

Macrolide use shortens fever duration in *Mycoplasma pneumoniae* infection in children: a 2-year experience

Ying-Jen Lu¹, Tou-Hwei Chen¹, Lung-Huang Lin¹, Chung-Min Shen¹,
Ceng-Hua Huang²

Departments of ¹Pediatrics and ²Infection, Cathay General Hospital, Taipei, Taiwan

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Background and Purpose: *Mycoplasma pneumoniae* infection is a major cause of community-acquired respiratory tract infection in children. We performed a retrospective study to evaluate clinical and demographic data and compare outcomes with and without macrolide treatment in children with *M. pneumoniae* infection.

Methods: A total of 139 patients were included in the study and classified into two groups according to whether or not they received macrolide therapy during hospitalization. Data collected included demographic, clinical and laboratory characteristics.

Results: Cases were most prevalent during September. Fever and cough were the most common presenting symptoms/signs. The time to fever subsidence did not differ significantly between azithromycin and erythromycin usage. We also found significantly longer fever duration in the group without macrolide usage.

Conclusion: Treatment with macrolide shortens fever duration of *M. pneumoniae* infection in children.

Key words: Agglutinins; Azithromycin; Erythromycin; Immunoglobulin M; *Mycoplasma pneumoniae*

Introduction

Mycoplasma pneumoniae infection is a major cause of community-acquired respiratory tract infection in children. Proper treatment with macrolides shortens the duration of infection and decreases the severity of symptoms [1]. *M. pneumoniae* is notoriously difficult to culture in the microbiological laboratory [2]. Because of the lack of a commercial polymerase chain reaction (PCR) kit in widespread use, serology remains the most frequently used diagnostic method for *M. pneumoniae* infection [3]. We performed a retrospective study to evaluate the characteristics of *M. pneumoniae* infection in children and compare groups with and without macrolide usage.

Corresponding author: Dr. Lung-Huang Lin, Department of Pediatrics, Cathay General Hospital, College of Medicine, Fu-Jen Catholic University, Taipei, Taiwan.
E-mail: LHLINLH@yahoo.com.tw

Methods

Patients

The medical records of children admitted to Cathay General Hospital, Taipei during the period from January 1, 2004 to December 31, 2005 with positive *M. pneumoniae* immunoglobulin M antibodies during hospitalization were reviewed and were included in the study. The SeroMP EIA (Savyon Diagnostics, Ashdod, Israel) is a semiquantitative indirect microtiter enzyme-linked immunosorbent assay for the detection of *M. pneumoniae*-specific immunoglobulin M antibodies and was considered positive at ≥ 20 BU/mL, with sensitivity of 95% and specificity of 100%. The antigen used is a membrane preparation of *M. pneumoniae* that contains the P1 membrane protein. Patients were excluded if they had concomitant bacteremia, or positive urine pneumococcus antigen. Patients were classified into two groups according to whether they received

macrolides or not during hospitalization. There were 74 patients receiving azithromycin therapy (10 mg/kg/day for 3 days) and 5 patients receiving erythromycin therapy (40 mg/kg/day for 7 days). Data collected included age, gender, clinical symptoms and signs, initial white blood cell count and C-reactive protein level, serum cold agglutinin titer, duration of fever and chest radiographic findings.

Statistical analysis

Data were presented as mean \pm standard deviation and numbers of patients (%). Unpaired *t* test and Statistical Package for the Social Sciences (SPSS) for Windows (Version 10.0; SPSS, Chicago, IL, USA) software package were used for all analyses. A *p* value of ≤ 0.05 was considered statistically significant.

Results

139 children, ranging in age from 8 months to 142 months, were included in the study and all of them had fever during admission. Cases were most prevalent during September; the seasonal distribution of cases is shown in Fig. 1. Serum cold agglutinin titer was also checked in 99 patients (71.2%) and was positive ($\geq 1:32$) in 48 patients (34.5%). Comparison of age, gender, clinical symptoms and signs, initial white blood cell count and C-reactive protein level, duration of fever and chest radiographic findings are shown in Table 1. We found significantly longer fever duration in the group without macrolide use. There was no statistically significant difference in the duration of fever between patients receiving azithromycin and erythromycin (mean \pm standard deviation [SD], 1.92 ± 1.37 and 2.2 ± 0.84 , respectively; $p=0.416$).

