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在线全文

不同剂量糖皮质激素治疗儿童重症肺炎支原体肺炎的临床研究*

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【摘要】 **目的** 本研究基于倾向性评分匹配法，分析不同剂量糖皮质激素（GC）治疗重症肺炎支原体肺炎（SMPP）患儿的临床特征及GC治疗不同疗效的临床特征。**方法** 回顾性收集2021年1月1日–2022年12月31日期间天津市儿童医院住院并接受GC治疗的271例SMPP患儿临床资料，按GC剂量分为低剂量组〔甲泼尼龙≤2 mg/(kg·d)〕和高剂量组〔甲泼尼龙>2 mg/(kg·d)〕。采用1∶1倾向性评分匹配（匹配变量包括发病至住院时间、发热至GC使用时间、GC使用至复查胸部X线时间）以减少混杂因素，低剂量组和高剂量组共计成功匹配90对患儿，比较匹配后两组的临床特征，进一步应用多因素logistic回归分析使用高剂量GC的危险因素。又以临床疗效将90对患儿分为无效组（*n*=38）和有效组（*n*=142），比较两组临床特征，并用多因素logistic回归分析使用GC后临床无效的风险因素。**结果** 高剂量组患儿年龄较小、血小板计数较高、肺不张发生率较高（均*P*<0.05）。高剂量组较低剂量组体温恢复时间及热程较短，药物不良反应（恶心、呕吐、腹痛、腹泻、皮疹等）发生率较高（均*P*<0.05），但两组均未见高血糖、高血脂、高血压、消化道出血或穿孔等严重不良反应。影像学评估显示，高剂量组显著吸收的病例明显多于低剂量组（*P* = 0.009）。但两组住院时长、咳嗽缓解时间及湿啰音吸收时间差异无统计学意义（均*P*>0.05）。多因素logistic回归分析显示，年龄小、合并肺不张及血小板偏高是选择高剂量GC治疗的危险因素。与GC治疗有效组相比，无效组难治性肺炎支原体肺炎（RMPP）比例、胸痛发生率及中性淋巴细胞比值、热峰、降钙素原、铁蛋白、乳酸脱氢酶、谷丙转氨酶、谷草转氨酶和D-二聚体水平均显著升高（均*P*<0.05），而淋巴细胞计数降低（*P*<0.05）。两组在年龄及高剂量GC使用率上差异无统计学意义（均*P*>0.05）。多因素分析显示，RMPP和高热峰是GC治疗无效的独立危险因素。**结论** 高剂量GC治疗虽可促进体温恢复、缩短发热病程并提高肺部病变吸收率，但其总体疗效与低剂量组无明显差异，且不良反应发生率更高。年龄较小、合并肺不张及血小板计数偏高是患儿接受高剂量GC治疗的主要影响因素。值得注意的是，RMPP和高热峰是GC治疗无效的独立危险因素，与GC剂量无关。临床需严格评估高剂量GC治疗的个体化风险收益比。

【关键词】 重症肺炎支原体肺炎 糖皮质激素 倾向性评分 儿童

Clinical Study of Different Doses of Glucocorticoids in the Treatment of Severe *Mycoplasma pneumoniae* Pneumonia in Children

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[**Abstract**] **Objective** To analyze the clinical characteristics of children with severe *Mycoplasma pneumoniae* pneumonia (SMPP) treated with different doses of glucocorticoids (GC) and to investigate factors associated with GC treatment efficacy on the basis of propensity score matching (PSM). **Methods** Clinical data from 271 children who were hospitalized at Tianjin Children's Hospital between January 1, 2021 and December 31, 2022, and who received GC treatment for SMPP were retrospectively collected. The patients were divided into low-dose (methylprednisolone ≤ 2 mg/[kg·d]) and high-dose (methylprednisolone > 2 mg/[kg·d]) groups. A 1∶1 PSM based on the matching variables, including time from onset to admission, time from fever onset to GC administration, and time from GC administration to follow-up chest X-ray, was performed to reduce confounding factors, resulting in 90 matched pairs in total in the low-dose and high-dose groups. Clinical characteristics were compared between the two groups after PSM. Multivariate logistic regression was performed to identify risk factors for high-dose GC use. The 90 pairs of children were further divided into an ineffective group (*n* = 38) and an effective group (*n* = 142) on the basis of clinical treatment outcomes, and multivariate logistic regression was conducted to determine risk factors for clinical GC treatment failure. **Results** Children in the high-dose group were younger and had higher platelet counts and a higher incidence of atelectasis (all *P* < 0.05). The high-dose group showed a shorter time to fever resolution and overall duration of fever, but higher rates of

