Efficacy of Azithromycin Injection Combined with Levofloxacin Capsule and Ambroxol Injection in the Treatment of Mycoplasma Pneumonia

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Abstract
Objective: To investigate the clinical efficacy and safety of combining azithromycin injection with levofloxacin capsule and ambroxol injection for the treatment of Mycoplasma pneumonia. Methods: A total of 160 cases of patients with mycoplasma pneumonia were randomly assigned to either the control group or the experimental group, with 80 cases in each group. In the control group, azithromycin injection was administered at a dosage of 10 mg/kg once daily via intravenous drip. The experimental group received treatment based on the control group regimen, supplemented with levofloxacin capsules at a dosage of 0.2 g (2 capsules) twice daily and ambroxol injection at a dosage of 1.2-1.6 mg/(kg.d), given 2-3 times per day through slow intravenous injection lasting for 2-3 minutes. Both groups underwent a treatment duration of 7 days. Clinical efficacy, antipyretic time, cough extinction time, lung rales extinction time, and adverse drug reactions were compared between the two groups. Results: The test group exhibited an effective treatment rate of 88% for mycoplasma pneumonia, whereas the control group was 74%. The test group demonstrated significantly shorter durations for fever, cough, and lung rale disappearance compared to the control group. Conclusion: The combination of azithromycin, levofloxacin, and ambroxol significantly enhances the efficacy in treating mycoplasma pneumonia. It can further shorten improvement signs and has high safety. It is worth application for non-pediatric patients with mycoplasma infection.
1 Introduction

Mycoplasma pneumonia is an acute inflammation of the lung caused by Mycoplasma pneumoniae infection, a common respiratory tract infection [1-4]. Mycoplasma pneumonia accounts for more than 30% of non-bacterial pneumonia, or 10% of pneumonia caused by various causes, and its incidence is on the rise worldwide [5-8]. Mycoplasma pneumonia occurs more frequently in autumn and winter. The initial symptoms include fever, rhinorrhea, headache, general discomfort, myalgia, sore throat, loss of appetite and so on. After 2 to 3 days, dry cough began to appear, and then white sticky sputum could appear. Among them, more than 35% of patients need to be hospitalized for intervention [9]. In addition, the clinical manifestations of mycoplasma pneumonia infection are not typical, which are similar to the clinical symptoms of pharyngitis, bronchitis and other diseases. Especially for some elderly patients with complex underlying diseases, it is easy to cause missed diagnosis or misdiagnosis of mycoplasma pneumonia infection. At present, the laboratory detection of Mycoplasma pneumoniae mainly includes serum method, culture method and PCR detection method [10]. In clinical diagnosis, the combination of PCR detection method and serum method is recommended, and the comprehensive diagnosis is made based on the clinical symptoms of patients [10].

Mycoplasma pneumoniae is a prokaryotic cell organism without a cell wall and capable of self-replication. Therefore, mycoplasma pneumoniae is naturally resistant to β-lactam drugs. Mycoplasma pneumoniae can invade the epithelial cells of the respiratory system through the adhesion of some proteins, and induce excessive immune response in the body, which then damages the respiratory system tissue and causes inflammation [10,11]. Although Mycoplasma pneumoniae infection in the human body can produce certain antibodies, and the antibody duration can generally last 1-2 years. However, due to the overuse of antibiotics in the treatment and the differences between different serotypes of Mycoplasma pneumoniae, the level of antibodies is low and the protective effect is limited, and the phenomenon of repeated infection is easy to occur. The main drugs used in clinical treatment of mycoplasma pneumonia infection are erythromycin and azithromycin [12,13]. Among them, azithromycin belongs to the second generation of macrolide antibiotics, which has the advantages of rapid absorption, wide distribution, long half-life and high cell concentration. Related studies have shown that although the antibacterial mechanism of azithromycin and erythromycin against mycoplasma pneumonia pathogens is the same, the bioavailability, adverse reaction rate and stability in gastric acid of azithromycin are better than those of erythromycin [12]. Azithromycin can regulate and improve the immune function of children and destroy the protein synthesis reaction of mycoplasma pneumonia, which will reduce the damage caused by inflammation to the body tissue [14]. Therefore, azithromycin is one of the preferred drugs in the treatment of mycoplasma pneumonia in children [15,16]. Azithromycin and levofloxacin have the effect of treating mycoplasma pneumonia, and the effect is obvious. Ambroxol has the effect of promoting sputum excretion, improving respiration and repairing mucus secretion [17,18]. However, it is not clear whether the combination of the three drugs can shorten the course of disease, improve clinical symptoms, prognosis and safety in patients with mycoplasma pneumonia. Therefore, this study aims to investigate the clinical efficacy and safety of azithromycin injection combined with levofloxacin capsule and ambroxol injection in the treatment of mycoplasma pneumonia.
2 Materials and methods