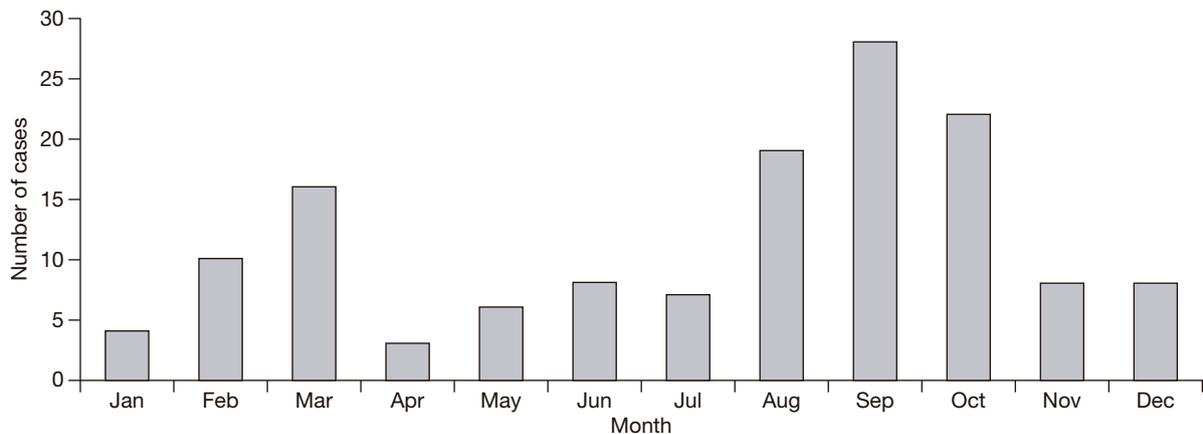


Fig. 1. Seasonal distribution of 139 cases of *Mycoplasma pneumoniae* infection in children (2004-2005).

Discussion

M. pneumoniae infection is a major cause of community-acquired respiratory tract infection in children. In children 5 to 15 years of age, a macrolide antibiotic is the most reasonable first choice, unless the child appears to have sepsis or the chest radiograph shows lobar infiltrates (with or without effusion) [4]. The age group most commonly affected by *M. pneumoniae* infection was 5 to 9 years, followed by children aged 1 to 5 years [5]. In our study, 70 patients (50.4%) were younger than 5 years of age, 58 patients (41.7%) were 5 to 9 years of age and 11 patients (7.9%) were older than 9 years of age. A few investigators have reported a peak incidence in the fall (autumn) [6], and our study showed similar findings. This is not surprising, since late summer and fall coincide with the time of return to schools.

In our study, fever (100%) and cough (100%) were the most common symptom/signs in both groups, as has been documented in other studies [7]. Gastrointestinal symptoms/signs were not apparent, again in agreement with other studies [8]. A wide variety of transient dermatologic manifestations have been reported with *M. pneumoniae* infection, including macules, morbilliform and papulovesicular eruptions as well as erythema nodosum and urticaria [9]. We observed two patients with urticaria. The role of antibiotic therapy in the development of exanthems seen during *M. pneumoniae* infection is unknown [10]. The association between *M. pneumoniae* infection and erythema multiforme or Stevens-Johnson syndrome is also well documented [11,12], but we did not find any case of erythema multiforme or Stevens-Johnson syndrome.

Table 1. Comparison of demographic, clinical and laboratory characteristics in children with *Mycoplasma pneumoniae* infection with and without macrolide treatment

| Variable | With macrolide (n = 79) No. (%) | Without macrolide (n = 60) No. (%) | p |
|--|------------------------------------|---------------------------------------|-------|
| Gender | | | |
| Male | 41 (51.9) | 32 (53.3) | |
| Female | 38 (48.1) | 28 (46.7) | |
| Age (months; mean \pm SD) | 56.6 \pm 30.5 | 49.4 \pm 31.9 | 0.181 |
| Duration of fever (days; mean \pm SD) | 4.90 \pm 1.89 | 5.63 \pm 2.22 | 0.037 |
| White blood cell count (μ L; mean \pm SD) | 9827 \pm 4476 | 9313 \pm 4417 | 0.501 |
| C-reactive protein (mg/dL; mean \pm SD) | 3.12 \pm 3.40 | 2.92 \pm 3.79 | 0.745 |
| Symptoms/signs | | | |
| Cough | 79 (100.0) | 60 (100.0) | |
| Coryza | 50 (63.3) | 37 (61.7) | 0.846 |
| Sore throat | 21 (26.6) | 15 (25.0) | 0.834 |
| Skin rash | 1 (1.3) | 1 (1.7) | 0.846 |
| Headache | 12 (15.2) | 10 (16.7) | 0.815 |
| Vomiting | 7 (8.9) | 5 (8.3) | 0.913 |
| Diarrhea | 4 (5.1) | 3 (5.0) | 0.987 |
| Pleural effusion on chest radiograph | 9 (11.4) | 7 (11.7) | 0.960 |

Abbreviation: SD = standard deviation

Cold agglutinin titer usually appears by the end of the first week of *M. pneumoniae* infection and disappears 2 to 3 months later. Approximately 30-75% of patients with *M. pneumoniae* infection will have positive cold agglutinin titer ($\geq 1:32$) [13]. Our data showed positive cold agglutinin titer ($\geq 1:32$) presented in 48 of 99 patients tested (34.5%), a finding similar to previous studies. Pleural effusion (usually a small amount) occurs in 5 to 20% of patients with *M. pneumoniae* infection [14,15] and was observed in 16 of our patients (11.5%).

Comparing patients using erythromycin and azithromycin, we found no statistically significant difference in the time to subsidence of fever after initiation of antibiotic treatment and also demonstrated in other studies [16]. Since only 5 patients received erythromycin in our study, more data are needed to clarify this observation. In adults, macrolide antibiotics have been shown to reduce the length and severity of pneumonia caused by *M. pneumoniae* compared with penicillin or no antibiotic treatment at all [17], but there are no similar studies in children [18]. In our study, children who did not receive macrolides had significantly longer fever duration than macrolide-treated patients. We conclude that if a child is admitted with *M. pneumoniae* infection, macrolides can be used empirically to shorten fever duration.

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