ejpmr, 2015,2(2), 235-249

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 3294-3211

EJPMR

COMPARISON OF EFFICACY AND SAFETY OF PIPERACILLIN/TAZOBACTAM PLUS AMIKACIN (PTA) VERSUS CEFTRIAXONE PLUS AMIKACIN (CA) IN MANAGEMENT OF COMPLICATED PNEUMONIAS IN CHILDREN

Jyoti Kaushal, Dhiren M Pranami*, Sanjiv Nanda, Madhu Sharma

A 202, Stadium Plaza, Motera Stadium Road Ahmedabad, Gujarat, India

Article Received on 29/12/2014 **Article Revised on 21/01/2015** **Article Accepted on 12/02/2015**

***Correspondence for Author**

Dr. Dhiren Pranami

A 202, Stadium Plaza, Motera Stadium Road Ahmedabad, Gujarat, India

ABSTARACT

Objectives: This study aimed to compare the efficacy and safety of piperacillin/tazobactam plus amikacin versus ceftriaxone plus amikacin for treating complicated pneumonias in children. **Materials and Methods:** A prospective, randomized, comparative, open label & parallel study was done on 40 children of either sex and age between 2 to 14 years having complicated pneumonia.They were randomly allocated with the help of computer generated random numbers to receive either piperacillin/tazobactam plus amikacin(PTA group) or ceftriaxone plus amikacin(CA group). Efficacy assessment was done by observing sign and symptoms of pneumonia i.e fever, cough (productive or non-productive), dyspnoea, chest pain etc. & laboratory investigations like chest X-ray & pleural fluid examination. The number of days patients were hospitalized, was noted and a record was maintained. The number of patients who required oxygen inhalation and needed mechanical ventilation, was also noted. Safety assessment was done by observing the side effects of antibiotic therapy. **Results:** Duration of fever in PTA group was 3.70 ± 0.46 days while in CA group it was 5.30 ± 0.51 days. This difference was statistically significant ($p < 0.05$). Duration of hospital stay in PTA group was 12.00 ± 0.95 days and in CA group was 14.70 ± 0.70 days and this difference was statistically significant with the p value of 0.028. Sixteen (80%) patients in PTA group were cured whereas in CA group thirteen (65%) patients were cured. Regarding the therapeutic success of medication, no statistically significant difference was observed between the two groups, although more patients were cured and less had failure with treatment in PTA group as compared to CA

group. Both the treatment regimens were well tolerated with minor ADRs. **Conclusions :** Both the treatment groups i.e. piperacillin/tazobactam plus amikacin (PTA) and ceftriaxone plus amikacin (CA) were found to be safe & efficacious in management of complicated pneumonia in children. On comparing the above mentioned treatment groups, better response was observed in PTA as compared to CA group.

KEYWORDS: Childhood Pneumonias, Complicated Pneumonias, Piperacillin/Tazobactam, Ceftriaxone, Amikacin.

INTRODUCTION

Pneumonia is an infection of the pulmonary parenchyma characterized by symptoms and signs of lower respiratory tract infection.[1] Revised classification system categorized pneumonia as either community acquired pneumonia (CAP) or health care associated pneumonia (HCAP). Health care associated pneumonia (HCAP) is further subcategorised into hospital acquired pneumonia (HAP) and ventilator associated pneumonia (VAP).[2] Pneumonia is the leading single cause of childhood mortality. India accounts for the maximum 43 million new cases followed by China (21 million cases) and Pakistan (10 million cases). It is estimated to kill 410,000 children in India every year.[3] It takes the life of one child every 20 seconds (more than AIDS, malaria and measles combined) and is responsible for nearly 20 percent of deaths in young children.[4] Complicated pneumococcal pneumonia is defined by the presence of the one or more of the following features : 1) loculated pleural fluid (PF) on chest X-ray, chest ultra sound or computed tomography 2) any pleural fluid (PF) parameters consistent with empyema(cloudy, bloody, or purulent appearance: white blood cell count ≥ 50,000 × 109 / L; pH ≤ 7.1; lactic dehydrogenase level ≥ 1,000 IU/L; glucose level ≤ 40 mg/dl; positive gram stain or culture) 3) chest tube (CT) placement; and/or 4) thoracotomy/ decortication.[5,6]

