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Original Article

Effect of azithromycin combined with ambroxol in children with Mycoplasma pneumoniae pneumonia

Yan Ni[1], Meixin Fang[2], Juping Jiang[1], Qiongqing Lou[1], Licheng Wu[1], Zhiyun Liu[1]

[1]Department of Pediatrics, Fuyang District Hospital of Traditional Chinese Medicine of Hangzhou, Hangzhou 311400, Zhejiang, China; [2]Department of Hematology-Oncology, The Children's Hospital of Zhejiang University School of Medicine, National Clinical Research Center for Child Health, Hangzhou 310003, Zhejiang, China

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Abstract: Objective: This study was designed to investigate the clinical efficacy of azithromycin combined with ambroxol in children with Mycoplasma pneumoniae pneumonia (MPP). Methods: The clinical data of 103 children with MPP treated in Fuyang District Hospital of Traditional Chinese Medicine of Hangzhou from December 2020 to August 2021 were selected and retrospectively analyzed, and these children were divided into a control group (n=51, azithromycin treatment) and a study group (n=52, azithromycin plus ambroxol treatment) according to the different treatment methods. The immunoglobulin level, pulmonary function score, treatment efficacy, serum cytokine level, disappearance time of signs and symptoms, and myocardial enzyme indices were observed and compared between the two groups. Univariate and multivariate analyses were conducted to screen the factors affecting the prognosis of MPP patients. Results: After treatment, the study group showed significantly lower levels of immunoglobulin E, immunoglobulin G, immunoglobulin M and immunoglobulin A; higher pulmonary function scores, and lower levels of interleukin-6, human interferon-gamma, and monocyte chemoattractant protein-4 compared with the control group (all $P < 0.05$). The total incidence of adverse reactions such as nausea, diarrhea, abdominal pain, and vomiting was 15.38% in the study group, which was slightly lower than that in the control group (17.65%), exhibiting no significant difference ($P > 0.05$). The disappearance time of cough and lung rales, time required to restore to a normal body temperature, and hospital stay in the study group were shorter than those in the control group ($P < 0.05$). After treatment, aspartate aminotransferase, lactate dehydrogenase, creatine kinase, and creatine kinase isoenzyme in the study group were lower than those in the control group (all $P < 0.05$). The course of disease before admission, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), anemia, albumin < 30 g/L, drug initiation time, pulmonary consolidation, and complications involving multiple systems were the main factors affecting the efficacy of azithromycin combined with ambroxol in the treatment of MPP. Conclusion: Azithromycin combined with ambroxol can effectively improve the immunoglobulin level and lung function, reduce the level of inflammatory factors, improve the therapeutic effect, shorten the recovery process, and reduce the degree of myocardial damage, which is effective in the treatment of MPP and is worth promoting.

Keywords: Mycoplasma pneumoniae pneumonia, azithromycin, ambroxol, clinical efficacy, pulmonary function

Introduction

Mycoplasma pneumoniae pneumonia (MPP) is a common respiratory infection that mainly affects children because of their low immunity and underdeveloped organs and tissues [1]. Mycoplasma pneumoniae infection is a major cause of MPP, leading to pulmonary emphysema and pleural effusion, and in severe cases, it can affect the entire system and hinder physical development [2]. MPP can also induce a variety of extrapulmonary complications, including functional damage to the blood system, digestive system, and nervous system. In addition, pneumonia and bronchopneumonia in children mostly occur in closed environments such as families and schools and in places where people are concentrated, and there are no obvious restrictions on gender and season. However, due to the great differences in the climate and environment, the incidence of pediatric bronchopneumonia varies greatly in different regions of China. MPP is characterized by long course of disease and severe symptoms, while

early detection and treatment have a positive impact on prognosis [3]. Azithromycin is a macrolide drug commonly used in the treatment of MPP, with rapid absorption, good tissue distribution, acid resistance, and long half-life, but with long-term administration individuals can develop a resistance to it [4]. Ambroxol is an expectorant that facilitates sputum removal, relaxes the bronchial smooth muscle, and eliminates cough triggers [5]. Therefore, this study was designed to explore the clinical efficacy of azithromycin combined with ambroxol in children with MPP. This study comprehensively analyzed the effects of azithromycin combined with ambroxol on the levels of immunoglobulin, pulmonary function scores, serum cytokine levels, time to disappearance of signs and symptoms, and myocardial enzymes in children with MPP; as well as explored the factors affecting the prognosis of patients with MPP.