2.1 Study design

This study was designed as a randomized, open, controlled, single-center clinical study.

2.2 General information

A total of 160 patients (84 males and 76 females) with mycoplasma pneumonia admitted to Luohe Central Hospital from January 2020 to December 2021 were selected as the research objects. Their age ranged from 18 to 65 years old. This study was approved by the Ethics Committee of Luohe Central Hospital, and all patients and their families signed informed consent. The control group of 80 patients (42 males and 38 females) aged 18-64 years old, with an average age of 40.29 ± 12.04 years old and a disease course of 4-10 days, with an average disease course of 5.96 ± 1.74 days. The Test group consists of 80 patients (42 males and 38 females) aged 22-65 years old, with an average age of 42.55 ± 11.62 years old and a disease course of 3-9 days, with an average disease course of 5.26 ± 1.43 days. There was no statistically significant difference in general information between the two groups (p > 0.05).

2.3 Exclusion criteria

Patients with serious primary diseases such as cardiovascular and cerebrovascular diseases, liver and kidney diseases and mental patients could not participate. Patients with severe lung diseases such as chronic obstructive pulmonary disease and lung cancer were excluded. Patients with drug intolerance could not participate.

2.4 Diagnosis and inclusion criteria

Diagnosis and inclusion criteria meet the diagnostic criteria for mycoplasma pneumonia in the Criteria for Diagnosis of Clinical Diseases and Judgment of Efficacy [3]: (1) Persistent fever for more than 1 week; (2) Cough as the prominent symptom, mostly severe cough, or paroxysmal irritating cough, with or without expectoration; (3) The lung signs were low, medium and fine wet rales or with dry rales on auscultation; (4) Mycoplasma pneumoniae detection (anti-MP-Ab in pharyngeal secretions and/or serum); (5) Chest DR or CT showed large patches of consolidation, occupying more than one lung segment or lobe, or single or multiple lobar lesions, pleural effusion, atelectasis, necrotizing pneumonia, etc.; (6) The temperature did not decrease or the lung imaging did not improve after standard use of macrolide antibiotics for more than 7 days; (7) Direct detection of Mycoplasma pneumoniae antigen in respiratory tract specimens can be used for rapid clinical diagnosis. Patients who met the above criteria were included in the observation.

2.5 Treatment options

A total of 160 patients were divided into experimental group and control group according to the random number table method, with 80 cases in each group. (1) The control group was given azithromycin injection 10 mg/kg, i.v QD intravenous drip; (2) On the basis of the treatment of the control group, the test group was given levofloxacin capsules 0.2 g once (2 capsules), 2 times a day and ambroxol injection: 1.2-1.6 mg/(kg.d), 2-3 times, within 2-3 minutes. Patients in both groups were treated for 7 days.

