A retrospective study of azithromycin and ceftizoxime for the management of children with Mycoplasma pneumoniae pneumonia

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Abstract

The aim of this study was to compare the clinical efficacy of azithromycin and ceftizoxime (AC) and erythromycin and amoxicillin/sulbactam (EAS) in the treatment of children with Mycoplasma pneumoniae pneumonia (MPP).

In this retrospective study, a total of 92 eligible children with MPP were included, and they were divided into a treatment group (n = 46) and a control group (n = 46). All patients were treated with intravenous ambroxol, and nebulized inhalation of budesonide and terbutaline. In addition, patients in the treatment group received AC. Patients in the control group underwent EAS. All patients in both groups were treated for a total of 10 days. Outcomes consist of erythrocyte sedimentation rate, C-reactive protein, serum lactate dehydrogenase, and interleukin 6, fever clearance time, time of cough disappearance, time of rale disappearance, time of signs disappeared by X-ray, and adverse events. All outcomes were measured after 10-day treatment.

After treatment, patients who received AC exerted better improvements in erythrocyte sedimentation rate (P < .01), C-reactive protein (P < .01), serum lactate dehydrogenase (P < .01), interleukin 6 (P < .01), fever clearance time (P < .01), time of cough disappearance (P < .01), time of rale disappearance (P < .01), and time of signs disappeared by X-ray (P < .01), than those in patients who received EAS. In addition, there were not significant differences in adverse events between 2 groups.

The results of this study showed that AC may benefit more than EAS for the children with MPP.

Abbreviations:  AC = azithromycin and ceftizoxime, CRP = C-reactive protein, EAS = erythromycin and amoxicillin/sulbactam, ESR = erythrocyte sedimentation rate, IL-6 = interleukin 6, LDH = serum lactate dehydrogenase, MP = Mycoplasma pneumoniae, MPP = Mycoplasma pneumoniae pneumonia.

Keywords: azithromycin, ceftizoxime, Mycoplasma pneumoniae pneumonia

1. Introduction

Mycoplasma pneumoniae pneumonia (MPP) is a common respiratory disease resulted from mycoplasma infection, especially in pediatric population. It accounts for about 10% to 40% of all pediatric community-acquired pneumonia in children and young adult population and 18% to 20% of them require hospitalization. Its typical symptoms and signs are fever and persistent dry cough. It has been reported that the overall incidence of MPP varies from 7.1% to 54.4% in China. Although it is a self-limited and benign condition, it still proceeds to severe complications, such as respiratory failure and hypoxia.

Considering that pediatric population with MPP are mostly under the phase of physical development, proper antibiotics are very important to manage this condition. Currently, macrolide antibiotics are the most commonly utilized medication for children with MPP. Studies have reported that erythromycin and amoxicillin/sulbactam (EAS) can effectively alleviate clinical symptoms, enhance lung function, and decrease the period of MPP in children. However, other study has also reported that EAS has limited efficacy and causes gastrointestinal adverse events. Additionally, it also results in pain on the local puncture site and phlebitis, which may lead to poor compliance in pediatric population.

Azithromycin is often recommended as the first choice to effectively perform bacteriostatic and bacteriological cleaning. It also has good tolerance and long half-life, which can reduce the management period. However, it still suffers from unsatisfied efficacy and high risk of drug resistance. Ceftizoxime is a highly resistant beta-lactam antibiotic, which is active against bacterial infections. Thus, azithromycin combined ceftizoxime (AC) is highly suggested as the advanced treatment for children with MPP.

Presently, there is insufficient evidence to compare the efficacy and safety of AC and EAS for the treatment of pediatric population with MPP. Therefore, this study aims to compare the
efficacy and safety of AC and EAS for the management of children with MPP.

2. Patients and methods

2.1. Ethical consideration

This retrospective study was approved by the Ethics Committee of The Second Affiliated Hospital of Mudanjiang Medical University. All patients provided written informed consent by their guardians.