Materials and methods

General data

The clinical data of 103 children with MPP treated in Fuyang District Hospital of Traditional Chinese Medicine of Hangzhou from December 2020 to August 2021 were selected and retrospectively analyzed, and children were divided into a control group (n=51) and a study group (n=52) according to the different treatment methods. This study was approved by the Ethics Committee of Fuyang District Hospital of Traditional Chinese Medicine of Hangzhou (No. 2022001).

Inclusion criteria [6]: Children diagnosed as having MPP by imaging and laboratory tests and symptoms.

Exclusion criteria: Children with congenital immune disorders; contraindications to the study drugs; those who took hormones or immunomodulatory drugs two weeks before the study; those with viral or bacterial pneumonia; those with liver and kidney dysfunction.

Diagnostic criteria for MPP: 1. Clinical manifestations: Mainly fatigue, sore throat, headache, cough, fever, loss of appetite, diarrhea, myalgia, earache and other symptoms. Cough is mostly irritating, choking, coughing up a small amount of mucus. Fever can last for 2-3 weeks, cough may still occur after body temperature returns to normal, and a few patients present with severe pneumonia. Extrapulmonary manifestations are more common, including nausea, loss of appetite, vomiting, diarrhea and other digestive system manifestations, as well as arthralgia, myocarditis, pericarditis, hepatitis, peripheral neuritis, meningitis and skin maculopapular rash. 2. X-ray imaging manifestations: X-ray examination may show various forms of infiltrates in the lungs which are segmented and scattered with exudative lesions in both lungs. The lesions often dissipate spontaneously after 3-4 weeks, and some patients have a small amount of pleural effusion. 3. Blood test: The total number of white blood cells in the blood of patients with mycoplasma pneumonia is normal or slightly increased, being mainly neutrophils, and there may be decreased lymphocytes. The positive titer of laboratory cold agglutination test is $\geq$ 1:32, and if the titer gradually increases, it has more diagnostic value. In addition, the determination of serum mycoplasma immunoglobulin M (IgM) antibody can further confirm the diagnosis of mycoplasma pneumonia. If the double serum titer is 4 times higher in the acute phase and the recovery phase, it is positive, which has certain diagnostic significance for mycoplasma pneumonia. 4. Antigen test: Direct detection of Mycoplasma pneumoniae antigens in respiratory specimens can be used for early clinical rapid diagnosis. Although it has a low detection rate and high technical requirements, and it takes a long time for decisive diagnosis.

Methods

Both groups were given conventional treatments, including nutritional support, correction of electrolyte and acid-base disorders, oxygen inhalation, and expectoration.

Children in the control group were administrated Azithromycin for Injection (Hainan Beite Pharmaceutical Co., Ltd., H20067075, 0.5 g). Azithromycin (10 mg/kg) dissolved in 200 mL of 5% glucose solution was intravenously infused once a day for consecutive 7 days.

Children in the study group were additionally administrated Ambroxol hydrochloride (Jiangsu Hengrui Pharmaceuticals Co., Ltd., H19980178, 100 mL:0.3 g) on the basis of the treatment in the control group. Ambroxol was taken orally, 3 times a day, and the therapeutic efficacy was

observed for 7 days. According to the prognosis, the patients were divided into good prognosis and poor prognosis groups. Good prognosis: after 7 days of treatment, the symptoms including fever and cough disappeared completely or improved significantly but with temperature still higher than normal. Poor prognosis: after 7 days of treatment, the symptoms were not improved, or even aggravated, and the treatment plan needed to be adjusted.

Outcome measurements

Immunoglobulin levels [7]: Fasting morning venous blood (3 mL) was collected for centrifugation, and the immunoglobulin levels, including immunoglobulin E (IgE), immunoglobulin G (IgG), IgM, and immunoglobulin A (IgA) were detected using laser immunoturbidimetric method (Siemens).

Pulmonary function score [8]: Maximum expiratory flow at 50% vital capacity (MEF50), forced expiratory volume in 1 second (FEV1), the peak expiratory flow (PEF), and forced vital capacity (FVC) were determined using MasterScreen (Germany).

