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小儿肺热咳喘口服液联合阿奇霉素对肺炎支原体肺炎患儿肺功能和炎性因子的影响 *

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摘要 目的:探讨小儿肺热咳喘口服液联合阿奇霉素对肺炎支原体肺炎患儿肺功能和炎性因子的影响。**方法:**选取 2016 年 1 月~2017 年 12 月期间我院收治的 175 例肺炎支原体肺炎患儿,根据随机数字表法将其分为对照组($n=87$,阿奇霉素治疗)和研究组($n=88$,小儿肺热咳喘口服液联合阿奇霉素治疗),比较两组患儿临床疗效、临床症状消失时间、肺功能指标[第 1s 用力呼气容积(FEV1)、用力肺活量(FVC)、FEV1/FVC]、炎性因子指标[肿瘤坏死因子- α (TNF- α)、白介素-6(IL-6)、C 反应蛋白(CRP)],记录两组患儿不良反应发生情况。**结果:**研究组患儿治疗后临床总有效率为 94.32%(83/88),高于对照组患儿的 80.46%(70/87)($P<0.05$)。研究组患儿咳嗽、发热、湿啰音、哮鸣音的消失时间均短于对照组($P<0.05$)。两组患儿治疗后 FEV1、FVC、FEV1/FVC 均升高,且研究组高于对照组($P<0.05$)。两组患儿治疗后 IL-6、CRP、TNF- α 水平均降低,且研究组低于对照组($P<0.05$)。两组患儿不良反应发生率对比无统计学差异($P>0.05$)。**结论:**小儿肺热咳喘口服液联合阿奇霉素治疗肺炎支原体肺炎患儿的疗效优于单用阿奇霉素,且可有效改善患儿肺功能和炎性因子水平,快速缓解临床症状,促进患儿恢复。

关键词:小儿肺热咳喘口服液;阿奇霉素;肺炎支原体肺炎;肺功能;炎性因子

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Effects of Xiaer Feire Kechuan oral Liquid Combined with Azithromycin on Pulmonary Function and Inflammatory Factors in Children with Mycoplasma Pneumonia*

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ABSTRACT Objective: To investigate the effects of Xiaer Feire Kechuan oral liquid combined with azithromycin on pulmonary function and inflammatory factors in children with mycoplasma pneumoniae pneumonia. **Methods:** 175 children with mycoplasma pneumoniae pneumonia who were admitted to our hospital from January 2016 to December 2017 were selected, and they were divided into control group ($n=87$, azithromycin treatment) and study group ($n=88$, Xiaer Feire Kechuan oral liquid combined with azithromycin treatment) according to random number table method. The clinical efficacy, disappearance time of clinical symptoms and pulmonary function indexes [forced expiratory volume in 1st second (FEV1), forced vital capacity (FVC), FEV1/FVC], inflammatory factor indexes [tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), C-reactive protein (CRP)] of the two groups were compared, and the occurrence of adverse reactions in two groups of children were recorded. **Results:** The total clinical effective rate of the study group was 94.32% (83/88), which was higher than 80.46% (70/87) of the control group ($P<0.05$). The disappearance time of cough, fever, moist rale and wheezing in the study group were shorter than those in the control group ($P<0.05$). The FEV1, FVC and FEV1/FVC in both groups after treatment increased, and the levels in the study group were higher than those in the control group ($P<0.05$). The levels of IL-6, CRP and TNF- α in both groups after treatment decreased, the levels of the study group were lower than those in the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** The curative effect of Xiaer Feire Kechuan oral liquid combined with azithromycin in treating children with mycoplasma pneumonia is better than that of azithromycin alone. It can effectively improve the pulmonary function and inflammatory factor level of children, quickly relieve clinical symptoms, and promote the recovery of children.

