Efficacy of different antibiotics in treatment of children with respiratory mycoplasma infection

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Abstract

BACKGROUND
Respiratory infections in children are common pediatric diseases caused by pathogens that invade the respiratory system. Children are considerably susceptible to *Mycoplasma pneumoniae* infection. There has been widespread clinical attention on treatment strategies for this disease.

AIM
To analyze the clinical efficacy of different antibiotics in treating pediatric respiratory mycoplasma infections.

METHODS
We included 106 children with a confirmed diagnosis of respiratory mycoplasma infection who were admitted to our hospital from April 2017 to July 2019 and grouped them using a random number table. Among them, 53 children each received clarithromycin or erythromycin. The clinical efficacy of both drugs was evaluated and compared. We performed the multiplex polymerase chain reaction (MP-PCR) test and determined the MP-PCR negative rate in children after the end of the treatment course. We compared the incidence of toxic and side effects, including nausea, diarrhea, and abdominal pain; further, we recorded the length of hospitalization, antipyretic time, and drug costs. Additionally, we evaluated and compared the compliance of the children during treatment.

RESULTS
The erythromycin group showed a significantly higher total effective rate of...
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Clinical treatment than the clarithromycin group. MP-PCR test results showed that the clarithromycin group had a significantly higher MP-PCR negative rate than the erythromycin group. Moreover, children in the clarithromycin group had shorter fever time, shorter hospital stays, and lower drug costs than those in the erythromycin group. The clarithromycin group had a significantly higher overall drug adherence rate than the erythromycin group. The incidence of toxic and side effects was significantly lower in the clarithromycin group than in the erythromycin group ($P < 0.05$).

CONCLUSION
Our findings indicate that clarithromycin has various advantages over erythromycin, including higher application safety, stronger mycoplasma clearance, and higher medication compliance in children; therefore, it can be actively promoted.

Key Words: Clarithromycin; Erythromycin; Mycoplasma respiratory infection; Children; Clinical efficacy; Drug compliance; Toxic side effects

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Core tip: This study aimed to explore the efficacy of different antibiotics for treating respiratory mycoplasma infection in children. Compared with erythromycin, clarithromycin showed numerous advantages, including high safety, a strong mycoplasma clearance rate, and high drug compliance.

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INTRODUCTION
Respiratory infections in children are common pediatric diseases caused by pathogens that invade the respiratory system. Given that children have worse lung and immune function than adults, they are more susceptible to infection with *Mycoplasma pneumoniae*, are more susceptible to disease after infection, have difficulty in breathing, and experience respiratory failure or critical illness[1]. Epidemiological studies have suggested that respiratory infections are among the main mortality causes in children in China[2]. Pediatric mycoplasma infections are common pediatric respiratory infections observed in clinical practice[3], with their proportion among non-bacterial pneumonia cases reaching $> 30\%$[4]. There has been widespread clinical attention on the treatment of these infections.

Currently, erythromycin is the most commonly used drug for treating pediatric mycoplasma infection and efficiently kills mycoplasma[5]; however, it has numerous disadvantages regarding gastrointestinal adverse reactions[6-8]. An additional disadvantage is that its main administration route is intravenous. During drug administration, children are prone to resist treatment given their young age and a strong sense of fear; consequently, medication compliance is low[9,10].

With the development of modern medicine, clarithromycin has been gradually applied to treat mycoplasma infection-related diseases[11]. Moreover, studies have reported that it is better and safer for clinical treatment than erythromycin[9,10,12,13]. We aimed to perform a comprehensive review to investigate the clinical utility of clarithromycin for treating pediatric respiratory mycoplasma infection.
MATERIALS AND METHODS

Baseline data
From April 2017 to July 2019, we included 106 children with mycoplasma respiratory infections. All children met the diagnostic criteria for mycoplasma respiratory infection based on the Chinese Expert Consensus for Laboratory Diagnosis of Mycoplasma pneumoniae respiratory infections.

The inclusion criteria were as follows: (1) Aged 3–12 years; (2) Having positive multiplex polymerase chain reaction (MP-PCR) test results; (3) Presenting with fever, cough, and other symptoms; (4) Their guardians understanding the treatment plan after voluntary enrollment; (5) No previous history of drug allergy; and (6) Having normal intellectual development as well as no typical mental retardation or mental developmental disability manifestations.