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adverse drug reactions (nausea, vomiting, abdominal pain, diarrhea, rash, etc.) compared with the low-dose group (all $P < 0.05$). No severe adverse events, such as hyperglycemia, hyperlipidemia, hypertension, gastrointestinal bleeding, or perforation, were observed in either group. Radiographic assessment showed a significantly higher rate of marked absorption in the high-dose group ($P = 0.009$). There were no significant differences between the groups in the length-of-stay, time to cough relief, or time to disappearance of pulmonary rales (all $P > 0.05$). Younger age, atelectasis, and elevated platelet count were identified as risk factors for selecting high-dose GC therapy using multivariate logistic regression analysis. Compared with the GC-effective group, the GC-ineffective group had a higher proportion of refractory *Mycoplasma pneumoniae* pneumonia (RMPP), a higher incidence of chest pain, and significantly increased levels of neutrophil-to-lymphocyte ratio, peak fever, procalcitonin, ferritin, lactate dehydrogenase, alanine aminotransferase, aspartate aminotransferase, and D-dimer (all $P < 0.05$), along with decreased lymphocyte counts ($P < 0.05$). There were no significant differences between the 2 groups in age or the proportion of children receiving high-dose GC (all $P > 0.05$). Multivariate analysis showed that RMPP and high peak fever were independent risk factors for GC treatment failure. **Conclusion** High-dose GC therapy may facilitate fever resolution, shorten the duration of fever, and enhance radiological improvement. However, its overall efficacy is not significantly superior to low-dose therapy and is associated with a higher incidence of adverse reactions. Younger age, atelectasis, and elevated platelet count are key factors influencing the use of high-dose GC in children. Notably, RMPP and high peak fever are independent risk factors for GC treatment failure, irrespective of the GC dosage. Clinicians should carefully evaluate the individualized risk-benefit profile when considering high-dose GC therapy for pediatric SMPP.

[Key words] Severe *Mycoplasma pneumoniae* pneumonia　Glucocorticoid　Propensity score matching　Children

肺炎是儿童常见疾病，是导致5岁以下儿童感染性疾病死亡的首位疾病[1]。肺炎支原体肺炎（*Mycoplasma pneumoniae* pneumonia, MPP）是我国5岁及以上儿童最主要的社区获得性肺炎（community acquired pneumonia, CAP）。MPP通常表现为轻症且具有自限性。然而，随着相关抗生素耐药率的增高，重症或难治性肺炎病例不断增多。约12%的住院MPP患儿可进展为重症肺炎支原体肺炎（severe MPP, SMPP）[2]。SMPP多发生于病程1周左右，伴有肺内和肺外并发症，若出现肺内并发症，患儿可出现气促或呼吸困难等；发生肺外并发症时可出现相应脏器损伤的临床表现，对儿童健康构成严重威胁。SMPP的发病机制曾被认为主要与病原体的直接作用及其诱发的炎症免疫反应间接作用相关[3]。因此，重症和危重症患儿主要用糖皮质激素（glucocorticoid, GC）进行治疗[4]。但目前GC在MPP的治疗中仍然存在治疗方案、疗效、安全性等争议。本研究通过分析不同剂量GC治疗SMPP的临床特征及初始选择应用高剂量GC的危险因素，以及使用GC治疗后的临床疗效评估，为临床医生提供一些治疗思路。

1　资料与方法

1.1　研究对象

本研究采用回顾性病例对照研究方法，纳入2021年1月1日–2022年12月31日于天津市儿童医院住院的SMPP并在住院期间使用GC治疗的患儿为研究对象，纳入标准：①年龄在1月龄至18岁之间。②住院期间均使用了GC治疗。③使用GC治疗前，患儿符合儿童肺炎支原体肺炎诊疗指南（2023年版）[4]中SMPP的诊断标准及使用GC治疗的指征。排除标准：①患有免疫缺陷病、先天性支气管肺发育不良或先天畸形、心脏病或慢性肾小球肾炎、风湿病、糖尿病等遗传代谢疾病。②合并支气管异物；结核、病毒、细菌等其他病原体感染。③30 d内再因肺炎入院以及3个月内接受免疫调节剂及激素治疗。④临床资料不完整，无法完成统计学分析。本研究通过天津市儿童医院伦理委员会批准（审批号：022-LXKY-004）。豁免知情同意。