2.2. Study design

This retrospective study analyzed a total of 92 eligible patient case records. All patients were performed between January 2018 and December 2019 at The Second Affiliated Hospital of Mudanjiang Medical University. They were assigned to a treatment group (n=46) and a control group (n=46). All patients in both groups received intravenous amoxicillin, and nebulized inhalation of budesonide and terbutaline. In addition, patients in the treatment group received AC, whereas subjects in the control group underwent EAS.

2.3. Patients

In this retrospective study, 92 patients with confirmed diagnosis of MPP by biochemical and imaging examinations according to the guideline of “Expert Consensus on the Diagnosis and Treatment of Mycoplasma Pneumoniae Pneumonia in Children (2015 Edition)” were included. In addition, patients were included if they had complete case record information; no treatment of hormone and antibiotics; aged between 3 and 10 years old; Mycoplasma pneumoniae (MP) antibody titer ≥1:160 or a single MP-IgM antibody positive; and provided written informed consent by their guardians.

Patients were excluded if they meet the following criteria: congenital immune dysfunction or deficiency; congenital heart disease, hereditary metabolic diseases; allergic to study medicine; abnormal function of liver or kidney; viral pneumonia, bacterial pneumonia, and tuberculosis; long-term use of immunosuppressive agents; no written informed consent was provided; and insufficient information of patient case records.

2.4. Treatment approach

All children in both groups received intravenous amoxicillin (15-30 mg/kg each time (depending on different ages), once daily), and budesonide and terbutaline (budesonide 1 mg and terbutaline 0.1 mg/kg, nebulized inhalation twice daily). All medications were administered for a total of 10 days.

In addition, patients in the treatment group received azithromycin (5-10 mg/kg, once daily for 5 days), and ceftizoxime (30 mg/kg, twice daily for a total of 10 days). Patients in the control group underwent erythromycin (10 mg/kg, once daily for a total of 10 days), and amoxicillin/sulbactam (30 mg/kg, twice daily for a total of 10 days).

2.5. Outcome measurements

Outcomes include serum factors (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum lactate dehydrogenase (LDH), and interleukin 6 (IL-6)), symptoms and signs (fever clearance time, time of cough disappearance, time of rale disappearance, time of signs disappeared by X-ray), and adverse events. All outcomes were measured after 10 days treatment.

2.6. Statistical analysis

This retrospective study utilized SPSS software (SPSSV.15.0, IBM Corp., Armonk, NY). All dichotomous data was presented as number and percentage, and was analyzed by χ2 test or Fisher exact test. All continuous data was estimated as mean and standard deviation, and was appraised by t test or Mann–Whitney U test. A value of 2-side P < .05 indicates statistical significance.

3. Results

A total of 92 eligible patients with MPP were included in this retrospective study. Of those, 46 patients who received AC were assigned to the treatment group, whereas the other 46 subjects who underwent EAS were assigned to the control group. We presented all patient characteristics and demographics in Table 1. There were not significant statistical differences in age (year), race, gender, body mass index (kg/m²), disease duration (day), leukocytes (10⁹/L), and platelets (10⁹/L) between 2 groups (Table 1).

Before treatment, there were not significant differences in ESR (P = .64), CRP (P = .48), LDH (P = .59), and IL-6 (P = .77) between 2 groups (Table 2). However, after 10-day treatment, children with MPP in the treatment group found more improvement in ESR (P < .01), CRP (P < .01), LDH (P < .01), and IL-6 (P < .01), than those of children in the control group (Table 3).

### Table 1

| Characteristic | Treatment group (n=46) | Control group (n=46) | P value |
|---------------|------------------------|---------------------|--------|
| Age (yr) | 6.5 (2.1) | 6.8 (2.4) | .52 |
| Race (Asian Chinese) | 46 (100.0) | 46 (100.0) | – |
| Gender | | | |
| Boy | 24 (52.2) | 27 (58.7) | .53 |
| Girl | 22 (47.8) | 19 (41.3) | .53 |
| BMI (kg/m²) | 15.2 (2.0) | 15.0 (2.3) | .66 |
| Disease duration (d) | 7.3 (1.9) | 7.6 (2.0) | .46 |
| Leukocytes (10⁹/L) | 10.7 (6.7) | 10.8 (7.0) | .94 |
| Platelets (10⁹/L) | 291.5 (115.4) | 292.0 (113.9) | .98 |

Data are present as mean ± standard deviation or number (%).