Childhood mortality due to pneumonia can be taken care by timely intervention. Some experts have recommended that all children with pneumonia should receive antibacterial therapy, as it is impossible to exclude the presence of bacterial infection.[6,7] Other experts have suggested that anti-bacterial therapy may be withheld in young, ambulatory children with mild symptoms.[6,7] Owing to the lack of the rapid, reliable, cost effective tests to identify the aetiology of pneumonia, the selection of initial antibacterial therapy is usually empiric. The treatment of choice depends primarily on age, clinical features and epidemiology factors. Other relevant factors include the cost, tolerability, acceptability and

convenience of treatment.[8] The global spread of antibiotic resistance has increased the important influence on the selection of antibacterial therapy for childhood pneumonia. The development of new antibacterial agents is necessary to address the increasing prevalence of raised minimum inhibitory concentrations (MICs) among paediatric respiratory pathogens. With wide spread of resistance, new agents that are active against the full spectrum of paediatric respiratory pathogens are needed.[9]

Hence prescribing guidelines for antibiotics in the treatment of childhood pneumonia have limitations because there is no standard for establishing the proven diagnosis of pneumonia, it is difficult to define the etiology of pediatric pneumonia, the pharmacokinetic (PK)/pharmacodynamic (PD) data are limited, resistance has recently emerged among the bacteria responsible for pneumonia and vaccine coverage against respiratory pathogens varies.[10,11]

Piperacillin is a broad-spectrum penicillin that is bactericidal against many Gram-positive and Gram-negative aerobes and anaerobes.[12] Tazobactam does extend piperacillin's activity against most β-lactamase producing strains of *Enterobacteriaceae*, *H. influenzae*, *N. gonorrhoeae*, and *M. catarrhalis*.[13] Piperacillin/tazobactam combination increases the spectrum of antibacterial activity, provides good tissue penetration, tolerance & prevents development of resistance.[12] Ceftriaxone is a broad-spectrum third-generation cephalosporin, most active cephalosporin against penicillin-resistant strains of pneumococci and is recommended for empirical therapy of serious infections that may be caused by these strains.[14] Amikacin sulfate is a semi-synthetic aminoglycoside antibiotic, active against the vast majority of aerobic gram-negative bacilli, including most strains of *Serratia*, *Proteus*, *P. aeruginosa*, *Klebsiella*, *Enterobacter*, and *E. coli* that are resistant to gentamicin and tobramycin[15] Combination of ceftriaxone & amikacin provides broadspectrum coverage, high and more rapid bactericidal activity, synergistic effect, optimal therapy for Pseudomonas aeruginosa and limitation of the emergence of resistance[16] In this study we compared the efficacy of piperacillin/tazobactam and ceftriaxone in association with amikacin for the treatment of complicated pneumonia in paediatric patients.

MATERIAL AND METHODS

This was a prospective, randomized, comparative, open label, parallel, study conducted by department of pharmacology and paediatrics, Pt. B D Sharma PGIMS, Rohtak, India on 40 pediatric patients of either sex having complicated pneumonia. They were randomly allocated

with the help of computer generated random numbers in two groups of 20 patients each, to receive either piperacillin/tazobactam plus amikacin (PTA) or ceftriaxone plus amikacin.(CA). An informed consent was obtained from the parents of pediatric patients enrolled for the study. The study protocol was approved by Institutional Review Board (IRB) & Institutional Ethical Committee (IEC).

Patients included in the study were in the age group of 2 to 14 years. They had microbiological evidence of bacterial infection and sensitivity to the study medications. They had at least one or more of the following criteria of complicated pneumonia : [1] Loculated pleural fluid (PF) on chest X-ray, chest ultra sound or computed tomography [2] Any pleural fluid (PF) parameters consistent with empyema (cloudy, bloody, or purulent appearance; white blood cell count ≥ 50,000 × 109 / L; pH ≤ 7.1; lactic dehydrogenase level ≥1,000 IU/L; glucose level ≤ 40 mg/dl; positive gram stain or culture) [3] Chest tube (CT) placement; and/or [4] Thoracotomy/ Decortication [5] Evidence of other complications of pneumonia such as pneumothorax & lung abscess.

Patients were not eligible if they had known or suspected hypersensitivity to β-lactam antibiotics & amikacin, those who had known acute or chronic renal failure, liver disease, heart disease and those who refused to give informed consent. Patients with any known or suspected bacterial infection other than the disease under investigation which required concomitant use of a systemic antimicrobial agent other than the study drugs allocated were also excluded.