1.2　分组标准

将纳入的271例患儿按照使用GC的量[5-7]分为两组：低剂量组〔静脉注射甲泼尼龙≤2 mg/(kg·d)，174例〕和高剂量组〔静脉注射甲泼尼龙>2 mg/(kg·d)，97例〕。为了减少混杂因素采用倾向性评分匹配（propensity score matching, PSM）将两组儿童依据基本情况进行1∶1匹配，匹配变量包括发病至住院时间、发热至使用GC时间和GC使用至复查胸部X线时间。PSM后，低剂量组和高剂量组共计成功匹配90对患儿，两组比较，发病至住院时间、发热至使用GC时间、GC使用至复查胸部X线时间差异无统计学意义（均$P>0.05$），标准化均值差均<0.1，数据具有可比性。最终入组180例患儿，其中90例为低剂量组，90例为高剂量组。同时根据GC疗效，将全部患儿进一步分为有效组（$n=142$）与无效组（$n=38$）。流程图见图1。

GC使用剂量的换算：参照糖皮质激素类药物临床应用指导原则(2023版)[8]将不同种类的GC使用剂量按照药

效比统一等价换算成甲泼尼龙使用剂量。

GC疗效判定:(1)无效:用药后24 ~ 48 h内热峰无明显下降(< 1℃),临床体征较前无好转;(2)有效:用药后24 ~ 48 h内热峰明显下降或体温正常,临床体征较前好转,病情无反复[4, 9]。

影像学变化判断(由本院2名呼吸科中级及以上职称医生和1名影像学科中级职称医生共同阅片,最终纳入结果为3人达成一致结果):(1)显著吸收:炎性病变吸收范围> 50%。(2)部分吸收:炎性病变吸收范围30% ~ 50%。(3)无变化:炎性病变吸收范围< 30%。

1.3 收集资料

通过电子病历系统收集患儿的一般信息、临床表现、实验室检查、影像学检查、治疗等资料。收集数据由专业人员统一录入,双人核对准确性。静脉血实验室检查均为入院24 h内进行实验室指标检测。

1.4 统计学方法

应用R软件(http://www.R-project.org; version 4.4.2)和SPSS 27.0软件进行数据处理。使用MatchIt包nearest函数,PSM按照1∶1匹配,设置卡钳值为0.25。符合正态分布且方差齐的计量资料以$\bar{x} \pm s$表示,组间比较采用t检验;非正态分布的计量资料以M(Q1, Q3)表示,组间比较用Mann-Whitney U检验。计数资料以例(%)表示,组间比较采用χ^2检验或Fisher确切概率法,多重卡方检验使用Bonferroni校正。采用二分类logistic回归分析SMPP患儿使用高剂量GC治疗及GC治疗无效的危险因素,以双侧P< 0.05为差异有统计学意义。

2 结果

2.1 低剂量组和高剂量组患儿临床特征及临床结局

高剂量组与低剂量组患儿比较,年龄较小、血小板计数较高、合并肺不张占比高,差异均有统计学意义(均P< 0.05),见表1。

高剂量组与低剂量组患儿相比,体温恢复正常的时间更短、热程更短,但常见药物不良反应(包括恶心呕吐、腹痛腹泻、皮疹等)占比更高,差异均有统计学意义(均P< 0.05)。无论是高剂量组和低剂量组患儿均无

