they found that ceftriaxone was a safe and effective in all the 8 patients treated for pneumonia[7]. Similarly, in our study, clinical cure was observed in all the 10 pneumonia patients treated with ceftriaxone and all the 8 patients had no adverse effects with ceftriaxone treatment. In a study of Jaurequi et al ., [8] showed that twenty one out of thirty patients were cured treated with ampicillin- sulbactum and eight improved and seven treatment failures, and out of 16 cefotaxime treated patients, nine cured, four improved, two were treatment failure in treatment of lower respiratory tract infections in hospitalized patients. However, in the present study 11 patients were treated Cefotaxime and 12 were treated with ampiclox, all were clinically cured.

In a study of Brambilla. C, et al [9], reported that clinical success in the two treatment groups were very similar 223 of 258 (87.1%) were cured or improved with cefuroxime/ cefuroxime axetil compared to 220 of 256 (85.9%) with amoxiclav. In the treatment of lower respiratory tract infections. However in the present study clinical cure of the patients treated with amoxiclav and cefotaxime was similar.

In a study of pediatric patients suffering with bronchopneumonia, had observed skin reactions, gastrointestinal, hepatic and heamatological reactions when treated with amoxicillin/clavulanic acid (13%,4%,2% respectively) and this was significantly higher than amoxicillin (7%,1%,1% respectively) [10]. However in the present study none of the patient had no adverse effect with ampiclox and amoxiclav treatment, present study reveals that ampiclox and amoxiclav can be safe prescribed. In a review, Keller et al [11], had reported that two pilot trials in 29 patients suffering from severe lower respiratory tract infections. The observed clinical response indicate that ceftriaxone are as active as amoxicillin in the treatment of severe lower respiratory tract infections. The results of present study were also similar.

Another study showed that the clinical success rate was 93.6% and 89.8% respectively for cefotaxime –sulbactum and co-amoxiclav in the treatment of children with lower respiratory tract infections[12]. However, in the present study clinical cure of the patients treated with cefotaxime (11 out of 11) and amoxiclav (13 out of 13) was 100%. In a study of Higuera F, et al, [13] the most common drug related adverse experiences were gastrointestinal events, reported by 8% and 4% respectively of the patients in the amoxiclav and cefuroxime axetil groups in the treatment of community acquired pneumonia. The difference was not statistically significant, whereas in the present study, none of the patient had reported adverse effects in the treatment of pneumonia with amoxiclav.

Treatment with the antibiotic was continued throughout the length of hospital stay. As expected, temperature was normalized earlier with a median duration of 3 days followed by breathlessness and cough. Time to improvement of clinical signs such as crepitations, wheeze, and abnormal respiratory rate was more or less similar. Additionally, this improvement was parallel with normal ESR values.

All the patients recovered without any residual sequel. In one patient there was a change in antibiotic usage from amoxiclav to ceftriaxone. None of case sheets had data regarding adverse effects. However, we on questioning the mother of the patient, we found that none had suffered any adverse events.

Conclusion

In this study, the duration of antibiotic usage and length of hospital stay was significantly

less when treated with cephalosporins like ceftriaxone and cefotaxime as compared to penicillins like ampiclox and amoxiclav. Cephalosporins like ceftriaxone and cefotaxime appear to be as more effective than penicillins like ampiclox and amoxiclav in reducing the clinical symptom like cough, clinical signs like crepitations, wheeze, and abnormal respiratory rate in pediatric patients with lower respiratory tract infections. However the time to disappearance of fever and breathlessness was not significantly different between the two groups. Clinical cure was observed in all the patients without any residual sequel and no adverse effects were reported. Hence, by our study it can be concluded that both groups of antibiotics were effective and safe. However cephalosporins appears to be as more effective than penicillins.

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