The exclusion criteria were as follows: (1) Having conditions that simultaneously affect the lungs, heart, kidneys, and other organs or sexually transmitted diseases; (2) Experiencing meningitis and sepsis; (3) Having incomplete information for checking the basic information; (4) Failing to complete the treatment course, being transferred from the hospital, or requesting to withdraw from the study; and (5) Not meeting any of the aforementioned inclusion criteria.

Based on a random number table, 106 children were assigned to either a clarithromycin (n = 53) or an erythromycin group (n = 53). There was no significant between-group difference in the baseline data (P > 0.05). Table 1 presents details regarding the data and corresponding test values. This study was approved by the ethics committee of our hospital after comprehensive assessment, including drug safety and research significance evaluation.

Methods
After admission, all the children were allowed to rest on a bed, provided with water and electrolyte balance correction solutions, administered with oxygen as appropriate to maintain the airway open, and provided with ice/wet towels to cool down.

Erythromycin group: Children in this group were treated using erythromycin, which was provided by Northeast Pharmaceutical Group Shenyang First Pharmaceutical Co., Ltd. (National Drug Standard H21022427; intravenous drip, 10-15 mg/kg per time, 2 times/day, and continuous administration for 14 d).

Clarithromycin group: Children in this group were treated using clarithromycin, which was provided by Baiyunshan Pharmaceutical General Factory of Guangzhou Baiyunshan Pharmaceutical Group Co., Ltd. (National Medicine Standard H20063961; 5-10 mg/kg per time, 2 times per day, and continuous administration for 14 d).

Observation indicators
After 14 d of treatment, we obtained a deep throat swab; the PCR test was performed to record the results.

Efficacy evaluation
Efficacy was classified as follows: (1) Significant effect: After treatment completion, MP-PCR test results turned negative with the disappearance of clinical symptoms, including cough and fever; (2) Effective: After treatment, MP-PCR test results were positive but with significant improvement of serum mycoplasma antibody and immunoglobulin M levels and X-ray examination results as well as cough and other symptoms; and (3) Invalid: MP-PCR test results were positive without improvement or with worsening of clinical symptoms and various test results. The total clinical effectiveness rate was calculated as (total number of cases-invalid cases)/total number of cases × 100%.

The medication status of children was obtained using the Morisky medication compliance questionnaire. For children who were young and could not accept the questionnaire, it was completed by the parents. Based on the grading results, 8 points were considered as full compliance, 6 points ≤ score < 8 points as compliance, and < 6 points as non-compliance. The medication compliance rate was calculated as (number of complete compliance cases + number of compliance cases)/total number of cases × 100%.

Moreover, we recorded the antipyretic time, length of hospital stay, and medication costs and calculated the incidence of nausea and diarrhea during the treatment of children.
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Table 1 Baseline data comparison between the clarithromycin group and the erythromycin group, n (%)

| Baseline data     | Clarithromycin group (n = 53) | Erythromycin group (n = 53) | χ²/t | P value |
|-------------------|-------------------------------|----------------------------|------|---------|
| Gender            |                               |                            |      |         |
| Male              | 28 (52.83)                    | 29 (54.72)                 |      | 0.641   | 0.423   |
| Female            | 25 (47.17)                    | 24 (45.28)                 |      |         |
| School            |                               |                            |      |         |
| Kindergarten      | 11 (20.75)                    | 10 (18.87)                 |      | 0.111   | 0.739   |
| Primary school    | 38 (71.70)                    | 37 (69.81)                 |      | 0.086   | 0.769   |
| Junior high school| 4 (7.55)                      | 6 (11.32)                  |      | 0.832   | 0.362   |
| Age               | 6.74 (1.25)                   | 6.83 (1.22)                |      | 1.050   | 0.862   |

Statistical analysis
Statistical analyses were performed using SPSS 23.0 software. Measurement data are presented as the mean ± SD measurement and were compared using t test. Count data are presented as percentages and were compared using χ² test. Statistical significance was set at P < 0.05

RESULTS

Between-group comparison of MP-PCR test results
As shown in Figure 1, the clarithromycin group showed a significantly higher MP-PCR negative rate than the erythromycin group (χ² = 11.427, P = 0.001).

