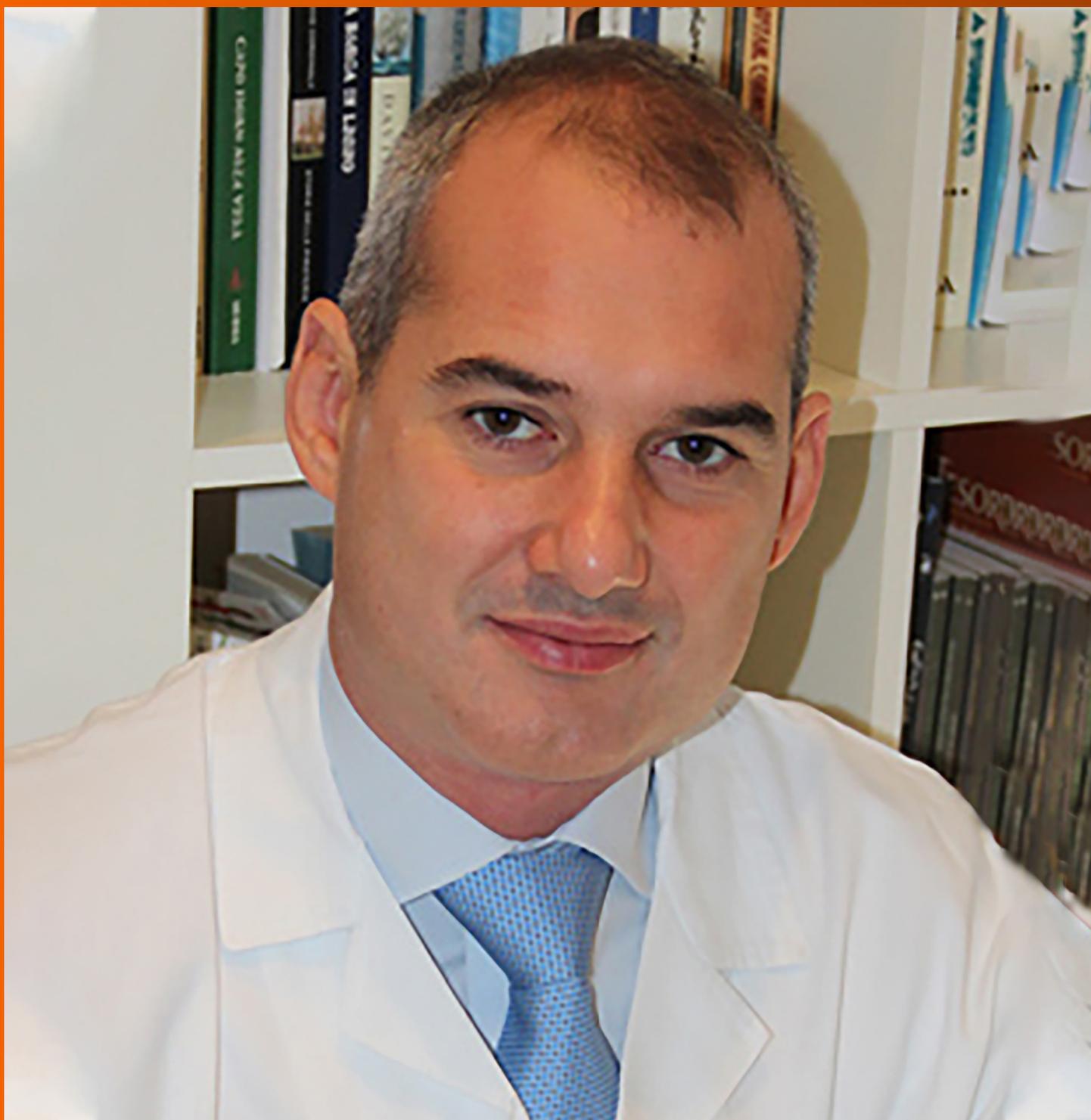


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**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: *Jia-Hui Li*; Production Department Director: *Xiang Li*; Editorial Office Director: *Jin-Lei Wang*.

**NAME OF JOURNAL**

*World Journal of Clinical Cases*

**ISSN**

ISSN 2307-8960 (online)

**LAUNCH DATE**

April 16, 2013

**FREQUENCY**

Thrice Monthly

**EDITORS-IN-CHIEF**

Dennis A Bloomfield, Sandro Vento, Bao-Gan Peng

**EDITORIAL BOARD MEMBERS**

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

**PUBLICATION DATE**

August 16, 2021

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<https://www.wjgnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

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**ONLINE SUBMISSION**

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## Retrospective Study

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

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**Author contributions:** Zhang MY and Zhao Y designed the study; Liu JF drafted the work; Liu GP and Zhang RY collected the data; Zhang MY analyzed and interpreted the data; Zhang MY, Zhao Y, and Wang LM wrote the article.

**Institutional review board statement:** The study was reviewed and approved by the Qingdao Municipal Hospital Institutional Review Board.