One group of patients ie PTA group (n = 20) received treatment with100 mg piperacillin/ 12.5 mg tazobactam per kg every 8 hourly by intravenous infusion over 20-30 minutes + 15 mg/kg/day amikacin intravenously in 2-3 divided doses for 14 days. Another group i.e. CA group (n=20) received 50 to 75 mg/kg ceftriaxone intravenously once a day. (Total daily dose did not exceed 2 grams) + 15 mg/kg/day amikacin intravenously in 2-3 divided doses for 14 days. The available commercial preparations were used.

Clinical and laboratory evaluation was carried out in all the patients in the terms of efficacy of the treatment along with safety estimation. Efficacy & safety assessment were done on days 1, 3, 5, 7, 10 and 14th day post-drug administrations. Efficacy assessment was done by observing sign and symptoms of pneumonia i.e fever, tachypnoea, tachycardia, cough (productive or non-productive), dyspnoea, chest pain etc. & laboratory investigations like

chest X-ray & pleural fluid examination were done. The number of days patients were hospitalized, was noted and a record was maintained. Also the number of patients who required oxygen inhalation and needed mechanical ventilation was also noted. All those patients who did not respond adequately to any of the study medications were provided with the best possible treatment required.

Safety Assessment was done by observing the side effects of antibiotic therapy e.g. skin rash, pruritus, diarrhoea/ constipation, nausea, vomiting, headache, abdominal pain, oedema, hearing loss, loss of balance, acute muscular paralysis, apnoea, elevation of serum creatinine, albuminuria, presence of red and white cells in urine, oliguria, hypersensitivity (rash, pruritus, fever or chills), eosinophilia, thrombocytopenia, leukopenia or any other local side effects like injection site reaction, thrombophlebitis, pain, induration and tenderness. Any other adverse effect reported by the patient/patient's guardian was recorded. The results of the study regarding efficacy and safety in both the groups were documented.

Therapeutic success was considered as resolution of all signs and symptoms without modification of the initial antibacterial regimen, failure was taken as the administration of any additional antibacterial agent due to persistent fever in a patient with signs of clinical deterioration, microbiological evidence, clinical progression of the presumed infection or adverse event associated with the antibiotic regime which necessitated stoppage of the treatment.

The primary objective of this study was to compare clinical success rates of both study drug regimens. Quantitative variables were given as Mean ± SEM. Differences between groups were compared with student's t-test or wilcoxon's rank-sum test where appropriate for quantitative variables and with a chi square test (with Fisher's correction where appropriate) for qualitative variables. For analysis of repeated measures in categorical data, cochran'Q test was used. A p-value < 0.05 was considered as statistically significant. For the analysis of data SPSS version 20 was used.

OBSERVATIONS

A total of 52 patients with clinical suspicion of complicated pneumonia were screened for this study. Out of this, 12 patients were excluded, as 7 patients did not fulfil the predefined inclusion criteria of study and 5 were not willing to give an informed consent. Rest 40 patients were randomized with the help of computer generated random numbers and were

allocated to either of the two treatment groups as described above. The baseline characteristics of the patients are tabulated in Table 1.

As shown in Table 1, the difference between ages of patients was not statistically significant ($p = 0.331$). There was no statistically difference between PTA & CA group for any baseline variables. The difference in duration of illness among the groups was also not statistically significant. ($p > 0.05$). All the patients presented with chief complaints of fever and cough. Dyspnoea was reported in 14(70%) patients in PTA group and 17(85%) patients in CA group.

After the treatment, comparison of duration of various symptoms like fever, cough dyspnoea, chest pain and was done in both the groups. As it is evident from Table 2, duration of fever in PTA group was 3.70 ± 0.46 days and in CA group was 5.30 ± 0.51 days. This difference was statistically significant ($p < 0.05$). However, no statistically significant difference was observed between the two groups regarding the duration of cough, dyspnoea and chest pain, although patients in PTA group suffered from these symptom for less duration. Duration of hospital stay in PTA group was 12.00 ± 0.95 days and in CA group was 14.70 ± 0.70 days and this difference was also statistically significant with the p value of 0.028.

The number of patients having fever & cough were observed and recorded in both the groups at baseline and on days 1, 3, 5, 7, 10 and 14th day post-drug administrations. As it is evident from Table 3, on day 3 only PTA group showed statistically significant improvement in incidence of fever whereas in CA group statistically significant improvement was observed on day 7. There was statistically significant decrease in the incidence of cough after 7th day of treatment with both the groups as compared to pre-treatment period. It was observed that fewer patients were having fever after day 3 and day 7 of treatment in PTA group as compared to CA group, but this difference was not statistically significant.

