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小儿肺热咳喘口服液联合布地奈德雾化吸入治疗小儿喘息性支气管炎的疗效及改善机体炎症反应和免疫力的效果研究*

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摘要 目的:探讨小儿喘息性支气管炎经布地奈德雾化吸入、小儿肺热咳喘口服液联合治疗后的疗效及改善机体炎症反应和免疫力的效果。**方法:**选取 2018 年 1 月~2022 年 6 月期间我院收治的 60 例小儿喘息性支气管炎作为研究对象,根据随机数字表法分为对照组($n=30$,接受布地奈德单药治疗)和观察组($n=30$,接受布地奈德联合小儿肺热咳喘口服液治疗)。对比两组临床疗效、临床症状改善情况、T 淋巴细胞亚群、炎症因子和不良反应。**结果:**与对照组 73.33%(22/30) 比较,观察组临床总有效率 93.33%(28/30)明显升高($P<0.05$)。与对照组相比,观察组热退时间和哮鸣音/咳嗽/喘息消失时间更短($P<0.05$)。与对照组相比,观察组治疗 5 d 后 $CD3^+$ 、 $CD4^+$ 、 $CD4^+/CD8^+$ 更高, $CD8^+$ 更低($P<0.05$)。与对照组相比,观察组治疗 5 d 后 C 反应蛋白(CRP)、白介素-6(IL-6)、降钙素原(PCT)更低($P<0.05$)。两组均未出现明显的药物不良反应。**结论:**小儿喘息性支气管炎采用小儿肺热咳喘口服液联合布地奈德雾化吸入治疗,可使症状缓解时间缩短,降低患儿炎症因子水平,提高其免疫力。

关键词:小儿肺热咳喘口服液;布地奈德;儿童;喘息性支气管炎;疗效;炎症反应;免疫力

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Study on the Therapeutic Effect of Xiaoer Feire Kechuan Oral Liquid Combined with Budesonide Aerosol Inhalation in Treating Children with Asthmatic Bronchitis and Improving the Body's Inflammatory Response and Immunity*

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ABSTRACT Objective: To investigate the therapeutic effect of budesonide aerosol inhalation combined with Xiaoer Feire Kechuan oral liquid in the treatment of children with asthmatic bronchitis and the effect of improving the body's inflammatory response and immunity. **Methods:** 60 children with asthmatic bronchitis who were admitted to our hospital from January 2018 to June 2022 were selected as research objects. According to the random number table method, they were divided into the control group ($n=30$, treated with budesonide monotherapy) and the observation group ($n=30$, treated with budesonide combined with Xiaoer Feire Kechuan oral liquid). The clinical efficacy, improvement of clinical symptoms, T lymphocyte subsets, inflammatory factors and adverse reactions were compared between the two groups. **Results:** Compared with 73.33% (22/30) of the control group, the total clinical effective rate 93.33% (28/30) in the observation group was significantly higher ($P<0.05$). Compared with control group, the heat withdrawal time and wheezing sound/cough/wheezing disappearance time of observation group were shorter ($P<0.05$). Compared with control group, $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ of observation group at 5 d after treatment were higher, and $CD8^+$ was lower ($P<0.05$). Compared with control group, C-reactive protein (CRP), interleukin-6 (IL-6) and procalcitonin (PCT) of observation group at 5 d after treatment were lower ($P<0.05$). There were no obvious adverse drug reactions in the two groups. **Conclusion:** Children's asthmatic bronchitis can be treated with Xiaoer Feire Kechuan oral liquid combined with budesonide aerosol inhalation, which can shorten the time for symptom relief, reduce the level of inflammatory factors in children, and improve their immunity.

