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EFFICACY OF SYSTEMIC GLUCOCORTICOIDS IN PEDIATRIC MYCOPLASMA PNEUMONIAE INFECTION

Mikołaj Szewczykowski ✉, ***Tomasz Klinkosz***, ***Ewa Otręba***, ***Magdalena Dorobek***

F. Ceynowa Specialist Hospital in Wejherowo, Poland

✉ ***m.szewczykowski98@gmail.com***

ABSTRACT

Aims: This review aimed to evaluate the clinical efficacy and safety of systemic glucocorticoids in children with Mycoplasma pneumoniae pneumonia (MPP), with particular focus on severe (SMPP) and refractory (RMPP) cases, based on prospective studies published between 2015 and 2025.

Methods: A structured literature search was conducted using PubMed and Google Scholar. Only English-language prospective studies involving pediatric patients were included. Eight studies met the eligibility criteria. Data were extracted and summarized thematically. No formal bias assessment was performed, but study limitations were analyzed narratively. Geographic distribution, study design, and outcome heterogeneity were taken into account.

Results: Combination therapy with glucocorticoids and antibiotics was associated with improved clinical outcomes in MPP, including reduced fever duration, improved pulmonary function, and lower inflammatory marker levels (CRP, IL-6, TNF-α). Intravenous methylprednisolone was the most commonly used steroid (1–2 mg/kg/day, up to 10 mg/kg/day in severe cases). Early administration (within 24–36 hours of hospital admission) was linked to better outcomes. No significant increase in adverse events was reported. One study suggested potential cost-effectiveness in RMPP. However, most data originated from East and Southeast Asia, limiting generalizability to European populations.

Conclusions: Glucocorticoid therapy may be beneficial in pediatric MPP, especially in severe and refractory forms. However, current evidence is limited by small sample sizes, heterogeneity in interventions, and regional concentration of studies. No standardized protocol for dosing, duration, or patient selection exists. High-quality, geographically diverse randomized controlled trials are urgently needed to support clinical decision-making in non-Asian populations.

Keywords: Mycoplasma pneumoniae, pneumonia, glucocorticoids, steroids, pediatrics, refractory pneumonia, treatment outcomes

INTRODUCTION

PNEUMONIA IN CHILDREN - ETIOLOGY, EPIDEMIOLOGY, SEASONALITY, RISK FACTORS

Community-acquired pneumonia (CAP) is a common pediatric condition and a significant public health concern. *Mycoplasma pneumoniae* (MP) is an important etiological factor responsible for this disease. In the USA, the

annual incidence rate of pneumonia in the study performed from January 2010 to June 2012 was 15.7 cases per 10,000 children. MP accounted for 19% of the reported cases in children five years of age or older and for 3% of cases in younger children [1]. In two studies conducted in Spain, detection of MP in pediatric CAP was 26.5% and 29.8% respectively [2,3]. In a similar study from Switzerland MP was established to be a cause of CAP in children and adolescence in 20.7% cases [4].

According to the 2013 study conducted by The Global Burden of Disease, lower respiratory infections were the leading cause of death in children under five years old. Among older children (aged five to nine years), they were the second most common cause of death. Due to the comparatively higher mortality rate among younger children, lower respiratory infections represent the single most significant cause of death across the entire population of children and adolescents [5].

Certain seasonality and epidemic patterns have been observed regarding *Mycoplasma pneumoniae pneumonia* (MPP). In a study conducted in the United States, pneumonia exhibited the strongest seasonal trend among common infectious diseases in the pediatric population. The peak season was winter [6]. Similarly in Italy the highest prevalence of MPP was reported from December to March [7]. Historically outbreaks of MPP epidemics occurred every few years. For example in Denmark and UK approximately every four years, with some authors suggesting that during this time interval the herd immunity decreases enough for the next outbreak to happen [8,9].

REFRACTORY AND SEVERE MYCOPLASMA PNEUMONIAE PNEUMONIA

MPP is often regarded as a self-limiting disease, but occasionally it may lead to refractory *Mycoplasma pneumoniae* pneumonia (RMPP). Although there is no universally accepted definition of RMPP, one commonly used set of diagnostic criteria is provided by the Chinese guidelines for CAP. According to these guidelines, RMPP may be diagnosed in patients who present with persistent fever, worsening clinical symptoms, and progressive radiological findings despite receiving macrolide antibiotic therapy for at least seven days. RMPP should not be confused with severe *Mycoplasma pneumoniae* pneumonia (SMPP), which focuses on the severity of the disease. In many cases, hospitalization in the intensive care unit is included in the criteria [10].