Treatment effect [9]: Markedly effective: fever and cough completely disappeared after treatment; effective: clinical signs and symptoms were significantly improved; ineffective: symptoms were not improved. Effective rate = (Markedly effective case + Effective case)/ Total case * 100%.

Serum cytokine levels [10]: The levels of interleukin-6 (IL-6), human interferon-gamma (IFN-γ), and monocyte chemoattractant protein-4 (MCP-4) were determined by enzyme-linked immunoassay using Thermo Multiskan Mk3 microplate reader (Art. No.: SP14708) before treatment and at 2, 5, and 7 days after treatment. The kits were provided by Wuhan Saipei Biotechnology Co., Ltd. (Art. No.: SP11988).

Adverse reactions: The incidence of nausea, diarrhea, abdominal pain, vomiting and nausea were recorded and compared between the two groups.

The disappearance time of signs and symptoms [11]: The disappearance time of cough and lung rales, time to return to normal body temperature, and hospitalization time were observed and compared between the two groups.

Myocardial enzyme indicators: Aspartate aminotransferase (AST), lactate dehydrogenase (LDH), creatine kinase (CK), and creatine kinase isoenzyme (CK-MB) were measured by enzyme-linked immunosorbent assay before treatment and at 2, 5, and 7 days after treatment. The kits were provided by Anhui IPROCOM Biotechnology Co., Ltd., (No.: 20160012).

Analysis of influencing factors: The factors that may affect the treatment effect and prognosis, including gender, age, course of disease before admission, body temperature > 38°C, fever course > 7 days, white blood cells (WBC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), anemia, albumin < 30 g/L, drug initiation time, pulmonary consolidation, and complications involving multiple systems were analyzed.

Statistical methods

Statistical Package for Social Science (SPSS) 22.0 software was used for data analysis, and GraphPad Prism 8 was used for figure plotting. The continuous variables with normal distribution were expressed as mean ± standard deviation (mean ± SD), the quantitative data in this study all conformed to a normal distribution, and independent sample t-test was used for comparison between two groups. Categorical variables were described as n (%), and chi-square test was used for comparison. Logistic regression analysis was used to screen the factors affecting the prognosis of patients. $P < 0.05$ indicated statistically significant differences.

Results

Comparison of general data

In the control group, there were 22 females and 29 males, with a mean age of 7.31±2.04 (ranged from 2-15) and a mean course of disease (6.94±2.33) days (ranged from 1-11). In the study group, there were 24 females and 28 males, with a mean age of 7.24±2.11 (ranged from 2-15) and a mean course of disease (6.73±2.29) days (ranged from 1-11). The general data of the two groups were comparable ($P > 0.05$).

Comparison of immunoglobulin levels

There was no significant difference in the levels of IgE, IgG, IgM, and IgA between the two

Table 1. Comparison of immunoglobulin levels ($\overline{x} \pm s$, g/L)

Groups	Number of cases	IgE		IgG		IgA		IgM	
		Before Treatment	After Treatment	Before Treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	51	0.51±0.13	0.49±0.08	10.91±1.43	10.36±1.21	1.98±0.36	1.75±0.15	1.73±0.27	1.58±0.19
Study group	52	0.58±0.16	0.39±0.07	11.04±1.46	9.98±1.23	1.96±0.38	1.53±0.16	1.72±0.29	1.21±0.09
t	/	1.739	6.755	0.456	1.580	0.274	7.196	0.181	12.669
P	/	0.085	< 0.001	0.649	0.117	0.785	< 0.001	0.856	< 0.001

IgE: Immunoglobulin E; IgG: Immunoglobulin G; IgA: Immunoglobulin A; IgM: Immunoglobulin M.

Table 2. Comparison of pulmonary function scores ($\overline{x} \pm s$)

Groups	Number of cases	MEF50 (%)		FEV1 (L)		PEF (L/min)		FVC (%)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After Treatment	Before treatment	After treatment
Control group	51	53.39±11.11	71.12±12.52	1.19±0.14	2.39±0.29	1.77±0.11	2.56±0.27	74.73±9.41	85.72±10.19
Study group	52	52.67±11.41	80.03±12.14	1.17±0.13	3.22±0.24	1.76±0.13	3.35±0.31	75.05±9.24	93.35±10.17
t	/	0.324	3.667	0.751	15.837	0.421	13.781	0.174	3.803
P	/	0.746	< 0.001	0.454	< 0.001	0.675	< 0.001	0.862	< 0.001

MEF50: Maximum Expiratory Flow at 50% Vital Capacity; FEV1: Forced Expiratory Volume In 1 Second; PEF: Peak Expiratory Flow; FVC: Forced Vital Capacity.