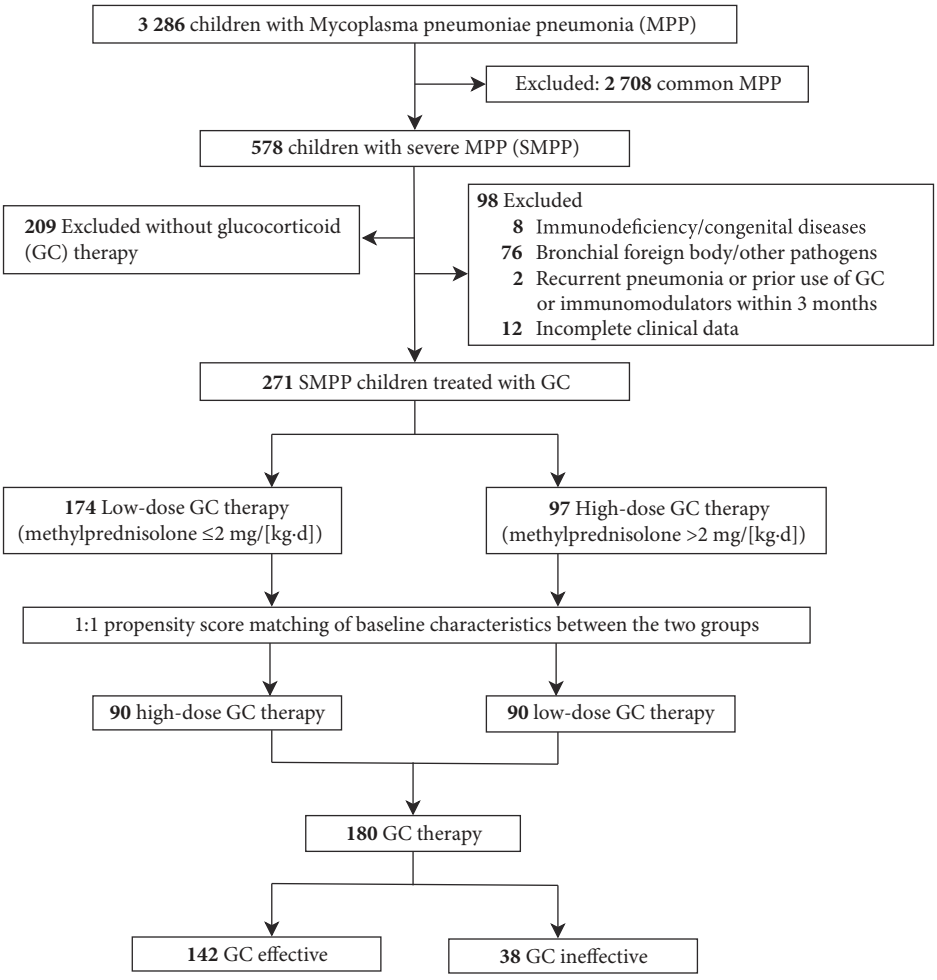

图 1 患儿筛选及分组流程图

Fig 1 Flowchart of patient enrollment and group assignment

表 1　低剂量组和高剂量组患儿临床特征比较

Table 1　Comparison of clinical characteristics between the low-dose and high-dose groups

Variable	Low-dose group (n = 90)	High-dose group (n= 90)	P
Male/case (%)	48 (53.33)	44 (48.89)	0.655
Age/yr., M (Q1, Q3)	7.00 (5.00, 9.00)	5.00 (3.00, 7.00)	0.007
RMPP/case (%)	29 (32.20)	17 (18.89)	0.059
Symptoms and signs			
Peak fever temperature/℃, M (Q1, Q3)	39.70 (39.30, 40.00)	39.80 (39.50, 40.00)	0.181
Productive cough/case (%)	84 (93.33)	88 (97.78)	0.278
Wheezing/case (%)	15 (16.67)	23 (25.56)	0.201
Crackles/case (%)	87 (96.67)	89 (98.89)	0.621
Diminished breath sounds/case (%)	35 (38.89)	23 (25.56)	0.079
Chest pain/case (%)	8 (8.89)	2 (2.22)	0.104
Hypoxemia/case (%)	4 (4.44)	10 (11.11)	0.162
Extrapulmonary complications/case (%)	14 (15.56)	13 (14.44)	1.000
Imaging findings			
Pulmonary consolidation/case (%)	49 (54.44)	56 (62.22)	0.364
Atelectasis/case (%)	26 (28.89)	40 (44.44)	0.044
Pleural effusion/case (%)	25 (27.78)	27 (30.00)	0.869
Pleural thickening/case (%)	60 (66.67)	54 (60.00)	0.439
Emphysema/case (%)	7 (7.78)	2 (2.22)	0.171
Laboratory tests			
WBC/10^9 L^{-1}, M (Q1, Q3)	8.12 (5.69, 10.24)	7.60 (6.21, 9.81)	0.985
N/10^9 L^{-1}, M (Q1, Q3)	5.31 (3.70, 7.07)	5.26 (3.80, 6.36)	0.940
L/10^9 L^{-1}, M (Q1, Q3)	1.68 (1.33, 2.17)	1.79 (1.39, 2.47)	0.240
NLR (M [Q1, Q3])	2.95 (2.20, 4.31)	2.48 (1.78, 4.19)	0.206
E/10^9 L^{-1}, M (Q1, Q3)	0.05 (0.03, 0.17)	0.04 (0.01, 0.14)	0.078
HGB/(g/L), $\bar{x} \pm s$	127.08 ± 10.34	125.47 ± 11.48	0.324
PLT/10^9 L^{-1}, M (Q1, Q3)	249.00 (208.00, 299.25)	273.00 (228.50, 326.00)	0.031
PLR (M [Q1, Q3])	157.71 (121.02, 192.77)	153.30 (109.30, 218.18)	0.864
SII (M [Q1, Q3])	757.03 (500.38, 1 126.12)	730.37 (464.36, 1 265.28)	0.989
CRP/(mg/L), M (Q1, Q3)	27.94 (12.26, 50.33)	29.99 (14.91, 53.33)	0.632
ESR/(mm/1 h), M (Q1, Q3)	30.00 (21.00, 39.75)	30.00 (25.00, 41.50)	0.283
PCT/(ng/mL), M (Q1, Q3)	0.14 (0.09, 0.26)	0.16 (0.09, 0.34)	0.271
FER/(ng/mL), M (Q1, Q3)	128.95 (99.17, 196.30)	136.95 (88.72, 237.20)	0.668
IL-6/(pg/mL), M (Q1, Q3)	27.42 (19.55, 43.54)	29.39 (17.86, 52.34)	0.482
LDH/(U/L), M (Q1, Q3)	362.50 (294.25, 477.00)	365.00 (306.00, 470.25)	0.902
ALT/(U/L), M (Q1, Q3)	13.00 (10.00, 17.75)	12.00 (10.00, 16.00)	0.836
AST/(U/L), M (Q1, Q3)	30.50 (24.00, 39.00)	31.00 (26.25, 37.75)	0.338
D-dimer/(mg/L), M (Q1, Q3)	1.09 (0.66, 1.65)	1.09 (0.83, 2.02)	0.313
Treatment			
Pre-hospital macrolide use/case (%)	44 (48.89)	37 (41.11)	0.369
Ventilator use/case (%)	1 (1.11)	2 (2.22)	1.000

