Original Article

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# Assessment of Treatment of Community Acquired Severe Pneumonia by Two Different Antibiotics

Paediatrics Section

KARIMELDIN MA SALIH[1], JALAL ALI BILAL[2], WIDAD ELDOUCH[3], ALI ABDIN[4]

## ABSTRACT

**Introduction:** Pneumonia is common presentation in the emergency room and is still a cause of morbidity and mortality. The rationale of this study was to test the trend of paediatricians to achieve rapid response facing severe pneumonia, the lack of agreed on plan for the management of community acquired pneumonia (CAP) and the few experiences regarding injectable form of β-lactam antimicrobial.

**Materials and Methods:** This is a prospective case control study, purposive randomized sampling, three patients were excluded since their information was incomplete, 132 patients were randomly divided into groups, one group named control group (penicillin according to the guidelines of WHO 2013), 33 patients; second group treated by β-lactam inhibitors (Augmentin IV) 50 patients; and third group treated by 3rd generation cephalosporin (ceftriaxone) 49 patients. The study was conducted at the main tertiary care and paediatrics teaching hospital in Khartoum capital of Sudan. The study was completed within the duration from 2010 to 2011.

**Results:** Both group showed more or less similar results regarding response, as well as the failure rate however, the Augmentin and ceftriaxone groups showed a little bit better survival than the control group.

**Conclusion:** Antibiotics decrease the mortality rate among the pneumonia patients provided that it is given early in the disease.

**Keywords:** Augmentin, Ceftriaxone, Community acquired pneumonia, Empirical treatment

## INTRODUCTION

The seriousness of pneumonia, delay and difficulty in investigations to establish accurate diagnosis, could lead to a morbid result, therefore empirical treatment should be considered early to avoid the complications of pneumonia, which is the leading cause of death in under five children [1-3] with some estimate of upto three million deaths in developing countries [4,5]. Susanna Esposito et al., stated that antibiotic guidelines faced by many challenges which might reduce its reliability such as absence of standard protocol to establish the diagnosis, difficulty to determine the exact aetiology in paediatric community acquired pneumonia, paucity of information regarding pharmacodynamics and pharmacokinetic, the emerging resistance to antibiotics used for community acquired pneumonia and finally the application of some vaccine against respiratory pathogen [6,7]. The explanation for the problem facing antibiotics guideline renders immediate therapy empirically an urgent decision [8,9]. The diagnosis of Community Acquired Pneumonia (CAP) is usually depending on combination of clinical, radiological and laboratory features [10]. *Streptococcus pneumonia* encountered in 27-44%, mixed infection of *Streptococcus pneumonia* and other infection occurred in 9-30%, respiratory viruses in 20-45% of the cases, *Hemophilus influenzae* is rare after vaccination and the remaining percentage due other agents. According to the International Vaccine Access Center (IVAC) by Johns Hopkins Bloomberg School of Public Health the Pneumonia Progress Report monitors coverage of the three GAPP interventions includes 15 countries with the high mortality of childhood pneumonia in 2010, Sudan is one of these 15 targeted country where pneumonia mortality is still high to deserve such intervention [11]. Once the diagnosis is established after many clinical, laboratory, radiological and epidemiological considerations careful selection of antibiotics should be an urgent decision particularly if the patient is toxic and very ill. β-lactam and 3rd generation cephalosporins are known modalities as intravenous treatment for CAP. The objective of early treatment in developing countries is to reduce mortality [12-14]. WHO guidelines allow alternative therapy in severe and very severe CAP instead of penicillin like β-lactam and 3rd generation cephalosporin which were both adopted in this study [15]. The β-lactam inhibitors have broad spectrum of activity, work against gram negative, gram positive, ananaerobic bacteria and this features it for treatment of severe and very severe CAP [16]. The third generation cephalosporin's are broad spectrum antibiotics useful in many clinical conditions in gram positive bacterial infection and in the form of ceftriaxone is quite suitable in inpatient as well as outpatient settings since it has relatively long half life and minimum side effects [17]. Very little experiences exist regarding the injectable form of β-lactam.