Table 3. Comparison of treatment efficacy [n (%)]

Groups	Number of cases	Markedly effective	Effective	Ineffective	Total effective rate
Control group	51	11 (21.57)	26 (50.98)	14 (27.45)	72.55%
Study group	52	25 (48.08)	24 (46.15)	3 (5.77)	94.23%
χ^2	/	/	/	/	8.783
P	/	/	/	/	0.003

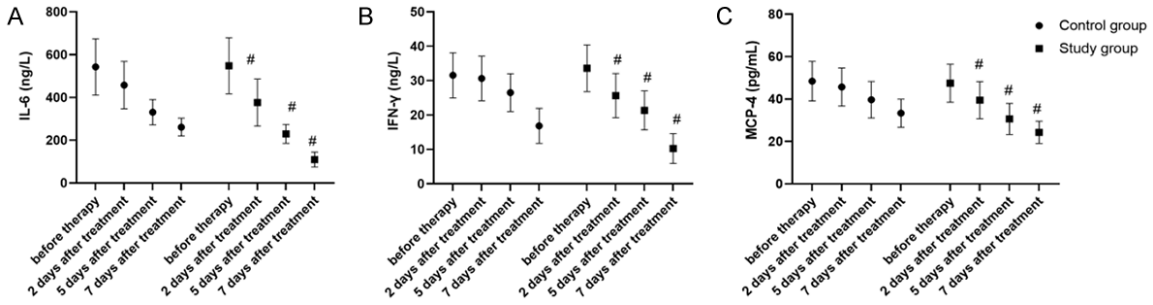

Figure 1. Comparison of serum cytokine levels. A: Interleukin-6 (IL-6); B: Interferon-gamma (IFN-γ); C: Monocyte chemoattractant protein-4 (MCP-4). The levels of IL-6, IFN-γ, and MCP-4 were significantly decreased in both groups after treatment, and were lower in the study group than in the control group ($P < 0.05$). Compared with the control group, $^{\#}P < 0.05$.

Table 4. Comparison of adverse reaction [n (%)]

Groups	Number of cases	Nausea	Diarrhea	Abdominal pain	Vomiting	Total effective rate
Control group	51	1 (1.96)	3 (5.88)	2 (3.92)	3 (5.88)	17.65%
Study group	52	1 (1.92)	2 (3.85)	3 (5.77)	2 (3.85)	15.38%
χ^2	/	/	/	/	/	0.096
P	/	/	/	/	/	0.757

groups before treatment (all $P > 0.05$). After treatment, the levels of IgE, IgG, IgM, and IgA in both groups were decreased compared with those before treatment, and the levels in the study group were significantly lower than those in the control group (all $P < 0.05$) (**Table 1**).

Pulmonary function scores

There was no significant difference in MEF50, FEV1, PEF, and FVC between the two groups before treatment (all $P > 0.05$). After treatment, the pulmonary function scores of the two groups were increased compared with those before treatment, and the scores in the study group were higher than those in the control group (all $P < 0.05$) (**Table 2**).

Comparison of treatment efficacy

The total effective rate of treatment was 94.23% in the study group, which was higher than 72.55% in the control group, exhibiting a significant difference ($P < 0.05$) (**Table 3**).

Comparison of serum cytokine levels

There was no significant difference in the levels of IL-6, IFN-γ, and MCP-4 between the two groups before treatment (all $P > 0.05$). At 2, 5, and 7 days after treatment, the levels of IL-6, IFN-γ, and MCP-4 in the two groups were decreased compared with those before treatment, and the levels in the study group were lower than those in the control group (all $P < 0.05$) (**Figure 1**).

Comparison of adverse reactions

The total incidence of adverse reactions such as nausea, diarrhea, abdominal pain, and vomiting was 15.38% in the study group, which was lower than 17.65% in the control group, exhibiting no significant difference ($P > 0.05$) (**Table 4**).