Radiological assessment was done in both the groups at baseline and on days 1, 3, 7 and day 14 post drug administrations. Number of patients having various parameters e.g. pleural fluid, pneumothorax, lung abscess, pneumatocele and consolidation were noted.

Figure 1 shows the incidence of pleural effusion in both the groups at different time intervals. At the end of 14th day incidence of pleural effusion was 40% in the PTA group as compared to 80% at baseline and this difference was statistically significant. Although incidence of pleural effusion also decreased in CA group on 14th day as compared to baseline (65% versus

80%) but this difference was not statistically significant. On intergroup analysis, although incidence of pleural effusion at the end of 14th day was less in PTA group as compared to CA group (40% versus 65%) but this difference was not statistically significant.

A record was maintained for the number of patients who required additional supportive measures e.g. need for mechanical ventilation or oxygen inhalation. There was no statistically significant difference between both the groups for the requirement of additional supportive measures, although it was observed that the requirement was less in PTA group.

As shown in Figure 2, 16(80%) patients in PTA group were cured whereas in CA group 13(65%) patients were cured. At day 7 of post drug administration 4(20%) patients in PTA group had microbiological evidence of infection and the sign and symptoms of pneumonia were also not resolved whereas in CA group 7(35%) patients still had positive microbiological evidence of infection and clinical sign and symptoms of pneumonia. Regarding the therapeutic success of medication, no statistically significant difference was observed between the two groups, although more patients were cured and less had failure with treatment in PTA group as compared to CA group. The patients who did not respond to the study medication were given other antibiotics i.e. vancomycin and meropenem.

In PTA group, 6(30%) patients reported ADRs. Pruritus, nausea, abdominal pain, skin rash was reported by one patient each and 2 patients reported diarrhoea. Thus gastrointestinal side effects were seen in 4(20%) patients and skin related problems were observed in 2(10%) patients. In CA group, 5(25%) patients reported ADRs. Nausea, diarrhoea & skin rash were reported by one patient each and 2 patients reported vomiting. Thus gastrointestinal side effects were observed in 4(20%) patients and skin related problems in 1(5%) patient. On intergroup analysis, there was no statistically significant difference observed between the two groups regarding the incidence of adverse effects. No newer adverse reactions were reported in both the groups. None of the patients in both the groups withdrew from the study because of ADRs. This shows that all treatment regimens were well tolerated with minor ADRs.

Table

TABLE 1: DEMOGRAPHIC & BASELINE CLINICAL CHARACTERISTICS OF PNEUMONIA			
Variables	**PTA group (n=20)**	**CA group (n=20)**	**p value**
PATIENT CHARACTERISTICS			
Age in Years	3.62 ± 0.30	4.01 ± 0.26	0.331
Gender- **Male** **Female**	 14 (70%) 6 (30%)	 13 (65%) 7 (35%)	0.736
Socio-economic Status **Lower** **Middle** **Higher**	 17 (85%) 3 (15%) 0	 18 (90%) 2 (10%) 0	0.637
CLINICAL SYMPTOMS			
Duration of illness *	5.10 ± 0.45	6.35 ± 0.53	0.082
Fever	20 (100%)	20 (100%)	-
Cough	20 (100%)	20 (100%)	-
Dyspnoea	14 (70%)	17 (85%)	0.256
Chest Pain	4 (20%)	6 (30%)	0.465

* Duration of illness in Days ± SEM

- All other values are expressed as number of patients (percentage)

- PTA group: Piperacillin/tazobactam plus amikacin treated patients

- CA group: Ceftriaxone plus amikacin treated patients

TABLE 2: DURATION OF SYMPTOMS IN PTA VERSUS CA GROUP			
Duration (Days)	**PTA (Mean ± SEM)**	**CA (Mean ± SEM)**	**p value**
Fever	3.70 ± 0.46	5.30 ± 0.51	0.026*
Cough	4.95 ± 0.49	5.80 ± 0.45	0.212
Dyspnoea	2.20 ± 0.47	2.95 ± 0.48	0.272
Chest Pain	0.50 ± 0.25	0.90 ± 0.33	0.339
Hospital stay	12.00 ± 0.95	14.70 ± 0.70	0.028*

* p value < 0.05 Statistically significant

- All values are expressed as Mean ± SEM
- **PTA group**: Piperacillin/tazobactam plus amikacin treated patients
- **CA group**: Ceftriaxone plus amikacin treated patients.

