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糖皮质激素辅助治疗对肺炎支原体肺炎患儿肺功能、血清炎症因子及体液免疫功能的影响*

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摘要 目的:探讨糖皮质激素辅助治疗对肺炎支原体肺炎(MPP)患儿肺功能、血清炎症因子及体液免疫功能的影响。**方法:**选取2016年3月~2019年3月间在我院接受住院治疗的100例MPP患儿,根据随机数字表法将患儿分为研究组、对照组,各50例,其中对照组予以常规治疗,研究组则予以糖皮质激素辅助常规治疗,比较两组患儿临床疗效、肺功能[呼气峰流速值(PEF)、第1s用力呼气容积(FEV₁)、潮气量(V-T)]、血清炎症因子[白介素-6(IL-6)、白介素-10(IL-10)、肿瘤坏死因子-α(TNF-α)]及体液免疫功能[免疫球蛋白A(IgA)、免疫球蛋白M(IgM)、免疫球蛋白G(IgG)]等指标变化情况,记录两组治疗期间不良反应情况。**结果:**研究组治疗后的临床总有效率为92.00%(46/50),高于对照组的70.00%(35/50)($P<0.05$)。治疗后两组患儿IgG、IgA、IgM均较治疗前升高,且研究组高于对照组($P<0.05$)。治疗后两组患儿IL-6、IL-10、TNF-α均较治疗前降低,且研究组低于对照组($P<0.05$)。治疗后两组患儿PEF、FEV₁、V-T均较治疗前升高,且研究组高于对照组($P<0.05$)。两组不良反应发生率相比无差异($P>0.05$)。**结论:**糖皮质激素辅助治疗MPP患儿,可减轻机体炎症因子水平,改善患儿肺功能的同时还可缓解体液免疫紊乱,且联合用药安全性较好。

关键词:糖皮质激素;肺炎支原体肺炎;肺功能;炎症因子;体液免疫

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Effects of Glucocorticoid on Pulmonary Function, Serum Inflammatory Factors and Humoral Immune Function in Children with Mycoplasma Pneumoniae Pneumonia*

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ABSTRACT Objective: To investigate the effect of glucocorticoid on pulmonary function, serum inflammatory factors and humoral immune function in children with mycoplasma pneumoniae pneumonia (MPP). **Methods:** From March 2016 to March 2019, 100 children with MPP in our hospital were selected, they were divided into study group and control group according to the random number table method, 50 cases in each group. The control group received routine treatment, while the study group received glucocorticoid assisted routine treatment. The clinical effect, pulmonary function value [peak expiratory flow (PEF), forced expiratory volume in the first second (FEV₁), tidal volume (V-T)], serum inflammatory factors [interleukin-6 (IL-6) and interleukin 10 (IL-10), tumor necrosis factor-α (TNF-α)] and humoral immune function [immunoglobulin A (IgA), immunoglobulin M (IgM), immunoglobulin G (IgG)] indexes changes between two groups were compared. The adverse reactions of the two groups were recorded. **Results:** The total clinical effective rate of the study group was 92.00% (46/50), which was higher than 70.00% (35/50) of the control group ($P<0.05$). After treatment, IgG, IgA and IgM of the two groups were higher than before treatment, and those of the study group were higher than those of the control group ($P<0.05$). After treatment, the levels of IL-6, IL-10 and TNF-α of the two groups were lower than those before treatment, and those of the study group were lower than those of the control group ($P<0.05$). After treatment, PEF, FEV₁ and V-T of the two groups were higher than before treatment, and those of the study group were higher than those of the control group ($P<0.05$). There was no difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Glucocorticoid assisted treatment of MPP children can reduce the level of inflammatory factors, improve the lung function of children, but also it can alleviate the disorder of humoral immunity, and the combination of drug safety is better.