## AIM

To determine response to empirical therapy with β lactam inhibitors (augmentin IV) and the 3rd generation cephalsporin (ceftriaxone). To compare differences in response to 3rd generation Cephalosporin and β-lactam inhibitors.

## MATERIALS AND METHODS

This was a prospective case control study at the main tertiary care and paediatrics teaching hospital in Khartoum capital of Sudan. The study was completed within the time period between April 2010 and April 2011. Purposive randomized sampling, three patients were excluded since their information was incomplete, 132 (total of 135) patients were randomly divided into three groups, and one group named control group (penicillin was administered according to the guidelines of WHO 2013), 33 patients; the second group was treated by β lactam inhibitors (Augmentin IV) 50 patients and third group treated by 3rd generation cephalosporin (ceftriaxone) 49 patients. Age, gender, family history, physical examination and laboratory results were taken from the patient files, The 1st group is the control, the 2nd group received Augmentin, and the 3rd group was treated by ceftriaxone. the response was determined clinically

after 72 hours vital sign's; systemic examination and by laboratory investigation using complete blood count and C-reactive protein.

Demographic variables; age, gender, occupational history, family history, smoking habits, breast feeding, physical examination, laboratory results, vital sign after drug intake, complications were recorded. These variables were used to compare and look for correlations and clinical significance.

**Inclusion criteria:** All children below the age of 60 months who were having severe CAP according to WHO definition who visited the hospital during the study duration April 2010-April 2011.

**Exclusion criterion:** Exposure to any investigational drug or procedure within 1 month prior to study entry or enrolled in a concurrent study that may confound results of this study.

**Declaration of Interest:** The authors report no conflict of interest. The authors have not disclosed any affiliation or financial involvements.

**Ethical and legal considerations:** Ethical principles for medical research involving human subjects were followed by the investigaors i.e. protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects and written consent from the ethical committee of the hospital was taken.

## STATISTICAL ANALYSIS

SPSS version 18, was used to enter the data suitable coding methods was adopted by the researcher to ease the process of data entry. Descriptive statistics i.e. mean, standard deviation, maxima, minima, range, percentages of Sociodemographic variables and laboratory results were calculated. Chi-square test was used to determine the relationship between different discrete variables. The p value less than 0.05 was considered significant

## RESULTS

In the results depicting the gender wise age distribution of the sample size, mean±SD of the overall age was 22.9 ± 8.91 months, Out of 132 pqatient, 65 patients were males and 67 were females. The minimum age was 1 month while the maximum was 56. There was no significant difference among the age and gender distribution. (p-value 0.531) [Table/Fig-1].

Regarding the medications used the findings depicted the drug distribution among the study group 37.9% were from Augmentin, 37.1% were Ceftrixone and 25% were control group (penicillin) [Table/Fig-2].

There was no significant difference in complaints among the 3 medications groups before treatment (p=0.413). After three days of the treatment the study groups were further examined by means of several parameters i.e. complaint vital signs and investigations after 3 days utilizing CBC (WBC) and CRP, hospital stay and outcome. The response to augmentin (1st group) therapy and 3rd generation cephalosporin (2nd group) was 40% and 38% respectively after 72 hour as 41%,38% of the 1st and 2nd group showed return of vital signs to normal after 3 days respectively, 40% and 38% of 1st and 2nd group had their WBC and CRP returning to normal values, hospital stay was reported in 43% and 40% in the 1st and 2nd group respectively, 43%,44% achieved full recovery in the 1st and 2nd group respectively where complications encountered as 14% and 10% for the 1st and 2nd group respectively [Table/Fig-3,4].

The Survival rate was 85.75, 89.79% and 78.7% for augmentin, ceftrixone and penicillin (the control) respectively and among both first groups there was no significant difference, surprisingly the survival rate in both groups is more than the control group.

## DISCUSSION

In this study the objectives were to determine the response to empirical therapy with β-lactam inhibitors (Augmentin IV) and 3rd generation cephalosporin (ceftriaxone) and to compare differences in outcome to 3rd generation cephalosporin and β-lactam inhibitors.