TABLE 3: INCIDENCE OF FEVER & COUGH IN PTA VERSUS CA GROUP					
		Baseline	**Day 3**	**Day 7**	**Day 14**
Fever	PTA	20(100%)	9 (45%)**	4 (20%)***	0 (0%)***#
	CA	20(100%)	15 (75%)	7 (35%)***	0 (0%)***###
Cough	PTA	20(100%)	15 (75%)	3 (15%)***##	0 (0%)***###
	CA	20(100%)	18 (90%)	7 (35%)**##	0 (0%)***###

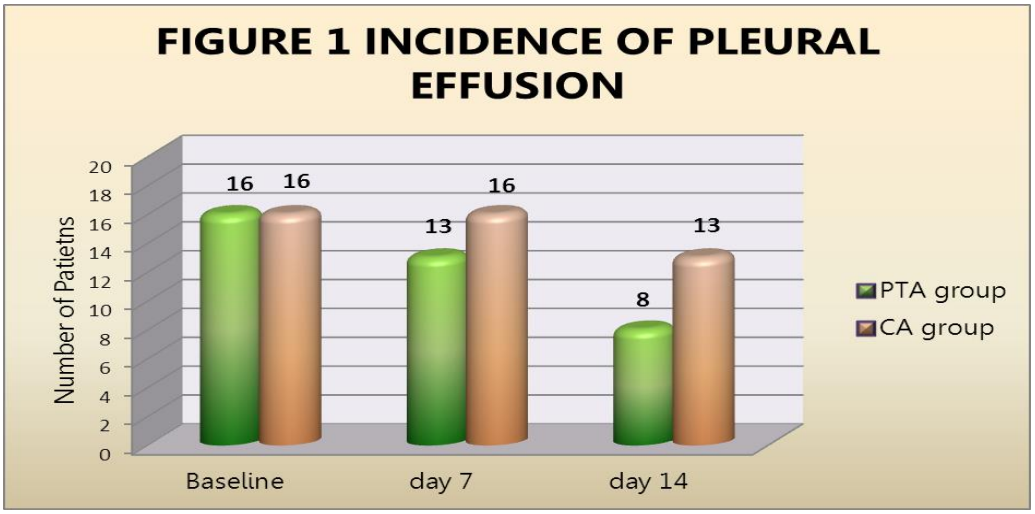
- All values are expressed as number of patients (percentage)
- **PTA group**: Piperacillin/tazobactam plus amikacin treated patients
- **CA group:** Ceftriaxone plus amikacin treated patients

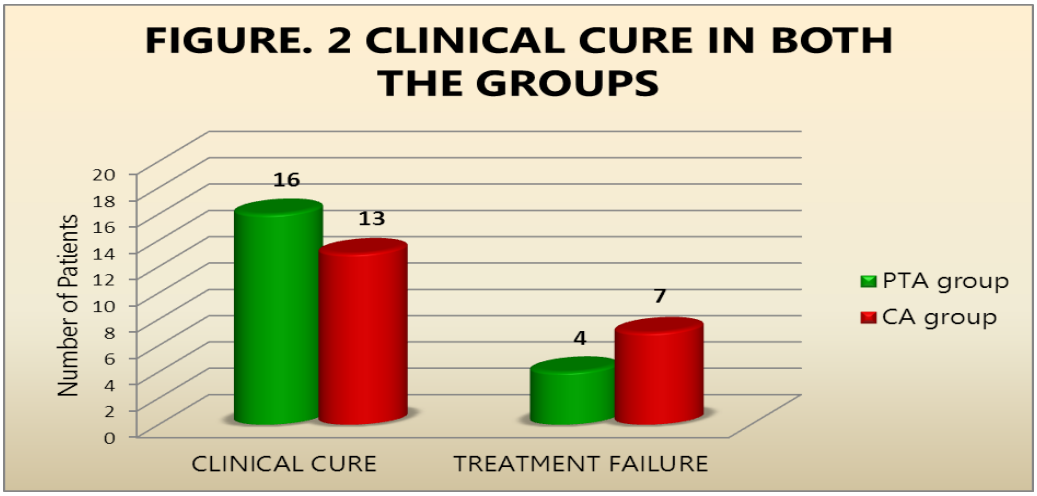
** Comparison of baseline values with values after 3rd, 7th and 14th day of treatment in PTA group and CA group*