MYCOPLASMA PNEUMONIAE PNEUMONIA COMPLICATIONS

MPP presents with significant variability in clinical presentation. The majority of cases are benign, but especially in RMPP, SMPP, and macrolide-resistant *Mycoplasma pneumoniae*, serious complications have been observed. MPP has been associated with necrotizing pneumonia, respiratory failure, Stevens-Johnson Syndrome, and life-threatening encephalitis [11,12,13]. Extrapulmonary manifestations occur in approximately 20% - 25% of infected children [14]. Additionally, a close connection between the MP infection and the development of asthma has been reported [15].

THE ROLE OF ANTIBIOTICS AND RISING MACROLIDE RESISTANCE

MPP has traditionally been treated with macrolides, tetracyclines, and fluoroquinolones, with macrolides serving as the first-line treatment due to their low minimal inhibitory concentrations and thereby potent effect on MP infection [16]. Azithromycin is the drug of choice, followed by erythromycin or clarithromycin. Regarding treatment of SMPP and RMPP, tetracyclines are recommended for children aged eight years and above, while macrolides are recommended for children under eight years old [17]. An increasing number of MP strains resistant to macrolides highlighted the need to reconsider this approach. Before the year 2000, macrolide resistance in MP was very rare. Since then, many studies have reported growing macrolide resistance. In the large meta-analysis covering 153 studies and 26 countries, an increasing trend in the prevalence of macrolide resistance was described. The highest proportion of macrolide-resistant infections was observed in Western Pacific regions (53.4%), with a lower percentage in America (8.4%) and the European region (5.1%). Authors found a higher proportion of macrolide-resistant MP infections in studies performed on children, compared to studies performed on adults and those including both adults and children [18]. Although baseline resistance levels may be lower in Europe compared to Asia, elevated macrolide resistance rates have been documented in pediatric and adult populations. Different studies have estimated the prevalence of macrolide-resistant MP during recent outbreaks in Italy, Scotland, England, Switzerland, and France at 26%, 19%, 9.3%, 9% and 8.3% respectively [19,20,21,22,23]. It was also reported in Germany, that macrolide resistance may be obtained by MP during an outbreak of disease [24].

Knowledge of the epidemiological situation in other countries may be clinically useful due to globalization and frequent international travel, as demonstrated in the report by Caballero et al. (2014). Following the deterioration of a 23-year-old patient treated with meropenem and azithromycin for MP infection, clinicians decided to switch to doxycycline, which subsequently led to clinical improvement. The decision was based on information indicating high rates of macrolide-resistant MP in China and Korea, countries the patient had visited prior to the onset of illness [25].

IMMUNOSUPPRESSIVE THERAPY

According to the Chinese Evidence-based guideline for the diagnosis and treatment of *Mycoplasma pneumoniae* pneumonia in children (2023), the addition of glucocorticoids (glucocorticoids, corticosteroids, and steroids will be used interchangeably) to antimicrobial drugs is recommended in both SMPP and RMPP. In contrast, the routine use of IVIG is not recommended for either SMPP or RMPP. Due to the lack of sufficient clinical evidence, these recommendations are made based on expert opinion [17]. So far, no universally accepted dosage schedule and drug of choice have been established for children with SMPP and RMPP [26,27].

Retrospective studies in the pediatric population have found that treatment of SMPP and RMPP with an antibiotic combined with a steroid significantly reduces inflammation, improves immune function, and shortens recovery time [28,29]. Although some studies have reported favorable outcomes, other investigations have found no evident benefits from corticosteroid use in the treatment of MPP in pediatric patients [30]. The potential effectiveness of corticosteroid therapy may depend on specific factors, such as dosage and the time of steroid administration. While high-dose corticosteroid therapy has the potential to offer therapeutic advantages, low-dose therapies have not demonstrated clinical efficacy [31,32]. Early administration of corticosteroids appears to reduce the duration of fever and shorten hospitalization compared to delayed initiation [33]. To optimize the timing and dosage of corticosteroid therapy in cases of SMPP and RMPP, monitoring specific biomarkers may provide valuable guidance [34,35].