Table 5. Univariate analysis of the factors affecting prognosis of MPP patients

Factor	Poor prognosis group (n=45)	Good prognosis group (n=58)	χ^2/t	*P*
Gender (male/female)	24/20	33/26	0.020	0.889
Age (years)	7.26±2.12	7.29±2.09	0.072	0.943
Course of disease before admission (d)	6.73±2.29	3.24±1.02	10.367	< 0.001
Body temperature > 38°C	23 (51.11)	30 (51.72)	0.000	0.979
Fever course > 7 days	24 (53.33)	31 (53.45)	0.000	0.991
WBC (× 10^9/L)	8.81±1.36	8.38±3.11	0.865	< 0.001
CRP (mg/L)	19.82±3.05	24.83±5.62	5.392	< 0.001
ESR (mm/1 h)	28.35±3.71	35.81±4.02	9.659	< 0.001
Anemia	30 (66.67)	24 (41.38)	6.500	< 0.001
Albumin < 30 g/L	24 (53.33)	18 (31.03)	2.155	< 0.001
Drug initiation time (d)	5.61±1.32	4.35±1.02	5.467	< 0.001
Pulmonary consolidation	27 (60.00)	22 (37.93)	4.948	< 0.001
Complications involving multiple system	36 (80.00)	19 (32.76)	22.726	< 0.001

WBC: White Blood Cells; CRP: C-Reactive Protein; ESR: Erythrocyte Sedimentation Rate.

Table 6. Multivariate analysis of the factors affecting prognosis of MPP patients

Factor	SE	Regression coefficient	*Wald* χ^2	*P*	*OR*	*95% CI*	
						Lower limit	Upper limit
Course of disease before admission (d)	0.765	0.901	10.073	< 0.001	1.858	1.395	9.252
CRP (mg/L)	0.855	0.162	10.308	< 0.001	1.286	1.011	2.561
ESR (mm/1 h)	0.903	0.874	11.276	< 0.001	2.836	1.376	5.633
Anemia	1.213	1.291	9.891	< 0.001	3.768	1.142	5.896
Albumin < 30 g/L	1.239	1.021	10.522	< 0.001	4.396	1.875	7.852
Drug initiation time (d)	0.884	0.866	9.126	< 0.001	4.029	1.368	8.033
Pulmonary consolidation	0.875	0.953	10.661	< 0.001	3.805	1.235	3.653
Complications involving multiple system	0.967	1.102	9.457	< 0.001	3.166	1.066	6.833

CRP: C-Reactive Protein; ESR: Erythrocyte Sedimentation Rate; SE: Standard Error; OR: Odds Ratio; 95% CI: Confidence Interval.

Univariate analysis of the factors affecting the prognosis of MPP patients

The course of disease before admission, CRP, ESR, anemia, albumin < 30 g/L, drug initiation time, pulmonary consolidation, and complications involving multiple systems showed statistical difference between the good prognosis and poor prognosis groups (all $P < 0.05$, **Table 5**).

Multivariate analysis of the factors affecting the prognosis of MPP patients

The course of disease before admission, CRP, ESR, anemia, albumin < 30 g/L, drug initiation time, pulmonary consolidation, and complications involving multiple systems were the independent factors affecting the prognosis of MPP patients (all $P < 0.05$, **Table 6**).

Time to the disappearance of signs and symptoms

The time to the disappearance of cough and lung rales, time to return to normal temperature, and hospital stay in the study group were shorter than those in the control group (all $P < 0.05$) (**Figure 2**).

Comparison of cardiac enzyme indices

There was no significant difference in the levels of AST, LDH, CK, and CK-MB between the two groups before treatment (all $P > 0.05$). At 2, 5, and 7 days after treatment, the levels of AST, LDH, CK, and CK-MB in both groups were significantly reduced than those before treatment, and the levels in the study group were lower than those in the control group (all $P < 0.05$) (**Figure 3**).