 # Comparison of 3rd day values with values after 7th and 14th day of treatment in PTA group and CA group

/# → p<0.05, **/## → p<0.01, */### → p<0.001*

Figures





DISCUSSION

Pneumonia is an infection of the pulmonary parenchyma characterized by symptoms and signs of lower respiratory tract infection, with new radiographic shadowing for which there is no alternative explanation.[1] Some of the essential diagnostic criteria and typical features of pneumonia are fever, cough and dyspneoa, abnormal chest examination (rales or decreased breath sound), abnormal chest radiograph (infiltrates and pleural effusion).[17] Complications associated with pneumonia include the development of necrotizing pneumonia, pleural effusion, pleural empyema, pyopneumothorax and lung abscess.[18-20]

One of the commonly used drugs in the treatment of pneumonia is ceftriaxone in combination with amikacin. Piperacillin is an extended spectrum beta-lactam antibiotic of the ureidopenicillin class. Piperacillin and related agents are important drugs for the treatment of serious infections caused by gram-negative bacteria, including infections acquired in the hospital.[21] Association of piperacillin and beta-lactamase inhibitor, tazobactam, allow to overcome resistance observed with piperacillin alone.[21] Combination therapy with an aminoglycoside plus piperacillin has commonly been recommended because this approach provides broad-spectrum coverage, bactericidal activity and potential synergic effects, and minimizes the development of resistance during treatment.[22]

Some studies have been done abroad that have compared the efficacy and safety of ceftriaxone and amikacin versus piperacillin/tazobactam and amikacin in febrile patients with haematological neoplasia and severe neutropenia.[23] But to the best of our knowledge no study has been done worldwide comparing the efficacy and safety of ceftriaxone and amikacin versus piperacillin/tazobactam and amikacin in paediatric patients having complicated pneumonia. In order to test if the substitution of piperacillin-tazobactam for ceftriaxone could improve the results in the treatment of complicated pneumonia, we had designed an open-labelled, randomized study to compare the efficacy of piperacillin/tazobactam and ceftriaxone in association with amikacin for the treatment of complicated pneumonia in paediatric patients.

This study reveals that both the groups showed significant improvement in symptoms of pneumonia in the patients over time. Fever got subsided with PTA treatment after 3.70 days as compared to 5.30 days with CA treatment. So patients became afebrile earlier with PTA treatment and this difference was statistically significant ($p = 0.026$). The improvement in cough, dyspnoea & chest pain also occurred earlier in PTA group as compared to CA group,

although the difference was not statistically significant. The patients were hospitalized for 12.00 ± 0.95 days in PTA group as compared to 14.70 ± 0.70 in CA group. This difference was also statistically significant (p = 0.028)

In a study done by Rossini et al, which compared same drugs that is ceftriaxone and amikacin versus piperacillin/tazobactam and amikacin in febrile patients with hematological neoplasia and severe neutropenia, mean duration of hospital stay were 6.7 in ceftriaxone plus amikacin group as compared to 7.6 in piperacillin/tazobactam plus amikacin group but this difference was not statistically significant. However better response was shown by PTA treatment as compared to CA treatment as far as the duration of hospital stay is concerned, in our study. The reason of disparity in the results could be because the patients in the mentioned study were suffering from fever because of neoplasia whereas the patients in our study were having fever because of complicated pneumonia, although treatment regimens compared were similar in both the studies.[23]

In the present study, on 3rd day only PTA group showed statistically significant improvement in incidence of fever whereas in CA group statistically significant improvement was observed on 7th day.

Although exact similar study was not available in which similar treatment groups were compared for incidence of fever. However in a study done by Cetinkaya et al in which two antibiotic regimens i.e. penicillin G plus chloramphenicol (n = 46) and ceftriaxone (n = 51) were compared for the empirical treatment of childhood pneumonia, it was seen that in both the groups high body temperature values (axillary) returned to normal values from third day on.[24] The findings of our study are quite similar to this study as in both the groups most of the patients became afebrile after 3rd day of the treatment although statistically significant improvement was seen only in PTA group on 3rd day.

At the end of 14th day incidence of pleural effusion was 40% in the PTA group as compared to 80% at baseline i.e. 50% of patients improved and this difference was statistically significant. Although incidence of pleural effusion also decreased in CA group on 14th day as compared to baseline (65% versus 80%) i.e. only 18.75% of patients improved and this difference was not statistically significant. When two groups were compared, although incidence of pleural effusion at the end of 14th day was less in PTA group as compared to CA group (40% versus 65 %) but this difference was not statistically significant.