GEOGRAPHIC VARIATION IN RESEARCH AND DISEASE BURDEN

Most of the prospective clinical studies evaluating systemic glucocorticoids in Mycoplasma pneumoniae pneumonia (MPP) have been conducted in East and Southeast Asia, particularly in China, South Korea, and Japan. This concentration of research reflects the high epidemiological burden in these regions, where cyclical MPP epidemics are common and macrolide-resistant *Mycoplasma pneumoniae* (MRMP) strains are highly prevalent. For example, resistance rates in some Chinese provinces exceed 80%, whereas the prevalence in the European region is approximately 5.1%, as shown in a recent global meta-analysis [18]. This lower resistance rate may partly explain the lack of large-scale prospective studies in Europe and North America. As a result, the current evidence base is geographically imbalanced, and caution is needed when generalizing findings to non-Asian pediatric populations. Further research in European contexts, including Poland, is warranted.

AIMS

Although *Mycoplasma pneumoniae* is a significant etiological agent of community-acquired pneumonia and a major concern in the pediatric population, potentially leading to fatal outcomes, retrospective studies have not provided definitive evidence regarding the efficacy of oral (p.o.) and intravenous (i.v.) glucocorticoids therapy in the treatment of MPP [5]. Despite the fact that generally lower levels of macrolide resistance in *Mycoplasma pneumoniae* pneumonia are described in Europe compared to Asia, recent European studies have reported resistance rates as high as 26% [19]. In the context of globalization and frequent international travel, understanding the epidemiological situation in other regions of the world may be valuable in certain clinical scenarios. This article aims to enhance understanding of potential benefits and highlight the absence of clear guidelines regarding the use of glucocorticoids in the management of MPP.

METHODS

This narrative review was based on literature retrieved from PubMed and Google Scholar. The search covered the period from 2015 to 2025 and focused on studies involving the pediatric population. The following search terms and their combinations were used: community-acquired pneumonia, CAP, Mycoplasma pneumoniae, pneumonia, children, pediatrics, paediatrics, steroids, glucocorticoids. Only English-language studies were considered. Special attention was given to prospective clinical trials evaluating the use of systemic glucocorticoids in pediatric Mycoplasma pneumoniae pneumonia.

Eight prospective studies meeting the inclusion criteria were selected and analyzed. No formal risk-of-bias assessment was performed, given the narrative character of the review. However, heterogeneity among the included studies was noted in terms of design, glucocorticoid regimens, dosing schedules, timing of administration, and patient populations. Most of the included trials were conducted in East Asian settings, where macrolide-resistant M. pneumoniae strains are prevalent. These factors limit the generalizability of findings to other regions and may introduce selection and publication bias.

FINDINGS

GLUCOCORTICOIDS AND CLINICAL PRESENTATION

In Kim et. al. (2017), the addition of methylprednisolone (1 mg/kg/day) to macrolide-based therapy in MPP resulted in a significantly shorter duration of fever post-admission (1.36 days vs. 2.17 days) as well as overall fever duration (4.42 days vs. 6.07 days) [35]. Another study reported a significantly higher total effective rate (complete or partial improvement of clinical and radiological features) in patients with MPP receiving methylprednisolone (2 mg/kg/day for three-five days followed by 1 mg/kg/day for three days) in conjunction with antibiotics, compared to the azithromycin-only group (95.35% vs. 78.07%). This combined therapy also led to a more rapid resolution of fever, cough, pulmonary rales, tonsillar congestion, and was associated with a reduced recurrence rate of MPP. There appears to be a discrepancy between the table and the narrative description - possible error [37]. Li et al. (2015) demonstrated that initial treatment with intravenous methylprednisolone (2 mg/kg/day) in combination with azithromycin, followed by oral prednisone (1 mg/kg/day) upon resolution of fever, was associated with a reduced duration of fever and cough [38].

Regarding RMPP in a study by Lan et al. (2015), 30% of patients treated with methylprednisolone (2 mg/kg/day) experienced fever resolution within three days, whereas fever persisted in all patients not receiving steroids. Despite this trend, the difference in total fever duration between the steroid and non-steroid groups did not achieve statistical significance. Cough duration was reduced in the steroid group (5.1 days vs. 7.0 days) [39]. Zhou et al. (2022) demonstrated that therapy with methylprednisolone (2 mg/kg/day for five days, then 1 mg/kg/day for two days, repeated for three cycles) combined with azithromycin in RMPP led to reduced cough and defervescence time, as well as a higher total effective rate (94.12% vs. 74.51%) compared to azithromycin monotherapy [40].

In SMPP seven days of continuous combined therapy with azithromycin and methylprednisolone reduced time of fever (6.30 ± 2.16 days vs 7.75 ± 2.84 days), cough (10.05 ± 2.36 days vs 12.37 ± 3.10 days), and lung rale (7.06 ± 1.95 days vs 12.30 ± 2.2), unfortunately the exact dosage of steroids is not given [41].