In this study no significant difference in outcome between augmentin and 3rd generation cephalosporin (the 1st group and 2nd group of the drugs), however this study showed similar response rate for both drugs and similar failure rate which is similar to studies done by other authors where effectiveness for ampicillin-sulbactam and 2nd or 3rd generation cephalosporins were studied [18-20], gender, and other confounding variables were examined in this study to measure the significant difference of demographic variables among the patients. According to Christopher et al., mortality was not significantly decreased by using two initial antibiotics instead of one, even in patients with septic shock or strep pneumonia infections, may appear to contradict earlier studies so only in the present study only one drugs was used [21]. Anıl Tapısız et al., among Turkish children found effectiveness of ampicillin-sulbactam and failure rate similar to our study [22]. The similarities in response might be well

| Characteristics | Augmentin | | Ceftriaxone | | Control | | Total | |
|---|---|---|---|---|---|---|---|---|
| | no | % | no | % | no | % | no | % |
| **Gender** | | | | | | | | |
| Male | 27 | 20.5 | 23 | 17.4 | 15 | 11.4 | 65 | 49.2 |
| Female | 23 | 17,4 | 26 | 19.7 | 18 | 13.6 | 67 | 50.8 |
| Total | 50 | 37,9 | 49 | 37,1 | 33 | 25 | 132 | 100 |
| **Age** | | | | | | | | |
| <18 month | 15 | 11,4 | 15 | 11,4 | 9 | 6,8 | 39 | 29,5 |
| ≥18 months | 35 | 26,5 | 34 | 25,7 | 24 | 18,2 | 93 | 70,5 |
| Total | 50 | 37,9 | 49 | 37,1 | 33 | 25 | 132 | 100 |

**[Table/Fig-1]:** Sex and age distribution among group study.

| Drugs | Number | % |
|---|---|---|
| Control(penicillin) | 33 | 25 |
| Augmentin | 50 | 37.9 |
| Ceftriaxone | 49 | 37.1 |
| Total | 132 | 100 |

**[Table/Fig-2]:** Drug distribution among the study group.

| Vital Signs& investigation Before Treatment | Number | % |
|---|---|---|
| Blood culture +ve | 24 | 18,2 |
| - ve | 108 | 81,8 |
| Total | 132 | 100 |
| WBC > 20000 | 39 | 39.4 |
| Cells/mcL ≤ 20000 | 60 | 60.6 |
| Total | 99 | 100 |
| CRPvery high | 39 | 39.4 |
| high | 60 | 60.6 |
| Total | 99 | 100 |
| Temp > 40 | 40 | 40.4 |
| ≤ 40 | 59 | 59.6 |
| Total | 99 | 100 |
| $O_2$ sats > 90% | 39 | 39.4 |
| ≤ 90% | 60 | 60.6 |
| Total | 69 | 100 |
| Chest X-ray +ve | 99 | 100 |
| - ve | - | - |
| Total | 99 | 100 |

**[Table/Fig-3]:** Vital signs (temperature, $O_2$ sats), Investigations (WBC, CRP, CXR, Blood Culture), Clinical Sequel.