Although exactly similar study was not found, the study conducted by Cetinkaya et al which compared the two antibiotic regimens i.e. penicillin G plus chloramphenicol (group I) and ceftriaxone (group II) in the empirical treatment of severe childhood pneumonia, showed that pneumonic infiltration was diagnosed in initial chest radiographs of all children by the radiologist. Mild improvement in chest films was seen on the fifth day of the study, but the radiologic findings manifestly improved in about half of the patients at the end of the study. Chest films were completely clear in 51% patients of group I and in 48 % of group II.[24]

It was seen that 16(80%) patients in PTA group were cured whereas in CA group 13(65%) patients were cured. Regarding the therapeutic success of medication, no statistically significant difference was observed between the two groups, although more patients were cured and less had failure with treatment in PTA group as compared to CA group. The patients who did not respond to the study medication were given other antibiotics i.e. vancomycin and meropenem.

In a study done by Cetinkaya et al in which two antibiotic regimens i.e. penicillin G plus chloramphenicol (group I) and ceftriaxone (group II) were compared for the empirical treatment of childhood pneumonia, at the end of the ten days treatment about 84.7% of the patients in group I and 80.4% of group II clinically recovered completely. This difference was not statistically significant. Rest of the patients in both groups took oral amoxicillin plus clavulanic acid for one week more. All patients were clinically well at the end of this period.[24]The findings of our study are in accordance to the findings of this study as no statistically significant difference was observed between the two groups.

In an another study done by Rossini et al, which compared same drugs that is ceftriaxone and amikacin versus piperacillin/tazobactam and amikacin in febrile patients with hematological neoplasia and severe neutropenia, the CA regimen was effective in 62/122 episodes (50.8%), and the PTA regimen in 64/121 (52.9%; P>0.2). This difference was not statistically significant.[23] The findings of our study are quite similar to the findings of this study as no statistically significant difference was observed between the two groups.

In PTA group, 6(30%) patients reported ADRs. Gastrointestinal side effects were seen in 4(20%) patients and skin related problems were observed in 2(10%) patients. In CA group, 5(25%) patients reported ADRs. Gastrointestinal side effects were observed in 4(20%) patients and skin related problems in 1(5%) patient. There was no statistically significant

difference observed between the two groups regarding the incidence of adverse effects. No newer adverse reactions were reported in both the groups. None of the patients in both the groups withdrew from the study because of ADRs. This shows that all treatment regimens were well tolerated with minor ADRs. In a study by Brun-Buisson et al, in which two antibiotic regimens i.e. piperacillin/tazobacatam plus amikacin (TAZ) was compared with ceftazidime plus amikacin (CAZ) in ventilator associated pneumonia, adverse events were recorded in 37 of 98 TAZ recipients (49 events) and 38 of 99 CAZ recipients (46 events); the adverse events were judged severe in 24 TAZ and 17 CAZ recipients. The frequency and distribution by site of all adverse events recorded were similar in both groups. The treatment was interrupted because of a nonfatal adverse event in 3 and 4 patients, respectively.[25] The incidence of adverse effects was comparatively less in our study as compared to above mentioned study as none of the patient had severe adverse effect and also treatment was not interrupted in any of the patient because of adverse effect profile.

CONCLUSIONS

Both the treatment groups i.e. piperacillin/tazobactam plus amikacin (PTA) and ceftriaxone plus amikacin (CA) were found to be safe & efficacious in management of complicated pneumonia in children. On comparing the above mentioned treatment groups, better response was observed in PTA group as patients became afebrile earlier and had to stay in the hospital for less duration as compared to CA group.

REFERENCES

1. Patterson CM, Loebinger MR. Community acquired pneumonia: assessment and treatment. Clin Med. 2012; 12(3):283-6.
2. Mandell LA, Wunderink R. Pneumonia. In: Fauci AS, Kasper DL, Longo DL, Braunwald E, Hauser SL, Jameson JL, et al, editors. Harrison's principles of internal medicine. 17th ed. New York: McGraw-Hill, Medical publishing division: 2008, P. 1619-28.
3. Pneumonia a major killer in children; prevention possible with safe & effective vaccines. 2009 [updated 02 Nov 2009]; Available from: http://www.whoindia.org/en/Section251.htm
4. "Fight Pneumonia. The Global Coalition against Child Pneumonia Save A Child." International Vaccine Access Center (IVAC). March 2012. Available from: www.worldpneumoniaday.org