Key words: Xiaer Feire Kechuan oral liquid; Azithromycin; Mycoplasma pneumoniae pneumonia; Pulmonary function; Inflammatory factors

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前言

肺炎是儿童常见的感染性疾病,也是导致儿童住院、死亡的重要疾病^[1,2]。其中肺炎支原体肺炎是临床常见的类型,在社区儿童获得性肺炎中占比高达 10%~40%^[3]。目前临床针对该病的治疗首选药物为大环内酯类药,阿奇霉素为其代表性药物^[4-6]。但不少临床实践证实^[7,8],单用阿奇霉素治疗易出现耐药性,疗效并不理想,因此寻找一种切实有效的治疗方案尤为重要。小儿肺热咳喘口服液是一种中成药,具有清热解毒、化痰平喘、宣肺止咳的作用^[9]。本研究针对肺炎支原体肺炎患儿的特点,在阿奇霉素治疗的同时辅以小儿肺热咳喘口服液治疗,并探讨上述联合药物对患儿肺功能和炎性因子的影响,以期为临床治疗提供方案参考。

1 资料与方法

1.1 一般资料

选取 2016 年 1 月~2017 年 12 月期间我院收治的 175 例肺炎支原体肺炎患儿,纳入标准:(1)均符合《儿童社区获得性肺炎管理指南》^[10]中的相关诊断标准;(2)临床表现为咳嗽、发热、呼吸困难,并经实验室检查及拍摄胸片等明确诊断;(3)血清特异性肺炎支原体抗体为阳性;(4)年龄 5~13 岁;(5)患儿家属或监护人知情本次研究且已签署同意书。排除标准:(1)合并严重肝肾等脏器功能不全者;(2)对本次研究使用药物过敏者;(3)伴有衣原体、病毒等其他病原体感染者;(4)合并先天性支气管肺疾病、先天性心脏病者;(5)高度不配合、未能完成肺功能测试者。根据随机数字表法将其分为对照组($n=87$)和研究组($n=88$),其中对照组男 48 例,女 39 例,年龄 5~13 岁,平均(7.12 ± 1.61)岁;病程 3~15d,平均(9.06 ± 1.46)d;病情严重程度^[10]:轻度 47 例,中度 40 例。研究组男 50 例,女 38 例,年龄 5~12 岁,平均(7.23 ± 1.73)岁;病程 3~13d,平均(9.11 ± 1.52)d;病情严重程度:轻度 46 例,中度 42 例。两组患儿一般资料对比无差异($P>0.05$),具有可比性。本研究已获取我院伦理委员会的批准。

1.2 治疗方法

所有患儿均给予退热、止咳、雾化吸入等常规治疗,在此基

础上,对照组给予静脉滴注阿奇霉素(Pfizer Inc., 国药准字: J20140073,规格:0.5g)10 mg/(kg·d)治疗,1 次/d,静滴 3d 后停用 4 d,随后口服阿奇霉素干混悬剂(Pfizer Inc., 国药准字 H10960112,规格:0.1 g)治疗,1 次/d,口服 3d 后停用 4d,序贯治疗 3 个周期。研究组在对照组基础上联合小儿肺热咳喘口服液(黑龙江葵花药业股份有限公司, 国药准字 Z10950080,规格:每支装 10 mL)治疗,5~7 岁患儿 10 mL/次,4 次/d,8~13 岁患儿 20 mL/次,3 次/d,14d 为一个治疗疗程,共治疗 3 个疗程。

1.3 观察指标

记录两组治疗后的临床疗效^[11],判定标准如下:无效:临床症状、肺部体征以及 X 线胸部摄片未见明显改善甚至加重;有效:X 线胸部摄片显示吸收不明显,临床症状、肺部体征有所好转;显效:X 线胸部摄片显示肺炎吸收期,临床症状、肺部体征明显好转;痊愈:X 线胸部摄片显示正常,临床症状、肺部体征消失;总有效率=痊愈率+显效率+有效率。记录所有患儿咳嗽、发热、湿啰音、哮鸣音等临床症状消失时间。记录所有患儿在治疗过程中发生的不良反应情况。于治疗前后采用德国 Carefusion 公司生产的 microUSB 肺功能仪检测两组患儿肺功能指标,包括第 1 s 用力呼气容积(Forced expiratory volume in 1st second, FEV1)、用力肺活量(Forced vital capacity, FVC),并计算 FEV1/FVC。于治疗前后采集患儿清晨空腹静脉血 4 mL,以 3500 r/min 离心 8 min,离心半径 8 cm,提取血清,置于 -20℃ 的冰箱中保存。采用酶联免疫吸附法检测血清中的肿瘤坏死因子- α (Tumor necrosis factor- α , TNF- α)、白介素-6(Interleukin-6, IL-6)、C 反应蛋白(C-reactive protein, CRP)的水平,试剂盒均购于 R&D Systems 公司。