2.6 Efficacy evaluation criteria

Clinical efficacy: (1) Markedly effect: the symptoms and signs of the patients basically disappeared, Mycoplasma pneumoniae antigen in respiratory tract specimens basically disappeared, pharyngeal secretions and/or serum anti-MP-Ab turned negative within 7 days, X-ray examination showed that the lung shadow disappeared. (2) Effective: the symptoms and signs of the patients were improved, the Mycoplasma pneumoniae antigen in respiratory tract specimens partially disappeared, the pharyngeal secretions and/or serum anti-MP-Ab partially turned negative within 7 days, and the lung shadow partially
disappeared by X-ray examination. (3) No effect: there was no significant improvement in clinical symptoms, no significant change in Mycoplasma pneumoniae antigen in respiratory tract specimens, no change in pharyngeal secretions and/or serum anti-MP-Ab within 7 days, and no change in lung shadow on X-ray film. The total effective rate was calculated as (number of markedly effective cases + number of effective cases)/number of each group [5].

Adverse reactions: the drug-related adverse reactions and the number of patients in the two groups during the treatment were recorded.

The number of fever patients in the two groups and the number of days needed for fever to disappear were recorded.

The number of pulmonary rales and the disappearance time of pulmonary rales in the two groups were recorded.

The number of patients with cough and the time of cough disappearance in the two groups were recorded.

### 2.7 Statistical methods

SPSS20.0 was used for statistical analysis. Measurement data was expressed as Mean ± Standard Deviation and processed by student’s t test. Counting data was expressed by % and processed by χ² test. ρ < 0.05 was considered to indicate statistical significance.

### 3 Results

#### 3.1 Comparison of clinical efficacy between the two groups

According to the symptoms and signs after treatment and mycoplasma antigen in respiratory tract specimens, the therapeutic effect was divided into three grades: markedly effective, effective and ineffective. The total effective rate of the test group was 87.5%, and the total effective rate of the control group was 70%. The total effective rate of the test group was significantly higher than that of the control group (ρ < 0.05), and detailed results were shown in Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of cases</th>
<th>Number of apparent effect</th>
<th>Significant figure</th>
<th>Number of nullity</th>
<th>Total effective rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test group</td>
<td>80</td>
<td>54</td>
<td>16</td>
<td>10</td>
<td>87.5% (70/80)</td>
</tr>
<tr>
<td>Control group</td>
<td>80</td>
<td>42</td>
<td>14</td>
<td>24</td>
<td>70% (56/80)</td>
</tr>
</tbody>
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\[
χ^2 = 8.45
\]

\[
ρ < 0.05
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#### 3.2 Comparison of the disappearance time of typical clinical symptoms or signs between the two groups

As shown in Table 2, the extinction time of fever, cough and lung rales in the test group was significantly lower than that in the control group, and there were significant differences between the two groups (ρ < 0.05). The extinction time of lung rales in the test group was 2.66 ± 2.32 days, while that was 6.90 ± 2.48 days in the control group. The cough extinction time was 1.91 ± 0.62 days in the test group and 4.46 ± 1.21 days in the control group. The extinction time of fever was 2.93 ± 1.56 days in the test group and 5.23 ± 2.23 days in the control group.
3.3 Comparison of adverse reactions

The main adverse reactions of the two groups after treatment were loss of appetite, nausea and vomiting, abdominal pain and diarrhea. There were no serious complications such as allergy, liver and kidney function damage in the two groups. In the Test group, 2 patients had loss of appetite, 2 patients had nausea and vomiting, and 3 patients had abdominal pain and diarrhea. In the control group, the number of patients with loss of appetite was 5 people, the number of patients with nausea and vomiting was 4 people, and the number of patients with abdominal pain and diarrhea was 4 people. As shown in Table 3, there were seven patients with adverse reactions in the Test group, accounting for 8.75% of the total number of patients in the test group, and thirteen patients with adverse reactions in the control group, accounting for 11.25% of the total number of patients in the control group. There was a significant difference between the two groups ($\rho < 0.05$).

4 Discussion

Mycoplasma pneumonia, also known as primary atypical pneumonia, is a kind of atypical pneumonia, which is caused by mycoplasma infection [19], accounting for more than 30% of non-bacterial pneumonia. Mycoplasmal pneumonia usually has a small amount of inflammatory exudate in the alveoli, may occur focal atelectasis, emphysema, and consolidation, and may cause tonsillitis, rhinitis, tracheitis, bronchiolitis, otitis media, and pneumonia. Mycoplasma pneumonia is one of the important pathogens of respiratory tract infection [2,20]. Antibiotic treatment of mycoplasma pneumonia is the main clinical strategy [21].