5. Hardie WD, Roberts NE, Reising SF, Christie CD. Complicated parapneumonic effusions in children caused by penicillin-nonsusceptible streptococcus pneumoniae. Pediatrics. 1998; 101: 388–92.
6. Bryant RF, Salmon CJ. Pleural empyema. Clin Infect Dis. 1996; 22:747–64.
7. Ruuskanen O, Mertsola J. Childhood community-acquired pneumonia. Semin Respir Infect. 1999; 14:163-72.
8. British T. British Thoracic Society Standards of Care Committee. British Thoracic Society guidelines for the management of community acquired pneumonia in childhood. Thorax. 2002; 57 Suppl. 1: i1-i24.
9. McCracken GH. Diagnosis and management of pneumonia in children. Pediatr Infect Dis J. 2000; 19: 924-8.
10. McIntosh K. Community-acquired pneumonia in children. N Engl J Med. 2002; 346: 429-37.
11. Pelton SI, Hammerschlag MR. Overcoming Current Obstacles in the Management of Bacterial Community Acquired Pneumonia in Ambulatory Children. Clin Pediatr (Phila). 2005; 44:1-17.
12. Felmingham D, Feldman C, Hryniewicz W, Klugman K, Kohno S, Low DE, et al. Surveillance of resistance in bacteria causing community acquired respiratory tract infections. Clin Microbiol Infect. 2002; 8 : 2:12-42.
13. Gin A, Dilay L, Karlowsky JA, Walkty A, Rubinstein E, Zhanel GG. Piperacillin–tazobactam: a β-lactam/β-lactamase inhibitor combination. Expert Rev Anti Infect Ther. 2007; 5:365–83.
14. Chambers HF, Deck DH. Beta-Lactam & Other Cell Wall- & Membrane-Active Antibiotics. In: Katzung BG, Masters SB, Trevor AJ, editors. Basic & Clinical Pharmacology. 11th ed. McGraw-Hill: 2009, p. 773-93.
15. Chambers HF. Aminoglycosides. In: Brunton LL, Parker KL, Blumenthal DK, Buxton ILO, editors. Goodman & Gilman's manual of pharmacology and therapeutics. 11th ed. McGraw-Hill: 2008, p. 751-61.
16. Klastersky J, Zinner SH. Synergistic combinations of antibiotics in gram negative bacillary infections. Rev Infect Dis. 1982; 4: 294-301.
17. Ogle JW. Antimicrobial Therapy. In: Hay WW, Levin MJ, Deterding RR, Sondheimer JM, editors. Current diagnosis and treatment Pediatrics. 19th edition. McGraw-Hill: 2009, p.1053-64.

18. Kerem E, Ziv YB, Rudenski B, Katz S, Kleid D, Branski D. Bacteremic necrotizing pneumococcal pneumonia in children. Am J Respir Crit Care Med. 1994; 149: 242–4.
19. Taryle DA, Potts DE, Sahn SA. The incidence and clinical correlates of parapneumonic effusions in pneumococcal pneumonia. Chest. 1978; 74: 170–3.
20. Murphy D, Lockhart CH, Todd JK. Pneumococcal empyema. Am J Dis Child. 1980; 134: 659–62.
21. MacDougall C, Chambers HF. Protein Synthesis Inhibitors and Miscellaneous Antibacterial Agents. In: Brunton LL, Chabner BA, Knollmann BC, editors. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. McGraw-Hill. p. 1521-47.
22. Hughes WT, Armstrong D, Bodey GP, Brown AE, Edwards JE, Feld R et al. 1997 guidelines for the use of antimicrobial agents in neutropenic patients with unexplained fever. Infectious Diseases Society of America. Clin Infect Dis. 1997; 25(3): 551-73.
23. Rossini F, Terruzzi E, Verga L, Larocca A, Marinoni S, Miccolis I, et al. A randomized clinical trial of ceftriaxone and amikacin versus piperacillin tazobactam and amikacin in febrile patients with hematological neoplasia and severe neutropenia. Support Care Cancer. 2005; 13(6): 387-92.
24. Cetinkaya F, Gogremis A, Kutluk G. Comparison of Two Antibiotic Regimens in the Empirical Treatment of Severe Childhood Pneumonia. Indian J Pediatr. 2004; 71(11): 969-72.
25. Brun-Buisson C, Sollet JP, Schweich H, Brière S, Petit C. Treatment of ventilator-associated pneumonia with piperacillin-tazobactam/ amikacin versus ceftazidime/ amikacin: a multicenter, randomized controlled trial. VAP Study Group. Clin Infect Dis. 1998; 26(2): 346-54.