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Research Article

Efficacy and Safety of Methylprednisolone Combined with Azithromycin in The Treatment of Children with Refractory Mycoplasma Pneumonia

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Abstract

Purpose: To investigate the efficacy of methylprednisolone combined with azithromycin in the treatment of refractory mycoplasma pneumonia in children. **Methods:** A total of 66 pediatric patients with refractory mycoplasma pneumonia received treatment in our hospital from May 2013 to December 2015 were selected and divided into control group and experimental group according to different treatment regimens. In addition to the same conventional symptomatic and supportive treatment, the control group was given intravenous infusion of azithromycin, and the experimental group was given methylprednisolone and azithromycin. After treatment, the efficacy of the two groups was observed. **Results:** After the above treatment, the efficacy of the experimental group was significantly better than that of the control group ($P < 0.05$); the hospital stay and body temperature returned to normal time of the experimental group were significantly lower than that of the control group ($P < 0.05$); CRP levels in both groups were significantly decreased, but the decrease was more significant in the experimental group, significantly lower than that of the control group ($P < 0.05$). **Conclusion:** Treatment of refractory mycoplasma pneumonia in children with methylprednisolone combined with azithromycin is safe and reliable and has the value of promotion and application.

Key words: Azithromycin, Mycoplasma pneumoniae refractory, Methylprednisolone.

1. Introduction

Mycoplasma pneumoniae has become one of the common pathogens of lower respiratory tract infections in children (1), and the incidence of mycoplasma pneumonia is increasing year by year

(2). Early studies suggested that mycoplasma pneumonia is self-limiting and most children will gradually improve without the need for specific treatment (3). However, recent studies have found that the incidence of refractory mycoplasma pneumonia (RMPP) is significantly increased, which may lead to extrapulmonary complications and progress to severe life-threatening pneumonia in children, making its treatment more difficult (3). In recent years, some children with RMPP have been treated with methylprednisolone and azithromycin in our hospital with good results.

2. Materials and methods

2.1 Materials

A total of 66 pediatric patients with refractory mycoplasma pneumonia received treatment in our hospital from May 2013 to December 2015 were selected. According to the criteria of clinical diagnosis and treatment guidelines for mycoplasma pneumonia, these patients met the diagnosis of mycoplasma pneumonia. Inclusion criteria for subjects(4): 1). Complicated with pulmonary interstitial fibrosis, pleural effusion, atelectasis, bronchiectasis or extrapulmonary complications. 2). Patients who fail to respond after one week of macrolide therapy. Criteria for exclusion of subjects: 1). History of corticosteroid use within the last three months. 2). Patient with tuberculosis. 3). The patient's family is unwilling to use hormone therapy. The children were divided into a control group (n = 33) and an experimental group (n = 33) according to the diagnostic criteria. This study has been approved by the Ethics Committee of the hospital and informed written consent from the parents of the children. The experimental group consisted of 15 females and 18 males, aged 4 – 13 years, with a mean age of (8.9 ± 2.3) years. The control group included: 14 females and 19 males, aged 3 – 14 years, with a mean age of (9.2 ± 2.2) years. There was no significant difference in age, gender, and other basic data between the two groups ($P > 0.05$), so statistical comparison could be made.

2.2 Methods

Both groups were given symptomatic and supportive treatment such as correction of acid-base balance disorder and conventional oxygen inhalation. The control group was given intravenous infusion of 10 mg/kg azithromycin aspartate once a day for 3 days; intravenous injection of 1.5 g/kg gamma globulin once a day for 3 days; intravenous injection of 10 mg/kg rifampicin for 12 hours/time for 48 hours. After 3 days of treatment, the drug was discontinued for 4 days, and then the patient was switched to Azithromycin (batch number: GYZZ H10980217) 10 mg/kg, which was produced by Shijiazhuang Ouyi Pharmaceutical Co., Ltd., once a day for 3 days, then discontinued for 4 days. One cycle was 7 days, and the treatment was continued for 3 cycles (5). In the experimental group, methylprednisolone (batch No.: H20110063) produced by Pfizer. ItaliaSrl was added to the above treatment regimen at a dose of 2 mg/kg/day. After 5 days of treatment, the dose was reduced to 1 mg/kg/day for 2 days(6).

2.3 Observation indicators

1). To observe the length of hospital, stay, the time of body temperature returning to normal, adverse reactions and C-reactive protein (CRP) levels before and after treatment. In the early morning, 2ml of cubital vein blood was collected from the patient under fasting state and placed in a vacuum test tube. After serum separation, the level of CRP was measured by immunoturbidimetry. 2). Efficacy evaluation. Significant effective evaluation criteria: cough symptoms disappeared, body temperature returned to normal, pulmonary rales and wheezing sounds disappeared, and chest X-ray lung shadow disappeared. Evaluation criteria for effective treatment: cough symptoms were significantly

relieved, body temperature was significantly decreased, pulmonary rales and wheezing sounds were significantly reduced, and chest X-ray showed significant absorption of pulmonary shadows; evaluation criteria for ineffective treatment: clinical symptoms and signs were not relieved, or there were aggravated conditions, and chest X-ray showed no absorption or increase of shadows. In this article, Significant effect and effectiveness are used as clinical effectiveness (7).