Key words: Glucocorticoid; Mycoplasma pneumoniae pneumonia; Pulmonary function; Inflammatory factors; Humoral immunity

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前言

肺炎支原体肺炎 (Mycoplasma pneumoniae pneumonia, MPP) 主要由肺炎支原体所引起, 据以往报道统计, 约有 10%~40% 的肺炎患儿由支原体感染所致^[1]。MPP 临床主要表现为发热、咳嗽、头痛、食欲不振等, 随着病情的进展, 还可导致患儿肺功能呈进行性下降及免疫功能失调, 引发多脏器功能损伤, 严重影响患儿生命健康^[2]。目前临床针对 MPP 的治疗多以阿奇霉素序贯疗法为主, 但由于阿奇霉素药理机制相对单一, 加之抗生素的大量应用, 易出现耐药现象, 致使部分患儿治疗后病情无明显改善, 效果受限^[3]。糖皮质激素具有调节免疫、抗炎等药理作用, 可用于辅助抗生素治疗呼吸道感染类疾病^[4]。本研究通过对我院收治的部分 MPP 患儿予以糖皮质激素辅助治疗, 取得了不错的疗效, 总结报告如下。

1 资料与方法

1.1 基线资料

选取 2016 年 3 月~2019 年 3 月间在我院接受住院治疗的 MPP 患儿 100 例。纳入标准: (1) 肺炎诊断标准符合《儿童社区获得性肺炎管理指南 2013 修订-上》的诊断标准^[5]; (2) 肺炎支原体 (Mycoplasma pneumoniae, MP) 的诊断符合任意一项: ① 血清 MP-IgM ≥ 1:160 ② 荧光定量实时 MP-PCR 阳性^[6]; (3) 患儿监护人或家属知情本研究且签署了同意书; (4) 年龄 5~14 岁。排除标准: (1) 入组前 1 个月内接受过其他治疗的患儿; (2) 对本次研究用药存在禁忌症的患儿; (3) 合并心肝肾等脏器不全者; (4) 合并肺部其他疾病的患儿; (5) 治疗依从性差, 中途退出本次研究的患儿; (6) 合并自身免疫系统疾病的患儿。本研究已获取我院伦理学委员会批准同意。根据随机数字表法将患者分为两组: 研究组、对照组, 其中对照组 50 例, 男 28 例, 女 22 例, 年龄 5~14 岁, 平均 (8.83±1.06) 岁; 病程 3~9d, 平均 (6.97±1.59)d; 体质指数 12.8~15.9kg/m², 平均 (14.26±0.42)kg/m²。研究组 50 例, 男 26 例, 女 24 例, 年龄 6~13 岁, 平均 (8.43±0.86) 岁; 病程 3~10d, 平均 (6.26±1.54)d; 体质指数 12.4~16.4kg/m², 平均 (14.37±0.55)kg/m²。两组患儿基本资料对比无差异 ($P>0.05$)。

1.2 方法

患儿接受常规血常规、肺功能等检查, 并给予相关对症治疗, 包括退热、化痰平喘、营养支持、纠正水电解质平衡、持续低流量吸氧、抗感染等。在以上基础的前提下, 对照组给予阿奇霉素干混悬剂 (辉瑞制药有限公司, 国药准字 H10960112, 规格: 0.1 g) 10 mg/kg, 口服, 1 次/d, 连服 5-7d, 停药 4d; 之后按照

连服 3d, 停药 4d 为 1 个治疗周期, 再连续服药治疗 3 个周期。研究组则在对照组的基础上联合糖皮质激素辅助治疗, 注射用甲泼尼龙琥珀酸钠 (进口药品注册证号 H20130301, 规格: 40 mg) 按 1 mg/kg, 溶于 100 mL 5% 葡萄糖注射液中, 静脉滴注, 1 次/d, 视患儿具体病情情况治疗 3~7d。

1.3 观察指标

1.3.1 临床疗效 记录两组患儿临床治疗效果, 疗效判定^[6]: 显效: 患儿发热、气急缺氧、干咳等临床症状基本消失, 肺部体征及 X 线胸片阴影消失; 有效: 患儿发热、气急缺氧、干咳等临床症状有所改善, 肺部体征及 X 线胸片阴影有所减少; 无效: 患儿发热、气急缺氧、干咳等临床症状未见改善甚至加重, 肺部体征及 X 线胸片阴影未见减少甚至增加。总有效率 = 显效率 + 有效率。

1.3.2 体液免疫功能、炎症因子 抽取所有患儿空腹肘静脉血 5 mL, 采血时间: 治疗前、治疗后清晨, 血液样本经 4300r/min 离心 12min, 分离上清液待测。采用酶联免疫吸附法检测白介素 -6 (Interleukin-6, IL-6)、白介素 -10 (Interleukin-10, IL-10)、肿瘤坏死因子 - α (Tumor necrosis factor- α , TNF- α)。采用美国库尔特公司 (COULTER) 生产的 EPICS XL 公司生产的流式细胞仪检测免疫球蛋白 A (Immunoglobulin A, IgA)、免疫球蛋白 M (Immunoglobulin M, IgM)、免疫球蛋白 G (Immunoglobulin G, IgG)。