Efficacy evaluation of the two groups
As shown in Table 2, the clarithromycin group showed a significantly higher total clinical effective rate than the erythromycin group (P < 0.05).

Between-group comparison of hospitalization time, drug cost, and antipyretic time
The clarithromycin group showed a significantly lower hospitalization time, antipyretic time, and drug cost than the erythromycin group (P < 0.05; Table 3).

Between-group comparison of side effects
As shown in Table 4, the clarithromycin group showed a significantly lower incidence of toxic and side effects than the erythromycin group (P < 0.05).

Between-group comparison of drug compliance
As shown in Table 5, the clarithromycin group showed a significantly higher compliance rate than the erythromycin group (P < 0.05).

DISCUSSION
We evaluated the efficacy of erythromycin and clarithromycin for treating respiratory mycoplasma infection in children. Our findings indicated that clarithromycin had various advantages over erythromycin, including higher application safety, stronger mycoplasma clearance, and higher medication compliance.

Human immunity gradually increases with age until the age of 35 years, peaking at the age of 22–35 years, and subsequently decreasing with age. Given the immature body development in children, they have relatively low immune function and are vulnerable to pathogen infection. Therefore, respiratory tract infections are more common in children than in adults. Studies have shown that respiratory infections caused by the invasion of various pathogens are among the main childhood mortality causes in China.

Mycoplasma belongs to a class of pathogens that infect viruses and bacteria. Epidemiological studies have shown that with the modernization process in China, there has been an increase in the urban population, population density, and risk of
multiple pathogen infections; accordingly, there has been an annual increase in the rate of mycoplasma-caused respiratory infections in children. Children with respiratory mycoplasma infections present with fever, headache, and cough. Failure to administer timely interventions can result in critical illnesses, including respiratory failure, which can seriously endanger the physical and mental health of children.

Currently, the main treatment for mycoplasma respiratory infections is antibiotic treatment, which involves drug interventions for suppressing and killing pathogens in children. For many years, a treatment regimen based on macrolide antibiotics has been used in clinical practice [14-16]. Macrolide antibiotics strongly affect protein synthesis in pathogens by blocking 50 S ribosome endopeptide acyltransferase activity in the pathogens, which quickly kills the pathogens. Therefore, significant therapeutic effects can be achieved in bacterial infection treatment [17].

Erythromycin and clarithromycin are both macrolide antibiotics, with the former being a first-generation macrolide antibiotic. Erythromycin has been used for many years in clinical practice and has been widely applied to treat respiratory mycoplasma infection in children. However, it has high toxicity and side effects, and causes poor metabolic capacity in children, which makes them prone to various gastrointestinal reactions after drug administration. Clarithromycin is a 14-ring semisynthetic derivative of macrolides that is similar to erythromycin and has good oral absorption. The peak blood concentration occurs within 2 h of clarithromycin administration; moreover, it has a higher drug bioavailability than erythromycin. The peak blood concentration of clarithromycin can be more than twice that of erythromycin. Further,
the half-life of clarithromycin is approximately 4–5 times that of erythromycin, with reduced gastrointestinal tract irritation and few toxic side effects[18-20].

In our study, the clarithromycin group had a significantly higher negative rate of MP-PCR and overall clinical effectiveness, as well as a significantly lower incidence of side effects ($P < 0.05$) than the erythromycin group. This indicates that clarithromycin has better clinical application than erythromycin. Moreover, compared with erythromycin, clarithromycin was less toxic, had fewer side effects, and had better safety. The clarithromycin group had a significantly shorter hospitalization length and antipyretic time than the erythromycin group ($P < 0.05$), which indicates that clarithromycin allows faster symptom relief and a better pathogen inhibitory effect than erythromycin. In addition, the clarithromycin group showed a significantly lower drug cost ($P < 0.05$), indicating that clarithromycin has higher bioavailability, and thus requires a relatively lower dosage with a concomitant reduction in the drug cost than erythromycin. Additionally, clarithromycin has great economic benefits.