RMPP: refractory mycoplasma pneumoniae pneumonia; WBC: white blood cell; N: peripheral neutrophils; L: peripheral lymphocytes; NLR: neutrophil-to-lymphocyte ratio; E: eosinophils; HGB: hemoglobin; PLT: platelets; PLR: platelet-to-lymphocyte ratio; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; FER: ferritin; PCT: procalcitonin; IL-6: interleukin-6; LDH: lactic dehydrogenase; AST: aspartate aminotransferase; ALT: alanine aminotransferase; SII: systemic immune-inflammation index.

GC严重不良反应, 如高血糖、高血脂、高血压、消化道出血或穿孔等, 且所有不良反应均在停药后自行缓解。在影像学表现方面, 显著吸收与无变化的占比差异均具有统计学意义(P< 0.016 7)。但住院时长、疗效、咳嗽缓解时间及湿啰音吸收时间差异均无统计学意义(均P> 0.05), 见表2。

表 2 低剂量组和高剂量组患儿临床结局比较

Table 2 Comparison of clinical outcomes between the low-dose and high-dose groups

Variable	Low-dose group (n = 90)	High-dose group (n = 90)	P
Duration of fever/d, M (Q1, Q3)	10.00 (8.00, 11.00)	9.00 (7.00, 10.00)	0.013
Hospitalization duration/d, M (Q1, Q3)	8.00 (7.00, 9.75)	8.00 (7.00, 10.00)	0.611
Febrile clearance time/d, M (Q1, Q3)	2.00 (1.00, 3.00)	2.00 (1.00, 2.00)	0.016
Time to cough resolution/d, M (Q1, Q3)	4.00 (3.00, 6.00)	4.00 (3.25, 6.00)	0.975
Time to crackles clearance/d, M (Q1, Q3)	5.00 (4.00, 6.75)	5.00 (4.00, 7.00)	0.866
Clinical effectiveness/case (%)	66 (73.33)	76 (84.44)	0.099
Adverse drug reactions/case (%)	11 (12.22)	23 (25.56)	0.035
Adiographic outcomes			0.009
Significant resolution/case (%)	36 (40.00)	56 (62.22)*	
Partial resolution/case (%)	34 (37.78)	24 (26.67)	
No change/case (%)	20 (22.22)	10 (11.11)*	

* indicate statistically significant differences between groups (P = 0.009, adjusted by the Bonferroni correction).