1.3.3 肺功能 于治疗前后采用日本杰斯特公司生产的肺功能仪 (HI101 型) 检测两组肺功能指标, 包括呼气峰流速值 (Peak expiratory velocity, PEF)、第 1s 用力呼气容积 (Forced expiratory volume in the first second, FEV₁)、潮气量 (Tidal volume, V-T)。

1.3.4 安全性评价 记录两组患儿治疗期间不良反应状况。

1.4 统计学方法

采用 SPSS25.0 进行数据分析, 计数资料以率表示, 行卡方检验, 计量资料以均值±标准差的形式表示, 行 t 检验。检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 临床疗效比较

研究组治疗后的临床总有效率高于对照组 ($P<0.05$); 详见表 1。

2.2 两组免疫功能指标比较

治疗前, 两组 IgG、IgA、IgM 比较无差异 ($P>0.05$); 治疗后两组患儿 IgG、IgA、IgM 均较治疗前升高, 且研究组高于对照组 ($P<0.05$); 详见表 2。

表 1 临床疗效比较 [例 (%)]

Table 1 Comparison of clinical effects [n (%)]

Groups	Markedly effective	Effective	Invalid	Total efficiency
Control group (n=50)	14 (28.00)	21 (42.00)	15 (30.00)	35 (70.00)
Study group (n=50)	19 (38.00)	27 (54.00)	4 (8.00)	46 (92.00)
χ^2				7.862
P				0.005

表 2 两组免疫功能指标比较($\bar{x}\pm s$)

Table 2 Comparison of immune function indexes between the two groups($\bar{x}\pm s$)

Groups	IgG(g/L)		IgA(g/L)		IgM(g/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=50)	8.49±0.73	9.75±0.82 ^a	0.78±0.08	0.98±0.11 ^a	1.52±0.33	1.85±0.46 ^a
Study group(n=50)	8.46±0.62	12.63±1.14 ^a	0.79±0.07	1.19±0.17 ^a	1.47±0.26	2.16±0.51 ^a
t	0.221	14.502	0.665	7.334	0.842	3.192
P	0.825	0.000	0.507	0.000	0.402	0.002

Note: compared with before treatment, ^a $P < 0.05$.

2.3 两组炎症因子水平比较

治疗前,两组 IL-6、IL-10、TNF- α 比较无差异($P > 0.05$);治

疗后两组患儿 IL-6、IL-10、TNF- α 均较治疗前降低,且研究组低于对照组($P < 0.05$);详见表 3。

表 3 两组炎症因子水平比较($\bar{x}\pm s$)

Table 3 Comparison of inflammatory factors between the two groups($\bar{x}\pm s$)

Groups	IL-6(ng/L)		IL-10(pg/mL)		TNF- α (pg/mL)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=50)	14.62±2.37	10.48±2.27 ^a	21.56±2.28	17.41±2.82 ^a	28.87±2.17	22.90±3.02 ^a
Study group(n=50)	14.48±1.54	6.47±1.34 ^a	21.74±3.21	13.95±2.97 ^a	29.52±2.46	17.16±2.30 ^a
t	0.350	10.757	0.323	5.974	1.401	10.692
P	0.727	0.000	0.747	0.000	0.164	0.000

Note: compared with before treatment, ^a $P < 0.05$.

2.4 两组肺功能指标比较

治疗前,两组患儿 PEF、FEV₁、V-T 比较差异无统计学意义

($P > 0.05$), 治疗后两组患儿 PEF、FEV₁、V-T 均较治疗前升高,且研究组高于对照组($P < 0.05$),详见表 4。

表 4 两组肺功能指标比较($\bar{x}\pm s$)

Table 4 Comparison of pulmonary function indexes between the two groups($\bar{x}\pm s$)

Groups	PEF(L)		FEV ₁ (L)		V-T(mL/kg)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=50)	3.26±0.39	4.83±0.42 ^a	1.36±0.23	1.85±0.31 ^a	8.18±0.95	11.17±1.33 ^a
Study group(n=50)	3.19±0.42	6.17±0.38 ^a	1.41±0.19	2.67±0.37 ^a	8.25±0.73	14.56±1.01 ^a
t	0.864	16.729	1.185	12.012	0.413	14.354
P	0.390	0.000	0.239	0.000	0.680	0.000

Note: compared with before treatment, ^a $P < 0.05$.