Early initiation of steroid therapy within 24 hours of admission demonstrated favorable outcomes regardless of the antibiotic class used. 74% of patients had fever resolution within 24 hours of the start of therapy, independent of the choice of antibiotic therapy (macrolide vs non-macrolide). The dosage of steroids depended on the severity of pneumonia. In mild cases, p.o. prednisolone (1 mg/kg/day) or i.v. methylprednisolone (1–2 mg/kg/day) was given. In more severe cases, i.v. methylprednisolone (5–10 mg/kg/day). 3% of patients (all of whom received oral prednisone or a lower methylprednisolone dose) needed an additive dose of steroid because of no response to treatment or progression of disease [42].

DURATION OF HOSPITALIZATION

Three studies showed that combining glucocorticoids with antibiotics reduced hospital stay compared to antibiotic monotherapy—one each for MPP, RMPP, and SMPP [38,40,41]. In contrast, one study reported no statistically significant difference in hospitalization time of patients with MPP [36]. In Yang et al. (2019), regardless of the antibiotic used in MPP treatment, early corticosteroid therapy (within 24 to 36 hours from admission) resulted in shorter hospitalization time compared to other studies in this review [42]. The corresponding data are summarized in Table 1.

Table 1. Time of hospitalization. In the last column, a comparison of the group treated with steroid plus antibiotic vs the control group treated only with antibiotic [36,38,40,41,42].

Study	Cause of hospitalization	Dose of steroids	Time of hospitalization
Kim et al. (2017) [36]	MPP	methylprednisolone i.v. 1 mg/kg/day	6.72 ± 1.54 days vs. 6.92 ± 1.87 days, P > 0.05 (no significant difference)
Li et al. (2015) [38]	MPP	methylprednisolone i.v. 2 mg/kg/day than prednisone p.o. 1 mg/kg/day	11.21 ± 2.65 days vs. 15.25 ± 3.22 days, P < 0.05
Zhou et al. (2022) [40]	RMPP	methylprednisolone i.v. 2 mg/kg/day for 5 days, then 1 mg/kg/day for 2 days, repeated for 3 cycles	11.39 ± 5.31 days vs. 14.82 ± 3.78, P < 0.001

Li (2021) [41]	SMPP	no information about exact dosage; methylprednisolone for 7 days	11.06 ± 2.07 days vs. 14.78 ± 2.61 days, P <0.05
Yang et al. (2019) [42]	mild to severe MPP	all treated with steroids; prednisolone p.o. 1 mg/kg/day or methylprednisolone i.v. 1–10 mg/kg/day depending on severity; If fever persists for 36 - 48 hours or progression: additive methylprednisolone i.v.	6.0 ± 1.8 days

BIOCHEMICAL MARKERS

Glucocorticoid plus antibiotic combination therapy has been shown to reduce levels of IL-6, TNF-α, and CRP in pediatric MPP. Additionally, it resulted in downregulation of CD8+ and upregulation of CD3+ and CD4+ T-cell subsets compared to non-steroid regimens [37]. In cases of SMPP, treatment with steroids and azithromycin led to decreased serum concentrations of CRP, IL-6, IL-10, and TNF relative to azithromycin alone [41]. However, in RMPP, the use of steroids did not significantly alter levels of IL-1β, IL-4, IL-6, IL-8, IL-10, or IFN-γ in bronchoalveolar lavage fluid [39].

PULMONARY FUNCTION

Patients treated with methylprednisolone demonstrated improved pulmonary function parameters, including FVC, FEV1, and FEV1/FVC, compared to those who did not receive steroids [36]. Furthermore, in RMPP cases, methylprednisolone therapy resulted in reductions in FeNO and eosinophil levels [40].

RADIOLOGICAL OUTCOMES

In MPP, steroid use did not significantly affect radiographic progression of lung pathology on chest X-ray conducted three days post-admission [36]. However, in RMPP, steroids accelerated the resolution of pulmonary infiltrates [40].

ADVERSE EFFECTS AND COST-UTILITY

The administration of steroids in pediatric MPP, including RMPP and SMPP cases, was not associated with an increase in adverse reactions [37,38,40,41]. The addition of corticosteroids in RMPP (after one week of macrolide therapy) has been shown to be cost-effective with higher quality-adjusted life years (QALY) and lower total costs per person [43].