2.2 SMPP患儿使用高剂量GC治疗的危险因素分析

二元logistic回归分析结果(表3)示: 年龄小、合并肺不张及血小板较高是使用高剂量GC治疗的危险因素。

2.3 PSM后SMPP患儿使用GC治疗后不同疗效临床特征比较

相较于有效组, 无效组患儿难治性肺炎支原体肺炎(refractory MPP, RMPP)占比及胸痛症状占比高、淋巴细胞计数低、中性淋巴细胞比值、热峰、降钙素原、铁蛋白、乳酸脱氢酶、谷丙转氨酶、谷草转氨酶、D-二聚体水平高, 差异有统计学意义(均P< 0.05), 两组在年龄、使用高剂量GC占比差异无统计学意义(P> 0.05), 见表4。

表 3 SMPP患儿使用高剂量GC治疗的多因素logistic回归分析

Table 3 Multivariate logistic regression for high-dose GC therapy in SMPP children

Variable	β	SE	Wald	OR (95% CI)	P
Intercept	1.240	0.885	1.964		0.161
Age	−0.142	0.054	6.886	0.867 (0.780-0.965)	0.009
PLT	0.004	0.002	4.546	1.004 (1.000-1.008)	0.033
Atelectasis	0.947	0.340	7.751	2.577 (1.323-5.020)	0.005

SE: standard error; PLT: platelets.

2.4 SMPP患儿使用GC治疗无效的危险因素分析

二元logistic回归分析结果(表5)示: RMPP和热峰高是使用GC治疗无效的危险因素。

3 讨论

MPP是儿童最常见的非典型病原体肺炎类型, 约占CAP住院患儿的三分之一[10]。近年来, SMPP的发病率持续上升。中国一项单中心研究报告示, SMPP的发病率高达50.6%[11], 提示疾病严重程度的流行病学变迁。SMPP的发病机制尚未完全明确, 现有研究表明其病因涉及病原体、理化因素、免疫功能异常、过敏反应及药物因素, 主要机制包括病原体的直接作用及其诱发的免疫炎症反应[12-13]。GC可用于治疗多种疾病。这类药物大多以药理剂量用于抗炎、抗毒、抗休克和免疫抑制治疗[8]。因此, GC治疗主要用于重症、危重症及难治性MPP[4, 9, 14], 且临床治疗推荐使用常规剂量〔2 mg/(kg·d)〕甲泼尼龙。YANG等[15]研究发现抗生素对肺炎支原体感染的疗效有限, 而根据疾病严重程度早期调整GC更有助于预防SMPP并减少GC的不良反应。

目前国内外应用GC治疗MPP临床应用尚未达成共识[5, 6, 16]。本研究发现低剂量〔≤2 mg/(kg·d)甲泼尼龙〕治疗SMPP疗效、住院时长、咳嗽缓解时间及湿啰音吸收时

表 4　GC治疗无效组和有效组患儿临床特征比较

Table 4　Comparison of clinical characteristics between the GC-ineffective and the GC-effective groups

Variable	Ineffective group (n = 38)	Effective group (n = 142)	P
Male/case (%)	21 (55.26)	68 (47.89)	0.532
Age/yr., M (Q1, Q3)	6.00 (4.00, 9.00)	5.00 (3.00, 7.00)	0.528
RMPP/case (%)	22 (57.89)	25 (17.61)	< 0.001
Symptoms and signs			
Peak fever temperature/℃, M (Q1, Q3)	40.00 (39.60, 40.30)	39.60 (39.30, 40.00)	< 0.001
Productive cough/case (%)	37 (97.37)	134 (94.37)	0.687
Wheezing/case (%)	9 (23.68)	31 (21.83)	0.981
Crackles/case (%)	37 (97.36)	139 (97.89)	1.000
Diminished breath sounds/case (%)	15 (39.47)	41 (28.87)	0.291
Chest pain/case (%)	4 (10.53)	3 (2.11)	0.037
Hypoxemia/case (%)	5 (13.16)	11 (7.75)	0.336
Extrapulmonary complications/case (%)	3 (7.90)	8 (5.63)	0.702
Imaging findings			
Pulmonary consolidation/case (%)	26 (68.42)	86 (60.56)	0.485
Atelectasis/case (%)	16 (42.11)	50 (35.21)	0.553
Pleural effusion/case (%)	16 (42.11)	38 (26.76)	0.102
Pleural thickening/case (%)	27 (71.05)	87 (61.27)	0.356
Emphysema/case (%)	1 (2.63)	4 (2.82)	1.000
Laboratory tests			
WBC/10^9 L^{-1}, M (Q1, Q3)	7.54 (5.86, 9.54)	7.88 (5.79, 10.05)	0.582
N/10^9 L^{-1}, M (Q1, Q3)	5.39 (3.97, 6.83)	5.07 (3.57, 6.47)	0.663
L/10^9 L^{-1}, M (Q1, Q3)	1.41 (1.17, 2.03)	1.83 (1.41, 2.62)	0.016
NLR (M [Q1, Q3])	3.41 (2.25, 5.10)	2.37 (1.71, 3.92)	0.022
E/10^9 L^{-1}, M (Q1, Q3)	0.05 (0.01, 0.15)	0.05 (0.02, 0.15)	0.368
HGB/(g/L), M (Q1, Q3)	123.50 (116.75, 132.75)	126.00 (119.25, 133.00)	0.411
PLT/10^9 L^{-1}, M (Q1, Q3)	244.00 (200.75, 323.75)	260.00 (227.00, 320.50)	0.346
PLT (M [Q1, Q3])	170.48 (124.81, 227.44)	150.16 (95.28, 205.30)	0.081
SII (M [Q1, Q3])	898.20 (583.64, 1 275.47)	636.48 (445.16, 1 161.08)	0.109
CRP/(mg/L), M (Q1, Q3)	22.12 (13.77, 54.41)	27.78 (13.23, 52.90)	0.851
ESR/(mm/1 h), M (Q1, Q3)	30.00 (24.00, 40.00)	30.00 (24.25, 36.00)	0.637
PCT/(ng/mL), M (Q1, Q3)	0.18 (0.12, 0.43)	0.14 (0.08, 0.25)	0.017
FER/(ng/mL), M (Q1, Q3)	190.60 (111.30, 293.78)	128.30 (86.86, 173.35)	0.001
IL-6/(pg/mL), M (Q1, Q3)	29.56 (22.39, 46.08)	26.88 (17.66, 39.46)	0.063
LDH/(U/L), M (Q1, Q3)	461.50 (334.75, 559.25)	351.50 (292.25, 417.50)	0.001
ALT/(U/L), M (Q1, Q3)	15.00 (12.00, 21.75)	12.00 (10.00, 16.00)	0.019
AST/(U/L), M (Q1, Q3)	36.50(27.25, 45.00)	31.00 (25.00, 37.00)	0.017
D-dimer/(mg/L), M (Q1, Q3)	1.46 (1.09, 3.20)	1.09 (0.67, 1.38)	< 0.001
Treatment			
Pre-hospital macrolide use/case (%)	21 (55.26)	57 (40.14)	0.137
High-dose methylprednisolone use/case (%)	14 (36.84)	76 (53.52)	0.100
Ventilator use/case (%)	0 (0)	3 (2.11)	1.000