1.4 统计学方法

采用 SPSS25.0 软件进行统计分析。计数资料以率的形式表示,采用卡方检验。计量资料以均值 $\pm$ 标准差($\bar{x} \pm s$)的形式表示,采用 LSD-t 检验。以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 临床疗效比较

研究组患儿治疗后临床总有效率为 94.32%(83/88),高于对照组患儿的 80.46%(70/87)($P<0.05$),详见表 1。

表 1 临床疗效比较[n(%)]
Table 1 Comparison of clinical efficacy [n(%)]

Groups	Recovery	Markedly effective	Effective	Invalid	Total effective rate
Control group($n=87$)	25(28.73)	24(27.59)	21(24.14)	17(19.54)	70(80.46)
Study group($n=88$)	37(42.04)	31(35.23)	15(17.05)	5(5.68)	83(94.32)
χ^2					7.645
P					0.006

2.2 临床症状消失时间比较

研究组患儿咳嗽、发热、湿啰音、哮鸣音的消失时间均短于对照组($P<0.05$),详见表 2。

2.3 肺功能指标比较

两组患儿治疗前 FEV₁、FVC、FEV₁/FVC 比较无差异($P>0.05$),两组患儿治疗后 FEV₁、FVC、FEV₁/FVC 均升高,且

研究组高于对照组($P<0.05$),详见表 3。

2.4 炎性因子比较

两组患儿治疗前 IL-6、CRP、TNF- α 水平比较无差异($P>0.05$),两组患儿治疗后 IL-6、CRP、TNF- α 水平均降低,且研究组低于对照组($P<0.05$),详见表 4。

表 2 临床症状消失时间比较($\bar{x} \pm s, d$)Table 2 Comparison of disappearance time of clinical symptoms($\bar{x} \pm s, d$)

Groups	Cough	Fever	Moist rale	Wheezing
Control group(n=87)	7.15± 1.26	3.48± 0.48	6.26± 0.91	5.35± 0.33
Study group(n=88)	5.46± 1.41	2.43± 0.54	5.35± 0.82	4.48± 0.26
t	8.357	13.590	6.951	19.384
P	0.000	0.000	0.000	0.000

表 3 肺功能指标比较($\bar{x} \pm s$)Table 3 Comparison of pulmonary function indexes($\bar{x} \pm s$)

Groups	FEV ₁ (%)		FVC(%)		FEV ₁ /FVC	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group(n=87)	75.39± 11.23	82.24± 10.42*	51.88± 5.78	54.34± 9.54*	1.45± 0.26	1.51± 0.24*
Study group(n=88)	76.11± 12.18	91.53± 11.37*	52.24± 5.46	57.38± 9.23*	1.46± 0.23	1.60± 0.34*
t	0.406	5.633	0.424	2.142	0.270	2.021
P	0.685	0.000	0.672	0.034	0.788	0.045

Note: Compared with before treatment, * $P < 0.05$.

表 4 炎症因子比较($\bar{x} \pm s$)Table 4 Comparison of inflammatory factors($\bar{x} \pm s$)

Groups	IL-6(ng/L)		CRP(mg/L)		TNF- α (ng/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group(n=87)	45.53± 8.54	14.77± 1.94*	31.27± 9.40	10.11± 1.87*	31.27± 8.17	11.90± 2.02*
Study group(n=88)	45.39± 9.27	8.79± 1.62*	31.19± 8.30	5.95± 1.97*	31.52± 9.46	6.86± 1.31*
t	0.104	22.143	0.060	14.324	0.187	19.605
P	0.917	0.000	0.952	0.000	0.852	0.000

Note: Compared with before treatment, * $P < 0.05$.