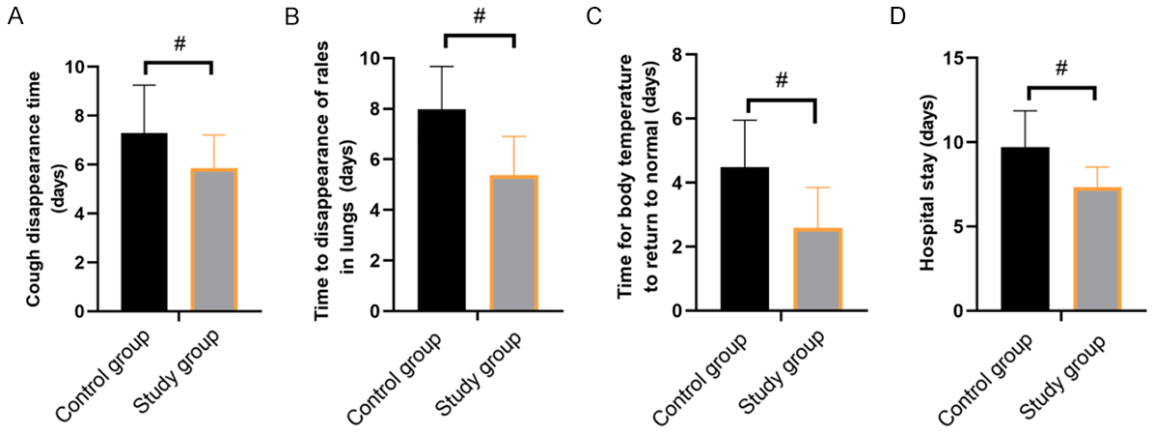

Figure 2. The disappearance time of signs and symptoms. A: Cough disappearance time; B: Time to disappearance of rales in lungs; C: Time to return to normal temperature; D: Hospital stay. The disappearance time of cough and lung rales, time to return to normal temperature, and hospital stay in the study group were shorter than those in the control group ($P < 0.05$). Compared with the control group, $^{\#}P < 0.05$.

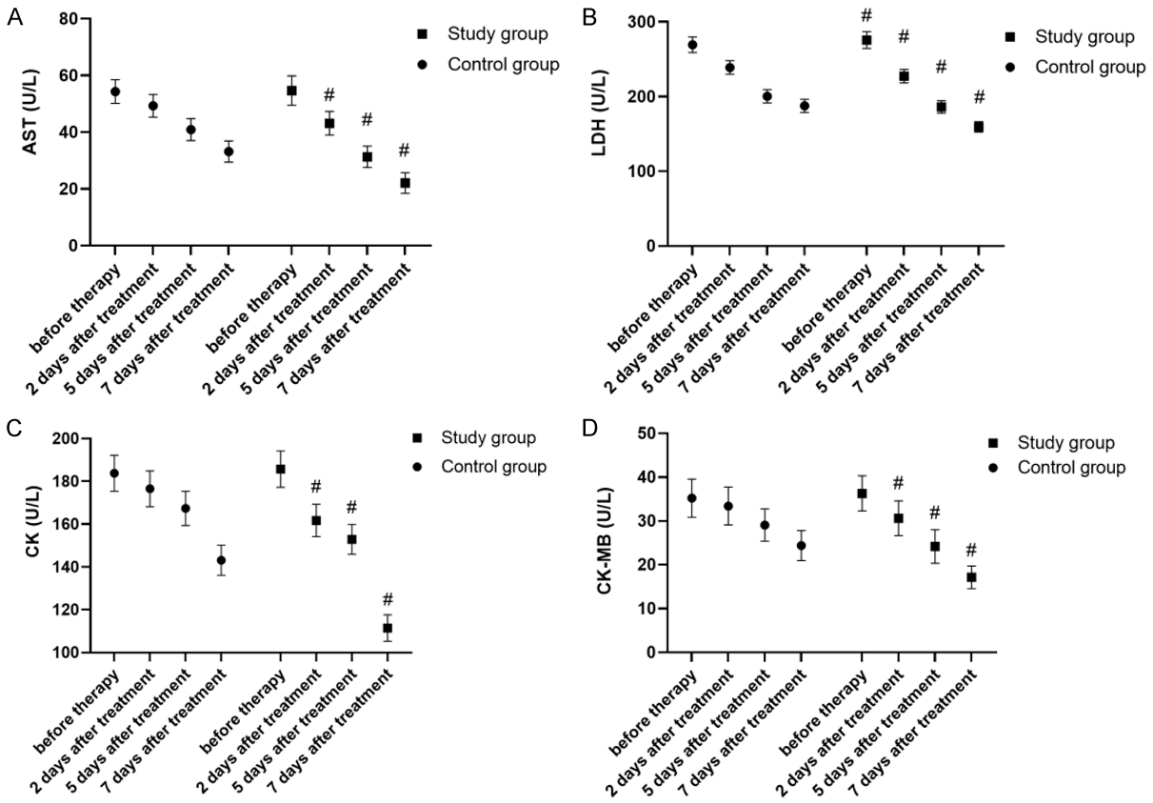

Figure 3. Comparison of cardiac enzyme indices. A: Aspartate aminotransferase (AST); B: Lactate dehydrogenase (LDH); C: Creatine kinase (CK); D: Creatine kinase isoenzyme (CK-MB). The levels of AST, LDH, CK, and CK-MB were significantly reduced in both groups after treatment, and were lower in the study group than in the control group ($P < 0.05$). Compared with the control group, $^{\#}P < 0.05$.