| | Augmentin | Ceftriaxone | Control(penicillin) | Total |
|---|---|---|---|---|
| **Complaint After 3Days** | | | | |
| Yes | 10(20%) | 11(22.45%) | 5(15.2%) | 26(19.7%) |
| No | 40(80%) | 38 (77.55%) | 28 (84.8%) | 106(80.3%) |
| Total | 50(100%) | 49(100%) | 33(100%) | 132(100%) |
| **Vital Signs After 3 Days** | | | | |
| Normal | 41(82%) | 38(77.55%) | 26(78,8) | 105(79.5%) |
| Abnormal | 9(18%) | 11(22.45%) | 7(21,2) | 27(20%) |
| Total | 50(100%) | 49(100%) | 33(100%) | 132(100%) |
| **Investigation After 3 Days** | | | | |
| Normal | 40(80%) | 38(77.55%) | 26(78,8) | 104(78.8%) |
| Abnormal | 10(20%) | 11(22.45%) | 7(21,2) | 28(21.2%) |
| Total | 50(100%) | 49(100%) | 33(100%) | 132(100%) |
| **Hospital Stay** | | | | |
| Less Than 7 Days | 43(86%) | 40(81.6%) | 26(78,8) | 83(83.8%) |
| More Than 7 days | 7(14%) | 9(18.4%) | 7(21,2) | 16(16.2%) |
| Total | 50(100) | 49(100%) | 33(100%) | 99(100%) |
| **Outcome** | | | | |
| Full Recovery | 43(86%) | 44 (89.8%) | 26 (78.8%) | 113(85.6%) |
| Empyema | 3(6%) | 1(2%) | - | 4(3%) |
| Meningitis | 4(8%) | 1(2%) | 2 (6.1%) | 7(5.3%) |
| Heart Failure | - | 2(4.1%) | 3 (9.1%) | 5(3.8%) |
| Sepsis | - | 1(2%) | 2 (6.1%) | 3(2.3%) |
| Complications | 7(14%) | 5(10%) | 7 (21.2 %%) | 19(14.4%) |
| Total | 50(100%) | 49(100%) | 33(100%) | 132(100%) |

**[Table/Fig-4]:** Vital signs, Clinical Sequel.

explained by the fact that streptococcal pneumonia which is the common bacterial cause usually respond well to wide spectrum antibiotics and the failure rate due to absence of good evidence of the exact cause in addition to possibilities of viral infection. This study showed the response to 3rd generation cephalosporins is similar to another study among Turkish children where they compare it with penicillin in addition to chloramphenicol however with this choice of treatment many nurse visits were necessary in contrast to our study where less nurse visits were necessary [23]. Penicillin and derivatives were the most commonly used empiric antibiotics. Linjie Zhang et al., study conducted at the teaching hospital of the Federal University of Rio Grande, Brazil [24] documented a failure rate of 4.8% which was better than the rate in our work and this result in Brazil might be due to rigid adherence to the guideline [25]. Despite our finding in this study where therapeutic success and failure for the two groups is the same other contradicting studies outcomes suggest that cephalosporin's are more effective than penicillin's, but another suggests the opposite [26]. In our study we attributed the failure rate to the misdiagnosis or the complication of the disease since 14% of the 1st group i.e. the augmentin group developed empyema in 6% and meningitis in 8% and 10% of the 2nd group i.e. the ceftrixone group developed (empyaemia 2%, meningitis 2%, heart failure 4%, sepsis 2%). This failure of the treatment in both groups was most probably due to the initial presentation in subtle or mild form or early stage that could not be detected clinically or radiologically.

## LIMITATIONS

Although the strength of this study is being prospective conducted in teaching tertiary hospital but factors like the small numbers, difficulty in making precise diagnosis of pneumonia, absence of accurate decision regarding failure to response after 72 hours might be the limitations of the study in addition to the confounders.

## CONCLUSION

Decision regarding treatment of severe pneumonia should be carried immediately as soon as diagnosis is suggested with the available injectable antibiotics although the two groups i.e. the augmentin and ceftrixone showed a little bit better survival than the control group i.e. the penicillin, however we highly recommend adherence to the penicillin since it is cheap and available in developing country in general and Sudan in particular. Should other options need either augmentin or ceftrixone could be good alternatives.

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**PARTICULARS OF CONTRIBUTORS:**
1. Associate Professor, Department of Pediatrics, College of Medicine, Bahri University, Sudan.
2. Assistant Professor, Department of Pediatrics, College of Medicine, Gasim University, KSA.
3. Pediatrician, Primary Health Care Department, MOH Sudan.
5. General Practitioner, MOH, Sudan.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. Karimeldin MA Salih,
King Khalid University, College of Medicine, PO box 641, Abha-61421, Kingdom of Saudi Arabia.
E-mail : karimeldin_salih@hotmail.com

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