The abbreviations are explained in the note to Table 1.

间与高剂量组〔> 2 mg/(kg·d)甲泼尼龙〕差异无统计学意义。但高剂量组体温恢复时间及热程较短，且影像学恢复表现为显著吸收占比更高，无变化占比更低，这一发现与既往研究结果一致[5, 16]，虽然也有研究发现高剂量GC可

表 5 SMPP患儿使用GC治疗无效的多因素logistic回归分析

Table 5 Multivariate logistic regression analysis of GC treatment failure in SMPP children

Variables	β	SE	Wald	OR (95% CI)	P
Intercept	−37.979	15.226	6.221		0.013
RMPP	1.825	0.437	17.463	6.200 (2.635-14.589)	< 0.001
Peak fever temperature	0.908	0.384	5.583	2.479 (1.167-5.264)	0.018

The abbreviations are explained in the note to Tables 1 and 2.

以缩短住院时长[7]，但其采用的GC剂量显著高于本研究。

在安全性方面，本研究发现高剂量组常见药物不良反应（恶心、呕吐、腹痛、腹泻、皮疹等）发生率相对较高，尽管有研究[5]报道类似症状在高剂量GC使用时更为常见，但组间差异未达统计学意义，且所有症状均在停药后自行缓解，本研究中出现不良反应的患儿亦均在停药后得到缓解。本研究中无论低剂量组还是高剂量组患儿均未发生严重不良反应（如高血糖、高血脂、高血压、消化道出血或穿孔等），这与多数文献报道相符[5, 7]。甚至，有研究[17]报道使用冲击剂量GC（≥200 mg/d甲泼尼龙）治疗时也未观察到明显不良反应，这可能与短期用药相关但现有研究普遍存在对轻度药物不良反应报告不充分的现象。