Azithromycin is currently widely used as the first-line drug for the treatment of mycoplasma pneumonia [22,23]. Expect it, azithromycin has a wide range of antibacterial activities against pneumococcus, staphylococcus aureus, anaerobic bacteria, gram-negative bacteria, gram-positive bacteria, and has a certain inhibitory effect on chlamydia pneumoniae, chlamydia humanoid and chlamydia trachomatis [24]. Nevertheless, long-term use of azithromycin can increase the incidence of adverse...
reactions in different tissues of patients, such as skin, respiratory, digestive and nervous systems [25]. In addition, due to the abuse of antibiotics, macrolide-resistant mycoplasma pneumoniae has emerged in the clinic, which greatly reduces the efficacy of conventional antibiotic therapy. Studies have found that compared with macrolide antibiotics, levofloxacin, a fluoroquinolone antibiotic, not only has good antibacterial activity against mycoplasma pneumoniae, but also has good penetration into lung tissue, with a higher intracellular concentration in phagocytes, and a higher effective drug concentration can be obtained at the site of respiratory tract infection after entering the body [18]. In this study, it was found that on the basis of azithromycin treatment, the experimental group with ambroxol injection and oral levofloxacin capsules had a total effective rate of 87.5% in the treatment of mycoplasma pneumonia, while the control group with only azithromycin treatment had a total effective rate of 70% (Table 1). This result is consistent with the previous report that levofloxacin combined with azithromycin can significantly improve the therapeutic effect of mycoplasma pneumonia [26-28].

Ambroxol hydrochloride has the properties of dissolving sticky phlegm. When treated with ambroxol hydrochloride, the secretion of mucus can return to normal, cough and sputum volume are usually significantly reduced, and the surfactant on the respiratory mucosa can thus exert its normal protective function [17]. In the present study, it was found that the extinction time of fever, cough and lung rale in the azithromycin combined with levofloxacin and ambroxol hydrochloride treatment group was significantly lower than that in the control group (Table 2). It indicated that this treatment strategy can significantly improve the efficacy of mycoplasma pneumonia. This treatment strategy focuses on the advantages of three drugs: azithromycin for the treatment of mycoplasma pneumonia, levofloxacin combined with azithromycin to kill other bacterial infections, ambroxol to promote sputum excretion, improve respiration, restore normal mucus secretion, and increase the concentration of azithromycin and levofloxacin in the lungs. It is important to note that levofloxacin cannot be used to treat mycoplasma pneumonia in children, and thus the treatment regimen in this study is not applicable to pediatric patients. This study showed that on the basis of azithromycin treatment in the control group, ambroxol injection and oral levofloxacin capsule, the antipyretic time, lung rales disappearance time and cough disappearance time were significantly better than those in the control group. Moreover, the incidence of adverse reactions after treatment in the test group was significantly lower than that of control group.

In conclusion, the combination of azithromycin, levofloxacin, and ambroxol significantly enhances the efficacy in treating mycoplasma pneumonia. It can further shorten improvement signs and has high safety. Therefore, azithromycin combined with levofloxacin capsules and ambroxol injection for injection has certain application value in the treatment of pneumonia caused by mycoplasma infection, and it is worthy of clinical promotion in non-pediatric patients with mycoplasma infection.

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Conflicts of Interest
The authors declare no competing interests.
Author Contributions
R.W. contributed to the conception of conceptualized the study; R.M., Z.W. and Q.S. performed the data analysis and wrote the manuscript experiments; R.M. contributed significantly to the analysis and reagents, materials and data analysis manuscript preparation; R.M. wrote the first draft of the manuscript. All authors read the manuscript and agreed to its contents.

Ethics Approval and Consent to Participate
This study was approved by Medical Ethics Committee, and patients were informed and agreed.

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Availability of Data and Materials
The analyzed data sets generated during the study are available from the corresponding author on reasonable request.

Supplementary Materials
Not applicable.

References