### Table 2

| Outcome measurements | Treatment group (n=46) | Control group (n=46) | P value |
|----------------------|------------------------|---------------------|--------|
| CRP (mg/L) | 29.8 (11.2) | 31.8 (13.4) | .48 |
| ESR (mm/h) | 52.4 (23.6) | 54.1 (21.9) | .64 |
| LDH (U/L) | 395.2 (115.7) | 408.5 (120.3) | .59 |
| IL-6 (pg/mL) | 7.7 (3.2) | 7.9 (3.4) | .77 |

Data are present as mean ± standard deviation.
After treatment, children who received AC also showed better efficacy in fever clearance time (P < .01, Table 4), time of cough disappearance (P < .01, Table 4), time of rale disappearance (P < .01, Table 4), and time of signs disappeared by X-ray (P < .01, Table 4), than those in children who received EAS.

In addition, there were not significant differences in incidence of each adverse event (local pain, P = .41; rash, P = .41; gastrointestinal reaction, P = .46; nausea, P = .46; vomiting, P = .65; Table 5), and total incidence of adverse events (P = .05, Table 5) between 2 groups.

4. Discussion

MP infection is the major pathogenic factor of MPP in pediatric population. Its incidence presents an increasing tendency in recent years. Macrolide antibiotics are the essential selected medications for the treatment of MPP. Of those, erythromycin is a frequent drug for patients with MP. Although, erythromycin alone can control the condition of MPP to a certain extent in pediatric population, its clinical efficacy is still limited, which may impact their prognosis. In addition, it may also accompany a variety of adverse events, such as gastrointestinal reactions, including nausea, vomiting, abdominal pain and diarrhea, especially for long-term administration. Fortunately, EAS are reported to have more powerful clinical efficacy and shorter treatment course for children with MPP.

Azithromycin is the other macrolide antibiotic, which has a good activity against MPP, and plays a very essential role in antimicrobial activity especially for the treatment of MPP in pediatric population. However, there is restricted clinical efficacy and drug resistance, which may affect its utilization to the clinical practice. Luckily, cefixime is reported to solve such issue. Thus, AC is found to be more effective intervention for children with MPP.

Studies report that azithromycin is superior to erythromycin in treating children with MPP. One study reported that the total effective rate of azithromycin was much higher than erythromycin in children with MPP. The other study found that azithromycin was much better than erythromycin in time of cough relief and rale in pediatric patients with MPP. In addition, study also reported the tolerance rates of azithromycin were less than those of erythromycin in treating MPP. However, there is still insufficient data to compare the clinical efficacy and safety of AC and EAS for the treatment of MPP in pediatric population.

The present study explored the efficacy and safety of AC compared with EAS in treating children with MPP. Our results are partly consistent with previous studies. The results of this study showed that patients in the treatment achieved better improvements in ESR, CRP, LDH, IL-6, fever clearance time, time of cough disappearance, time of rale disappearance, and time of signs disappeared by X-ray, than those of patients in the control group. It indicates that AC may be better than EAS for the treatment of children with MPP. In addition, there is a similar safety profile between 2 groups in this study.

This retrospective study still has several drawbacks. Firstly, this study was only conducted at 1 center of The Second Affiliated Hospital of Mudanjiang Medical University, which may restrict the generalization of its findings to other hospitals. Secondly, this retrospective study did not employ approach of randomization and blinding to both patients and investigators, which may cause risk of bias of study selection. Thirdly, this study only assessed short-term of 10-day treatment, and no further evaluation was performed in this study. Fourthly, this study only analyzed all outcome data at the time point of 10-day posttreatment, and no outcome data at other time points were collected and analyzed, because of insufficient information and incomplete data at other time points. Fifthly, the sample size of this study is relatively small, which may affect the present findings. Finally, the last limitation is a retrospective study in nature. Thus, future studies should avoid above limitations.

5. Conclusion

The results of the present study demonstrated that AC may exert more promising efficacy than EAS for the treatment of children with MPP.

### Author contributions

Conceptualization: Li-ping Han, Han-yan Xiao, Li-li Fang.
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