2.5 不良反应发生率比较

治疗期间,对照组出现 1 例心动过速、2 例面部潮红、1 例恶心呕吐、3 例胃肠道反应,不良反应发生率为 14.00%(7/50);研究组出现 3 例胃肠道反应、3 例面部潮红、2 例恶心呕吐、2 例心动过速,不良反应发生率为 20.00%(10/50);两组不良反应发生率对比未见统计学差异($\chi^2=0.638, P=0.424$)。

3 讨论

肺炎支原体是介于细菌与病毒之间的一种病原微生物,独立生存能力较强,是引起呼吸系统疾病和全身性病变的常见病原体,其中以 MPP 最为常见且严重^[7-9]。由于肺炎支原体可通过

呼吸道飞沫传播,易在幼儿园、学校等封闭环境中流行,加之小儿肺脏娇嫩,尚未完全发育成熟,极易遭受肺炎支原体的侵入而引发肺炎^[10-12]。MPP 发病后,由于肺炎支原体的感染,可对患儿呼吸道上皮及黏膜造成直接损伤,从而引起气道炎症性改变;同时肺炎支原体还可促进过氧化氢类有毒代谢产物大量释放,间接损伤上皮细胞并引发炎症反应;此外,既往也有研究结果显示,MPP 患儿发病时其免疫功能明显降低,即免疫紊乱在 MPP 的病情进展中发挥重要作用^[13-15]。现临床针对 MPP 的治疗,主要以抗肺炎支原体感染为主,阿奇霉素是大环内酯类抗生素的代表性药物,可有效控制 MPP 患儿病情,但不少临床实践结果表明大环内酯类药物治疗肺炎支原体肺炎会出现耐药,

效果欠佳^[16,17]。因此,临床逐渐尝试采用辅助药物联合进行治疗以提高治疗效果。糖皮质激素具有抗过敏、抗感染及抑制免疫反应等多重药理作用,在抗感染治疗中应用较为广泛^[18,19],因此本研究设置了对照试验,在阿奇霉素治疗的基础上辅以地塞米松磷酸钠注射液,以期取得更好的疗效。

本次研究结果中研究组治疗后的临床总有效率高于对照组,表明糖皮质激素辅助治疗 MPP 患儿,可优化治疗效果。分析其原因,阿奇霉素生物利用度较佳,抗菌谱广,进入人体后可选择性的抑制蛋白质合成,快速杀死致病性微生物,而与糖皮质激素联合使用后,糖皮质激素不仅自身具有多重药理作用,还可增强阿奇霉素的药效,发挥协同作用^[20-22]。既往研究结果显示^[23],MPP 的发病机制及其复杂,其中机体过强的炎症反应及免疫紊乱是 MPP 发生的重要原因。肺炎支原体入侵人体后,一方面可释放过氧化氢、核酸酶、磷酸酶等代谢产物,损伤白细胞,导致 IgG、IgA、IgM 分泌异常,引发机体产生免疫损害;另一方面可通过激活巨噬细胞、中性粒细胞,致使炎症细胞如 IL-6、IL-10、TNF- α 等大量分泌,引起患儿呼吸道呈持续性高反应性,间接影响患儿肺功能^[24-26]。PEF、FEV₁、V-T 是反映机体大气道及小气道功能的直观指标,当患儿肺功能受损时,上述指标水平明显下降。本次研究中,两组患儿炎症因子、肺功能及体液免疫功能指标均有所改善,且糖皮质激素辅助治疗者改善效果更佳。糖皮质激素作为一种非特异性消炎药,可促进局部炎症部位的毛细血管扩张,提高血管壁通透性,进而降低炎症细胞对肺实质细胞的浸润;其还具有较强的抗纤维化作用,可阻止或减缓肺纤维化形成,有利于患儿呼吸功能的恢复;此外,糖皮质激素还可通过减少炎症因子的分泌,减少机体毒性物质的产生,进而缓解患儿免疫功能的紊乱^[27-29]。另两组不良反应发生率对比未见差异,可见本次用药安全性较好,这可能与糖皮质激素可在一定程度上缓解阿奇霉素的耐药性,并纠正患儿免疫功能紊乱有关^[30],因而没有增加不良反应发生率。

综上所述,糖皮质激素辅助治疗 MPP 患儿,可减轻机体炎症因子水平,改善患者肺功能,纠正体液免疫功能紊乱,且用药安全性较好。

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(上接第 4467 页)

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