DISCUSSION

In the presented studies, the adjunctive use of corticosteroids (mostly intravenous methylprednisolone 1–2 mg/kg/day, up to 10 mg/kg/day) with standard antibiotic therapy was associated with improved clinical outcomes in MPP, RMPP, and SMPP. These included reduced duration of fever, cough, and auscultatory findings. The studies, although not unanimous, suggest that adding steroids may reduce the length of hospital stay. Early initiation of corticosteroids (preferably within 24 to 36 hours of admission) appears to be beneficial in mild and severe MPP irrespective of the choice of antibiotic used in therapy. Moreover, improvements in pulmonary function tests and favorable modulation of inflammatory biomarkers (e.g., IL-6, CRP, TNF-α) suggest that corticosteroids may help blunt the immune-mediated pathophysiological component of MPP. The effect of corticosteroids on radiological abnormalities resolution and bronchoalveolar lavage cytokine profiles remains inconclusive.

Despite promising results in several prospective studies, the evidence for the use of steroids in MPP remains inconsistent. For example, Kim et al. (2017) reported no statistically significant difference in hospitalization duration with steroid use [36], and Lan et al. (2015) observed no significant difference in total fever duration in RMPP [39]. These discrepancies may be attributed to heterogeneity in steroid dosing regimens, timing of therapy initiation, definitions of disease severity, and small sample sizes. Importantly, all but one study were conducted in Asia (specifically in China, Korea, or Japan), highlighting the need for further research in more geographically diverse populations.

Regarding safety, the reviewed studies reported no increase in adverse events associated with steroid use. Additionally, cost-utility analyses suggest that the addition of corticosteroids may be economically favorable in

RMPP cases [43].

LIMITATIONS OF THE CURRENT EVIDENCE

The limitations of the available literature must be acknowledged. First, the included studies are heterogeneous in terms of study design, glucocorticoid type and dose, timing of administration, outcome measures, and definitions of disease severity. Second, none of the studies applied blinding or placebo control, which increases the risk of performance and detection bias. Third, all but one study were conducted in East Asia, where the epidemiological context (especially the high prevalence of macrolide-resistant *M. pneumoniae*) differs significantly from that in Europe or North America. This limits the external validity and generalizability of the findings. Fourth, potential publication bias and selective outcome reporting cannot be excluded, as most studies reported positive results without sufficient discussion of negative or null outcomes. Finally, no studies assessed long-term respiratory outcomes or adverse effects associated with corticosteroid use in this patient population.

There is an urgent need for high-quality randomized controlled trials to determine optimal dosing, timing, indications, and long-term safety for corticosteroid therapy in pediatric MPP. Until such data are available, clinical judgment, supported by careful assessment of disease severity and biomarker profiles, should guide the decision to initiate steroid treatment.

CONCLUSIONS

- Systemic glucocorticoids may provide clinical benefit in pediatric Mycoplasma pneumoniae pneumonia, particularly in severe and refractory cases (SMPP, RMPP), when used in combination with antibiotics.
- The reviewed studies suggest improvements in clinical symptoms (fever, cough), reductions in inflammatory markers (CRP, IL-6, TNF-α), and enhancement of pulmonary function with adjunctive glucocorticoid therapy.
- Intravenous methylprednisolone was the most frequently used agent, typically at 1–2 mg/kg/day, with doses up to 10 mg/kg/day in severe presentations.
- Early administration (within 24–36 hours of hospital admission) appears to be associated with more favorable outcomes.
- No significant increase in adverse effects related to glucocorticoid use was reported in the included studies.
- One prospective study reported potential cost-effectiveness of glucocorticoid use in RMPP, but this finding requires independent confirmation.
- The current evidence base is limited by small sample sizes, heterogeneity of study designs, and regional concentration of available data.
- There is currently no universally accepted or internationally standardized protocol regarding glucocorticoid dose, duration, timing, or patient selection in pediatric MPP. Further high-quality, geographically diverse randomized controlled trials are necessary to support the development of consistent evidence-based guidelines.

DISCLOSURES

AUTHOR CONTRIBUTIONS

- Conceptualization: Mikołaj Szewczykowski.
- Literature search and data analysis: Mikołaj Szewczykowski; Tomasz Klinkosz.
- Writing – original draft preparation: Mikołaj Szewczykowski; Tomasz Klinkosz; Magdalena Dorobek ; Ewa Otręba.
- Writing – review and editing: Mikołaj Szewczykowski; Tomasz Klinkosz; Magdalena Dorobek ; Ewa Otręba.
- All authors approved the final version of the manuscript

USE OF AI TOOLS

We acknowledge the use of ChatGPT based on the GPT -4o (https://chatgpt.com/). Artificial intelligence (AI) was utilized during the preparation of this manuscript for language-related assistance, specifically to identify and correct grammatical, stylistic, and spelling errors in the text.

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