Discussion

MPP is a common pediatric disease characterized by sore throat, high fever, muscle pain, wheezing and cough, and it is also associated with risk of extra-pulmonary complications in children. The pathogenesis of MPP remains unclear, but it can impair organ function and lead to immune dysfunction and inflammation. MPP can be recurrent with a long course of

disease and affect the pulmonary function of children as well as cause hypoxia in the myocardial cells and affect the level of myocardial enzymes [12]. Therefore, it is vital to provide timely, effective and scientific treatment for children.

Azithromycin is a common antibiotic with high tissue permeability and higher drug concentrations in lungs or bronchus than in normal tissues. However, it has been shown in clinical practice that azithromycin alone is ineffective and individuals tend to develop resistance to it, and this prolongs the treatment cycle in children [13]. Moreover, it can cause myocardial damage to patients and reduce the safety of treatment.

Ambroxol is a common expectorant used in clinical practice, which has the characteristics of dissolving secretions, anti-inflammation, promoting the expelling of mucous sputum, and anti-oxidation properties. Meanwhile, it promotes the movement of cilia in the trachea, which facilitates the discharge of secretions. It can reduce alveolar surface tension and improve respiratory function. Moreover, ambroxol can inhibit the release of inflammatory mediators and reduce the degree of bronchial edema and alveolar epithelial damage in children.

MPP can lead to an immune response that alters the antigenic structure of host cells and leads to immune dysfunction. A study has shown elevated levels of IgM in children with MPP, and some scholars have found that the levels of immunoglobulins increase significantly in MPP children with severe immune response, and therefore aggravate the disease condition [14]. Another study has reported that children with refractory MPP have higher levels of immunoglobulins than normal children, confirming that MPP triggers immune dysfunction [15]. IgG is the most abundant immunoglobulin in the body, accounting for 75% of all immunoglobulins, and about 50% of them are distributed in the serum, mainly produced by the lymph nodes and spleen, which is known as the mainstay of the immune response. IgM cannot pass through the vascular walls and is mainly present in the blood. It is the earliest antibody that occurs in the primary immune response, known as the forerunner of the immune response. If IgM is detected in the serum, it may indicate a recent infection. Once the body is stimulated by an external source of infection, the levels of the above immunoglobulins increase rapidly, and when the infection in the body is effectively controlled, the serum levels gradually decrease. The results in this study showed that the levels of IgE, IgG, IgM, and IgA in the study group were lower than those in the control group after treatment, indicating that azithromycin combined with ambroxol can effectively improve the immunoglobulin levels of the children and facilitate their rehabilitation. It has been reported that the serum levels of IgG, IgA, and IgM were higher in children with MPP, especially in children with refractory MPP, which were higher than those in children with ordinary MPP, and humoral immune dysfunction was present in children [16]. Wu et al. found that serum levels of IgA, IgM, and IgE in the study group were higher than those in the control group, that is, the expression and secretion of immunoglobulins in MPP children were higher than those in healthy children [17]. In the hyperactivated state, the cellular hyperfunction and massive proliferation of B lymphocytes may be an important factor in triggering or exacerbating MPP.