现有研究[18-19]显示年龄小是进展为SMPP的危险因素，本研究也发现年龄小是使用高剂量GC治疗的危险因素。从病理生理学角度而言，年长患儿由于免疫系统发育相对成熟，可能产生更强烈的炎症反应，对高剂量GC的需求更高。然而，本研究显示使用高剂量组患儿年龄显著低于低剂量组，多因素logistic回归分析证实年龄偏小是高剂量GC治疗的独立影响因素。有研究显示在RMPP患儿中使用高剂量GC的年龄偏大[20]。得出的结论与病理生理学相反，推测临床决策过程可能受到非医学因素的影响。如低龄患儿反复发热等临床症状更容易引发家属焦虑情绪，这种心理因素可能无形中影响医生的治疗决策。血小板在调控宿主对损伤、炎症和感染的反应中具有生物学活性[21-22]。有证据表明，血小板及中性粒细胞均表达促炎受体（C-X-C chemokine receptor type 4, CXCR 4）和CXCR 7，在炎症过程中，这些受体表达升高，并促进血小板和中性粒细胞形成复合物[23]。有研究显示SMPP血小板计数高于MPP[24]。本研究结果显示高剂量GC治疗组患儿血小板计数显著高于低剂量组，多因素logistic回归分析进一步证实，血小板计数升高是高剂量GC治疗的独立影响因素。血小板在炎症过程表现为促炎作用，因此医生倾向于对血小板计数升高的患儿启动GC治疗。然而，目前尚缺乏高质量循证医学证据来明确血小板计数的具体临界值及不同血小板升高程度对应的最佳GC剂量。儿童胸部影像学存在肺不张是诊断SMPP其中一个重要的特征[4]，MPP不同的影像学表现中，以肺实变/肺不张组病情最重，其临床表现及实验室指标异常显著，且预后较差，包括发热和住院时间延长、住院费用增加，并更易发展为RMPP、坏死性肺炎及闭塞性细支气管炎。本研究结果显示，高剂量GC治疗组患儿的肺不张发生率显著高于低剂量组，并且肺不张是高剂量GC治疗的独立影响因素。我们推测这一临床决策可能与以下因素相关：合并肺不张的患儿临床表现更重，炎症浸润范围更广泛，其平均发热持续时间显著延长；肺不张是疾病预后不良的预测指标。这些因素可能共同促使临床医生对合并肺不张的患儿采取更积极的高剂量GC干预策略。

本研究证实，GC治疗无效的SMPP患儿具有更显著的炎症反应特征，表现为RMPP比例增高、胸痛发生率升高，以及中性淋巴细胞比值、热峰、炎症标志物（降钙素原、铁蛋白、乳酸脱氢酶、D-二聚体）和肝损伤指标（ALT、AST）水平升高，同时伴有淋巴细胞减少。然而，GC疗效与患儿年龄及GC剂量无明显相关性。多因素回归分析进一步明确，RMPP和高热峰是GC治疗无效的独立危险因素。这一结果提示治疗无效可能与过度免疫激活相关。RMPP患儿体内存在异常的细胞免疫应答和细胞因子风暴[25]，导致GC抗炎作用受限。持续高热可通过多重途径加重病情，包括直接组织损伤、促炎介质释放及全身炎症反应[26]。尤其值得注意的是，下呼吸道因其特殊的解剖结构和生理功能，可能对高热诱导的免疫损伤更为敏感[27]。

本研究存在一定局限性。首先，尽管通过多变量调整控制了混杂因素，但观察性研究设计仍可能存在残余混杂或未测量的偏倚。其次，单中心数据及有限的样本量可能影响研究结论的普适性，未来需要通过多中心、大样本的前瞻性队列研究加以验证。尽管如此，本研究仍为相关临床实践及决策提供了有价值的证据。

综上, 本研究证实低剂量GC治疗方案具有良好的临床疗效, 因此推荐临床首选低剂量GC治疗。同时发现临床医师在面对低龄、血小板计数偏高以及合并肺不张患儿时更倾向于选择高剂量GC治疗。对于具有RMPP特征或持续高热的SMPP患儿, 需警惕GC治疗失败风险, 并考虑早期联合其他免疫调节治疗策略。同时, 应加强体温管理, 以减轻高热对肺组织的继发损伤。这些治疗决策可能反映了临床医师对疾病严重程度的综合判断, 但目前尚缺乏高质量循证医学证据来验证这一临床实践的科学性。基于此, 未来研究亟需通过多中心协作, 建立整合临床指标与生物标志物的预测模型, 并开展治疗策略的优化研究, 从而为SMPP患儿的GC治疗提供更精准的决策依据。

*　　*　　*

作者贡献声明　王雪琳负责论文构思、数据审编、正式分析、调查研究、研究方法、可视化和初稿写作, 王一帆负责数据审编和审读与编辑写作, 李姣负责论文构思、研究方法、研究项目管理和监督指导, 邹映雪负责论文构思、经费获取、研究方法、研究项目管理、提供资源、监督指导和审读与编辑写作。所有作者已经同意将文章提交给本刊, 且对将要发表的版本进行最终定稿, 并同意对工作的所有方面负责。

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