In addition, the clarithromycin group showed a significantly higher compliance rate than the erythromycin group ($P < 0.05$). Generally, rational cognition in children is incomplete; accordingly, children are prone to fear intravenous injections in the clinical treatment process and are likely to show resistance. Clarithromycin is generally orally administered, which effectively solves the aforementioned problem. Children may have low compliance, including resistance and crying, during intravenous administration. Studies have reported the clinical efficacy of erythromycin and clarithromycin in children with respiratory mycoplasma infections. These previous findings have indicated that clarithromycin has a higher total effective rate and a lower incidence of adverse reactions than erythromycin, which is consistent with our findings and further confirms that clarithromycin has more application advantages than erythromycin.

CONCLUSION
In summary, different antibiotics for treating clinical mycoplasma respiratory infections in children have different treatment outcomes. Clarithromycin is superior to erythromycin with respect to its application, safety, and economic benefits; accordingly, it can be preferentially selected over erythromycin.

ARTICLE HIGHLIGHTS

Research background
Children are more susceptible to infection with *Mycoplasma pneumoniae*. At the same time, they are more susceptible to disease after infection and have difficulty breathing and can experience respiratory failure or critical illness. The treatment of this disease has received widespread clinical attention.

Research motivation
To search drugs that can replace erythromycin in the treatment of respiratory tract
infections in children.

**Research objectives**
This study aimed to analyze the clinical efficacy of different antibiotics in the treatment of pediatric respiratory mycoplasma infection.

**Research methods**
One hundred and six children diagnosed with respiratory mycoplasma infection were included in this study. The clinical efficacy was evaluated and compared between groups. The compliance of children during treatment was evaluated and compared between groups.

**Research results**
The total effective rate of clinical treatment of children in the clarithromycin group was significantly higher than that in the erythromycin group. The incidence of toxic and side effects in the clarithromycin group was significantly lower than that in the erythromycin group, and the above data comparisons were statistically significant.

**Research conclusions**
Clarithromycin has a variety of advantages over erythromycin, such as higher application safety, stronger mycoplasma clearance, and higher medication compliance in children, and can be actively promoted.

**Research perspectives**
Clarithromycin is superior to erythromycin in terms of application effect, safety, and economic benefits and can be preferentially selected.

**REFERENCES**

1. Mathur S, Fuchs A, Bielicki J, Van Den Anker J, Sharland M. Antibiotic use for community-acquired pneumonia in neonates and children: WHO evidence review. *Paediatr Int Child Health* 2018; 38: S66-575 [PMID: 29790844 DOI: 10.1080/20469047.2017.1409455]

2. Brown N, Kuika AJ, Mårtensson A. Efficacy of zinc as adjunctive pneumonia treatment in children aged 2 to 60 months in low-income and middle-income countries: a systematic review and meta-analysis. *BMJ Paediatr Open* 2020; 4: e000662 [PMID: 32685705 DOI: 10.1136/bmjpo-2020-000662]

3. Tagliabue C, Tchassensiri C, Torres JP, Katz K, Meek C, Kannan TR, Coalsjon JJ, Esposito S, Principi N, Leff R, Basevan JB, Hardy RD. Efficacy of increasing dosages of clarithromycin for treatment of experimental Mycoplasma pneumoniae pneumonia. *J Antimicrob Chemother* 2011; 66: 2323-2329 [PMID: 21791441 DOI: 10.1093/jac/dkr306]

4. Gentile D, Raymond J, Moulin F, Iniguez JL, Ravilly S, Habib P, Lebon P, Califa G. Etiology and response to antibiotic therapy of community-acquired pneumonia in French children. *Eur J Clin Microbiol Infect Dis* 1997; 16: 388-391 [PMID: 9228482 DOI: 10.1007/BF01726370]

5. Ruhrmann H, Bleik H. [Erythromycin vs amoxicillin for the treatment of pneumonia in children (author's transl)]. *Infection* 1982; 10 Suppl 2: S86-S91 [PMID: 7049959 DOI: 10.1007/BF01640862]

6. Nascimento-Cardalho CM, Souza-Marques HH. [Recommendation of the Brazilian Society of Pediatrics for antibiotic therapy in children and adolescents with community-acquired pneumonia]. *Rev Panam Salud Publica* 2004; 15: 380-387 [PMID: 15272984 DOI: 10.1590/s1020-49892004000600003]