AST, LDH, CK, and CK-MB are all cytoplasmic enzymes with varying degrees of activity in myocardial tissue. When myocardial tissue cells are damaged, the above-mentioned myocardial enzymes can be released from the myocardial cells into the blood, resulting in the presence of AST and CK-MB in the blood. The levels of myocardial enzymes such as LDH, CK, and CK-MB were increased, and combination of azithromycin and ambroxol improved the immune function [18, 19]. The results showed that the levels of AST, LDH, CK, and CK-MB in the study group were lower than those in the control group after treatment, indicating that the combination of two drugs can effectively alleviate the degree of myocardial injury and are beneficial for their early rehabilitation. Zhang et al. found that the combination of azithromycin and ambroxol could accelerate recovery of children with MPP [20], which was similar to the findings of this study. The reason may be that the combination of drugs not only protects the respiratory epithelium of children with MPP and improves respiratory reactivity, but also modulates the immune function of the children. The combination of drugs has strong anti-inflammatory effect and improves inflammatory damage [21]. The results of this study

showed that the MEF50, FEV1, PEF, and FVC in the study group were higher than those in the control group after treatment without increasing the incidence of adverse reactions, indicating that the combined treatment is more effective in improving the lung function of children with a good safety profile. The reason may be that the combination of drugs can effectively improve the pulmonary function in children with MPP while ensuring airway ventilation [22]. The inflammatory cytokines are mainly produced by macrophages or lymphocytes. It has been shown that IFN-γ is elevated in children with MPP compared with healthy children, and inflammatory factors such as IL-6 and IFN-γ are involved in the development of MPP [23]. It has been found that the imbalance of Th1/Th2 subpopulation is the main cause of inflammatory cell changes in children with MPP, and IL-6 is a cytokine of the Th2 subpopulation that induces an immune response and leads to an inflammatory cascade [24]. In contrast, IFN-γ is a cytokine of the Th1 subpopulation that activates macrophages [25]. MCP-4 plays a role in relieving immune inflammation damage [26]. It has been noted that the assessment of the above-mentioned indicators is beneficial to determining the effectiveness of treatment in children with MPP [27, 28]. The results of this study showed that the levels of IL-6, IFN-γ, and MCP-4 in the study group were lower than those in the control group after treatment, indicating that the combination of drugs can effectively improve the levels of inflammatory factors, which is conducive to the correct assessment of the treatment efficacy. The results also showed that the disappearance time of cough and lung rales, time to return to normal temperature, and hospital stay in the study group were shorter than those in the control group, indicating that the combined treatment can effectively accelerate the recovery. The reason may be that the combination of drugs has a synergistic effect. Ambroxol can increase the drug distribution concentration of azithromycin, improve the antibacterial effect, reduce the sputum secretion and the number of aspiration, thus reducing the damage to the respiratory tract; moreover, it can alleviate the symptoms of wheezing and cough and promote the rehabilitation of the children [29]. In this study, logistic regression was used to analyze various factors affecting the treatment effect and prognosis, and the results showed that the course of disease before admission, CRP, ESR, anemia, albumin < 30 g/L, drug initiation time, pulmonary consolidation, and complications involving multiple systems were the independent factors affecting the prognosis of MPP patients. Earlier visit and treatment are beneficial to the disease control and good prognosis. In addition, due to the severity of tissue damage in children with MPP, the degree of tissue damage can be judged by changes in CRP, but the severity of disease is not affected by gender and age. Changes in ESR index can be used to determine the erythrocyte sedimentation velocity. Children accompanied by severe infection may have a large number of erythrocyte aggregations, which affects the stability of ESR index. Albumin < 30 g/L indicates that nutritional indicators of children are not maintained in a reasonable range, which will affect the treatment effect in children. Furthermore, the presence of significant pulmonary consolidation indicates a more severe inflammatory response, which may increase the incidence of extrapulmonary complications and affect the prognosis of children.

There are a few areas for improvement in this study. The sample size was small and the study period was short which may greatly affect the accuracy of the study. Therefore, further studies with more eligible samples and longer study period are warranted to improve the accuracy of the study.

In conclusion, the combination of azithromycin and ambroxol can reduce the levels of immunoglobulin and inflammatory factors, improve the pulmonary function and therapeutic effect, shorten the recovery process, and reduce the degree of myocardial damage, which is effective in the treatment of MPP and is worth further promotion. In addition, the course of disease before admission, CRP, ESR, anemia, albumin < 30 g/L, drug initiation time, pulmonary consolidation, and complications involving multiple systems are independent factors that may affect the treatment effect and prognosis of children. Therefore, early and effective treatment is critical.

Disclosure of conflict of interest

None.

Address correspondence to: Yan Ni, Department of Pediatrics, Fuyang District Hospital of Traditional Chinese Medicine of Hangzhou, Hangzhou 311400,

Zhejiang, China. Tel: +86-13706815856; E-mail: amyni0327@163.com

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