**Informed consent statement:** Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

**Conflict-of-interest statement:** The authors declare that there is no conflict of interest to disclose.

**Data sharing statement:** No additional data are available.

**Open-Access:** This article is an

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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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**Manuscript source:** Unsolicited manuscript

**Specialty type:** Respiratory system

**Country/Territory of origin:** China

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

**Received:** March 2, 2021

**Peer-review started:** March 2, 2021

**First decision:** April 4, 2021

**Revised:** April 6, 2021

**Accepted:** May 15, 2021

**Article in press:** May 15, 2021

**Published online:** August 16, 2021

**P-Reviewer:** Printz C

**S-Editor:** Wang JL

**L-Editor:** Wang TQ

**P-Editor:** Wang LL



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.

**Citation:** Zhang MY, Zhao Y, Liu JF, Liu GP, Zhang RY, Wang LM. Efficacy of different antibiotics in treatment of children with respiratory mycoplasma infection. *World J Clin Cases* 2021; 9(23): 6717-6724

**URL:** <https://www.wjgnet.com/2307-8960/full/v9/i23/6717.htm>

**DOI:** <https://dx.doi.org/10.12998/wjcc.v9.i23.6717>

## 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  $\times 100\%$ .

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  $\leq$  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  $\times 100\%$ .

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.

**Table 1** Baseline data comparison between the clarithromycin group and the erythromycin group, *n* (%)

Baseline data	Clarithromycin group ( <i>n</i> = 53)	Erythromycin group ( <i>n</i> = 53)	$\chi^2/t$	<i>P</i> value
Gender			0.641	0.423
Male	28 (52.83)	29 (54.72)		
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  $\pm$  SD measurement and were compared using *t* test. Count data are presented as percentages and were compared using  $\chi^2$  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 ( $\chi^2 = 11.427$ , *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

**Table 2 Comparison of the total clinical effectiveness in the clarithromycin group and the erythromycin group, *n* (%)**

Group	Number of cases	Invalid	Effective	Marked effect	Total clinical effectiveness
Clarithromycin group	53	2 (3.77)	19 (35.85)	32 (60.38)	51 (96.23)
Erythromycin group	53	13 (24.53)	22 (41.51)	18 (33.96)	40 (75.47)
$\chi^2$	-	17.739	0.675	14.005	17.739
<i>P</i> value	-	0.001	0.411	0.001	0.001

**Table 3 Hospital stay time, drug cost, and antipyretic time of the clarithromycin group vs the erythromycin group (mean  $\pm$  SD)**

	Clarithromycin group ( <i>n</i> = 53)	Erythromycin group ( <i>n</i> = 53)	<i>t</i>	<i>P</i> value
Hospital stays (d)	15.14 $\pm$ 2.01)	20.63 $\pm$ 3.15	10.696	0.001
Drug cost (Yuan)	1654.63 $\pm$ 100.21	2152.14 $\pm$ 163.48	18.889	0.001
Antipyretic time (d)	2.63 $\pm$ 0.57	4.06 $\pm$ 0.75	11.051	0.001

**Table 4 Toxic side effects of the clarithromycin group compared with the erythromycin group, *n* (%)**

Group	Number of cases	Stomach ache	Diarrhea	Nausea	Other	Incidence of side effects
Clarithromycin group	53	2 (3.77)	1 (1.89)	2 (3.77)	3 (5.66)	8 (15.09)
Erythromycin group	53	8 (15.09)	7 (13.21)	10 (18.87)	11 (20.75)	36 (67.92)
$\chi^2$	-	7.502	9.179	11.357	9.934	57.479
<i>P</i> value	-	0.006	0.002	0.001	0.002	0.001

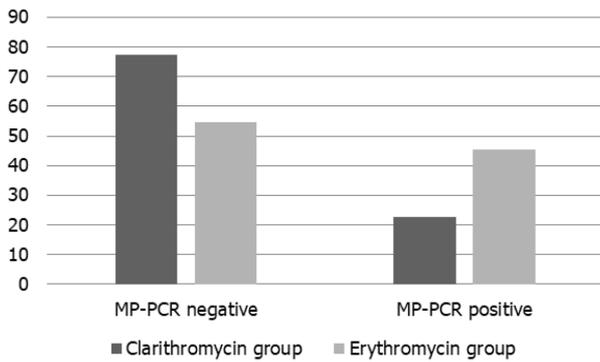
**Table 5 Comparison of medication compliance between the clarithromycin group and the erythromycin group, *n* (%)**

Group	Number of cases	Full compliance	Obey	Disobey	Medication compliance
Clarithromycin group	53	40 (81.13)	12 (22.64)	1 (1.89)	52 (98.11)
Erythromycin group	53	18 (33.96)	20 (37.74)	15 (28.30)	38 (71.70)
$\chi^2$	-	45.537	5.409	27.211	27.211
<i>P</i> value	-	0.001	0.020	0.001	0.001

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,



**Figure 1 Comparison of multiplex polymerase chain reaction negative conversion rate between the clarithromycin group and the erythromycin group.** MP-PCR: multiplex polymerase chain reaction.

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.

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