7. Han R, Yu Q, Zhang G, Li B, Han S, Li G. Comparison of azithromycin and erythromycin in the treatment of mycoplasma pneumonia in children. *Pak J Med Sci* 2020; 36: 156-159 [PMID: 32063951 DOI: 10.12669/pjms.36.2.1441]

8. Vasilos LV, Rumel' NB, Shchuka SS. [Chemotherapeutic effectiveness of erythromycin, rifampicin and tetracyclines in chlamydiosis and mycoplasmosis in children]. *Antibiot Khimioter* 1995; 40: 40-42 [PMID: 8593094]

9. Lee PI, Wu MH, Huang LM, Chen JM, Lee CY. An open, randomized, comparative study of clarithromycin and erythromycin in the treatment of children with community-acquired pneumonia. *J Microbiol Immunol Infect* 2008; 41: 54-61 [PMID: 18327427]

10. Alvarez-Elcoro S, Enzler MJ. The macrolides: erythromycin, clarithromycin, and azithromycin. *Mayo Clin Proc* 1999; 74: 613-634 [PMID: 10377939 DOI: 10.4065/74.6.613]

11. Block S, Hedrick J, Hammerschlag MR, Cassell GH, Craft JC. Mycoplasma pneumoniae and Chlamydia pneumoniae in pediatric community-acquired pneumonia: comparative efficacy and safety of clarithromycin vs. erythromycin ethylsuccinate. *Pediatr Infect Dis J* 1995; 14: 471-477 [PMID: 7667050 DOI: 10.1097/00006454-199506000-00002]

12. Chien SM, Pichotta P, Siepman N, Chan CK. Treatment of community-acquired pneumonia. *A...
multicenter, double-blind, randomized study comparing clarithromycin with erythromycin. Canada-Sweden Clarithromycin-Pneumonia Study Group. Chest 1993; 103: 697-701 [PMID: 8449054 DOI: 10.1378/chest.103.3.697]

13 Schönwald S, Gunja M, Kolacny-Babić L, Car V, Gosev M. Comparison of azithromycin and erythromycin in the treatment of atypical pneumonias. J Antimicrob Chemother 1990; 25 Suppl A: 123-126 [PMID: 2154431 DOI: 10.1093/jac/25.suppl_a.123]

14 Langtry HD, Brogden RN. Clarithromycin. A review of its efficacy in the treatment of respiratory tract infections in immunocompetent patients. Drugs 1997; 53: 973-1004 [PMID: 9179528 DOI: 10.2165/00003495-199753060-00006]

15 Fujii R, Meguro H, Arimasu O, Hiruma F, Sugamata K, Sugie N, Higa A, Shinozaki T, Abe T, Sunagawa K. [Bacteriological, pharmacokinetic and clinical studies on clarithromycin in the pediatric field. Pediatric Study Group of Clarithromycin]. Jpn J Antibiot 1989; 42: 512-541 [PMID: 2526259]

16 Ogura H, Kubota H, Nomura I, Tomoda T, Araki K, Ogura Y, Kurashige T. [Clinical efficacy of clarithromycin in the field of pediatrics]. Jpn J Antibiot 1989; 42: 401-410 [PMID: 2526253]

17 Rogozinski LE, Alverson BK, Biondi EA. Diagnosis and treatment of Mycoplasma pneumoniae in children. Minerva Pediatr 2017; 69: 156-160 [PMID: 28178776 DOI: 10.23736/S0026-4946.16.04866-0]

18 Watanabe K, Otabe K, Shimizu N, Komori K, Mizuno M, Katano H, Koga H, Sekiya I. High-sensitivity virus and mycoplasma screening test reveals high prevalence of parvovirus B19 infection in human synovial tissues and bone marrow. Stem Cell Res Ther 2018; 9: 80 [PMID: 29587847 DOI: 10.1186/s13287-018-0811-7]

19 Nishimura T, Tabuki K, Aoki S, Takagi M. [Laboratory and clinical studies of clarithromycin in pediatric fields]. Jpn J Antibiot 1989; 42: 353-369 [PMID: 2526248]

20 Ito S, Mayumi M, Mikawa H. [Clinical evaluation of clarithromycin in pediatric patients]. Jpn J Antibiot 1989; 42: 343-351 [PMID: 2526247]