2.5 不良反应比较

见表 5。

两组患儿不良反应发生率对比无统计学差异($P > 0.05$), 详

表 5 不良反应比较[n(%)]

Table 5 Comparison of adverse reactions [n(%)]

Groups	Diarrhea and abdominal pain	Tachycardia	Facial flushing	Rash	Total incidence rate
Control group(n=87)	6(6.89)	4(4.60)	3(3.45)	1(1.15)	14(16.09)
Study group(n=88)	7(7.95)	3(3.41)	4(4.55)	2(2.27)	16(18.18)
χ^2					0.135
P					0.714

3 讨论

肺炎支原体是一种可直接致病的病原微生物,其大小介于病毒和细菌之间,可在无细胞的培养基上生长,兼性厌氧,可独立存活,通常在空气中传播,也可引起小范围的流行^[12-14]。肺炎支原体感染可发生在任何年龄段,随着人们生活习惯改变、周遭环境污染加重等多重因素影响,该病的发病年龄有逐渐减小的趋势^[15,16]。目前临床治疗肺炎支原体肺炎患儿的方法为常规

基础治疗的基础上联合阿奇霉素,但存在临床症状消失缓慢、耐药性普遍存在以及患儿处于生长发育期致使可用药物受限等诸多不足^[17],故而在现有基础上如何进一步提高治疗效果具有积极的临床意义。中医认为肺炎支原体肺炎以肺经为病变位置,患儿肺脏娇嫩,卫外不固,津液失养,则化液生痰,故以清肺化痰、补气平喘治疗为宜^[18,19]。小儿肺热咳喘口服液由经典名方"麻杏石甘汤、白虎汤、银翘散"的基础上加减所得,主要适用于热邪犯于肺卫所致咳嗽、发热等,而这些证候与肺炎支原体

肺炎患儿的症状基本吻合^[20-22]。鉴于此,本研究通过设置对照试验,以探讨小儿肺热咳喘口服液联合阿奇霉素的确切疗效。

本次研究结果显示,研究组患儿治疗后临床总有效率为94.32%,高于对照组患儿的80.46%,且研究组各项临床症状消失时间均短于对照组,表明小儿肺热咳喘口服液联合阿奇霉素治疗可迅速改善患儿临床症状,进一步提高治疗效果,阿奇霉素组织渗透性高,经血液循环进入吞噬细胞后,存积于溶酶体,进而传送到感染部位,达到治疗目的^[23,24]。小儿肺热咳喘口服液主要成分为苦杏仁、金银花、麻黄、石膏、连翘、甘草、板蓝根、麦冬、知母、黄芩、鱼腥草,方中麻杏石甘汤具有宣肺止咳之效,配伍金银花、黄芩、连翘、甘草清热解毒,知母除烦解热,板蓝根、鱼腥草、麦冬祛风利咽、清热解毒,诸药合用,共奏清热化痰、活血化痰、清肺止咳之效^[25]。同时本次研究结果还显示,与单用阿奇霉素治疗相比,小儿肺热咳喘口服液联合阿奇霉素治疗可有效改善患儿肺功能,这可能是由于小儿肺热咳喘口服液中麻黄配伍黄芩可有效抑制气管炎性刺激,松弛支气管平滑肌,同时麦冬可发挥较好的养阴润肺功能,有效减少肺部损伤^[26]。当患儿处于肺炎支原体肺炎时,肺炎支原体进入人体后,可激活巨噬细胞、中性粒细胞产生IL-6、CRP以及TNF- α 等炎症因子,扩大炎症级联反应,加重组织损伤,而本研究中的两组经治疗后IL-6、CRP、TNF- α 等代表性炎症因子水平均降低,且研究组低于对照组,可见联合治疗在控制机体炎症反应方面效果显著。现代药理学研究表明^[27,28],麻黄具有减少气道局部浸润,抑制或拮抗炎性介质的释放作用;黄芩、连翘、麦冬、板蓝根均有抗菌、抗病毒、抗炎以及增强机体抵抗力之功效。此外,两组患儿不良反应发生率对比无统计学差异,可见此次联合治疗安全性较高,不会增加不良反应发生率,这可能是由于小儿肺热咳喘口服液为中成药,对机体毒副作用较小^[29,30]。

综上所述,小儿肺热咳喘口服液联合阿奇霉素治疗肺炎支原体肺炎患儿,显效快,疗效高,可有效改善患儿肺功能,减轻机体炎症应激,安全性好。

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