2.4 Data analysis

The data were analyzed and processed using SPSS 24.0 software, and the measurement data were expressed as (± s) and the enumeration data were expressed as percentage (%), $P < 0.05$, with statistical significance, and the comparison between groups was performed by t or chi-square test.

3. Results

3.1 Clinical Efficacy

After treatment, the clinical efficacy of the experimental group was significantly better than that of the control group ($P < 0.05$), Table 1.

Table 1: Inter-group comparison of clinical efficacy (n = 33, %).

Group	Significant effect	Effectiveness	Treatment futility	Effective rate of treatment (%)
Experimental	21	11	1	97.0
Control	14	13	6	81.8
X^2	-	-	-	12.19
P	-	-	-	<0.05

3.2 Treatment Results

The hospital stays and temperature recovery time of patients in the experimental group were significantly lower than those in the control group ($P < 0.05$). After treatment, the CRP levels in both groups decreased significantly, but the decrease was more significant in the experimental group, which was significantly lower than that in the control group ($P < 0.05$),Table 2.

Table 2: Comparison of treatment outcomes between the two groups.

Group	**CRP（mg/L）**		**Average hospitalization time(d)**	**Body temperature recovery time** (h)
	Before treatment	**Post-treatment**		
Experimental	69.2±22.3	13.2±5.6	9.6±2.3	7.5±1.6
Control	67.5±22.7	29.5±10.3	12.5±2.2	11.5±2.1
t	0.31	-7.99	-5.23	-8.70
p	>0.05	<0.05	<0.05	<0.05

3.3 Adverse reactions

In the experimental group, no serious adverse reactions occurred during the treatment, only 1 case showed facial flushing, and 1 case showed mild euphoria, which were relieved spontaneously.

4. Discussion

At present, the pathogenesis of refractory mycoplasma pneumonia is not clear in clinical practice, so there is no unified standard for the treatment of this disease in clinical practice(8). In the past, appropriate antibiotics were used for continuous treatment for 7 days, but the results were often unsatisfactory. According to related studies,

RMPP can be characterized by hypercytokinemia, including elevated interleukin 4 (IL-4), IL-2, IL-10, etc., and elevated urinary β2 microglobulin, lactate dehydrogenase, CRP and ferritin, suggesting that RMPP may be associated with severe cellular inflammatory reactions (9). Azithromycin, a macrolide antibiotic, has a broad antibacterial spectrum, especially against Mycoplasma pneumoniae, aerobic gram-positive bacteria, Streptococcus pneumoniae and so on. As a medium-potency glucocorticoid, methylprednisolone has a strong anti-infective effect, regulates inflammatory response and immune response by inhibiting inflammatory cytokines and lipid-mediated products, so as to promote the improvement of clinical symptoms (10). In this study, the results after treatment with azithromycin and methylprednisolone in the experimental group showed that the effective rate of treatment in the experimental group was significantly higher than that in the control group ($P < 0.05$), and the hospital stay and temperature recovery time of the patients were significantly lower than those in the control group ($P < 0.05$). This shows that the use of methylprednisolone adjuvant therapy can effectively promote the relief of symptoms in patients with RMPP, shorten the course of disease, significant effect. During the treatment period, no significant adverse reactions were observed in the experimental group. This treatment regimen has high safety and can be applied to the treatment of pediatric patients.

CRP is an acute protein produced by the body in response to infection or trauma, which can directly reflect the degree of RMPP inflammatory response(9). The results of this study showed that CRP significantly decreased after treatment in the experimental group and was significantly lower than that in the control group ($P < 0.05$), indicating that methylprednisolone combined with azithromycin treatment could significantly reduce the inflammatory response and promote the rehabilitation process.

5. Conclusion

In summary, methylprednisolone combined with azithromycin treatment in children with RMPP can promote the improvement of clinical symptoms, with reliable efficacy and high safety, which is of value for further study.

Declarations

1) ***Consent to publication***
We declare that all authors agreed to publish the manuscript at this journal based on the signed Copyright Transfer Agreement and followed publication ethics.
2) ***Ethical approval and consent to participants***
Yes.
3) ***Disclosure of conflict of interests***
We declare that no conflict of interest exists.
4) ***Funding***
None
5) ***Availability of data and material***
We declare that the data supporting the results reported in the article are available in the published article.
6) ***Authors' Contributions***
Authors contributed to this paper with the design (JHP and JH), literature search (JHP and

JH), drafting (JHP and JH), revision (JHP and JH and LCL), editing (JHP and LCL) and final approval (JHP and LCL).

7) ***Acknowledgement***

None

8) Authors' biography

None

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