Key words: Xiaoer Feire Kechuan oral liquid; Budesonide; Children; Asthmatic bronchitis; Therapeutic effect; Inflammatory response; Immunity

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前言

小儿喘息性支气管炎是临床上常见的呼吸系统疾病,临床主要表现为喘息、低热、咳嗽、痰多等,严重时会降低患儿的肺功能和免疫功能,导致全身炎症反应,严重危及患儿的生命健康^[1,2]。流行病学调查显示^[3],小儿喘息性支气管炎多发于3岁以内的婴幼儿,其中在1~3岁年龄段患儿的发生率占总发生率的30%~60%。目前临床上主要通过提高机体抵抗力、止咳祛痰等手段治疗小儿喘息性支气管炎,布地奈德是一种糖皮质激素,具有抗过敏、抗炎作用,有利于缓解患者哮喘症状^[4]。但此类药物疗效不稳定,停药后易反复发作。小儿肺热咳喘口服液具有强力镇咳作用,同时对致病病毒、细菌有抑制杀灭作用^[5]。本次研究通过探讨小儿肺热咳喘口服液联合布地奈德雾化吸入在小儿喘息性支气管炎中的临床应用价值,以期为临床治疗提供数据参考。

1 资料与方法

1.1 基线资料

选取2018年1月~2022年6月期间我院收治的60例小儿喘息性支气管炎,诊断标准:参考《诸福堂实用儿科学》^[6];常表现为喘息、咳嗽、发热、痰多、出气吸气不畅等症状,部分患儿会出现高热症状;行血常规检查、胸部X线检查、动脉血气分析检查明确诊断。纳入标准:(1)年龄1~5岁;(2)所有患儿家属均知情同意;(3)首次发作患儿;(4)符合上述诊断标准者;(5)入组前1个月内未进行调节免疫、祛痰止咳类相关治疗。排除标准:(1)患有精神障碍,不能配合治疗者;(2)先天免疫缺陷患儿;(3)对本次研究用药存在过敏症的患儿;(4)严重心、肺、肝、肾功能不全或血液系统疾病者;(5)先天性心脏病、支气管先天发育异常患儿;(6)肺结核、支气管异物患儿。根据随机数字表法分为两组,对照组和观察组,对照组接受布地奈德单药治疗,观察组接受布地奈德联合小儿肺热咳喘口服液治疗。其中对照组30例,女14例,男16例,病程2~10 d,平均病程(5.28±0.94)d;病毒感染类型:流感病毒10例,腺病毒4例,呼吸道合胞病毒10例,副流感病毒6例;年龄1~5岁,平均年龄(2.74±0.41)岁。观察组30例,女13例,男17例,病程3~12 d,平均病程(5.43±0.87)d;病毒感染类型:流感病毒8例,腺病毒4例,呼吸道合胞病毒12例,副流感病毒6例;年龄1~4岁,平均年龄(2.79±0.52)岁。两组一般资料均衡可比($P>0.05$),均衡可比。研究方案

通过我院伦理学委员会批准进行。

1.2 方法

对照组患儿雾化吸入吸入用布地奈德混悬液(Astrazenca Pty Ltd,批准文号H20140475,规格:2 mL:1 mg),0.25 mg加入到生理盐水3 mL,10 min/次,2次/d。基于对照组治疗,观察组口服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1 mL相当于饮片1.77 g)治疗,口服,一岁至三岁一次1支,一日3次;四岁至七岁一次1支,一日4次,或遵医嘱。两组患儿均治疗5 d。

1.3 疗效判定依据

总有效率=痊愈率+好转率。好转:体温恢复正常,喘息、咳嗽症状明显减轻,肺部粗喘鸣音、湿啰音明显减少。痊愈:咳嗽、喘息症状消失,体温恢复正常,肺部粗喘鸣音、湿啰音消失^[7]。无效:上述体征、症状无好转甚至加重。

1.4 观察指标

(1)比较两组患儿喘息消失时间、热退时间、咳嗽消失时间、哮鸣音消失时间。(2)治疗前、治疗5 d后抽取两组患儿的空腹肘静脉血6 mL,分为2管血液标本,一管经北京同生时代生物技术有限公司,FACS Calibur流式细胞仪检测CD3⁺、CD4⁺、CD8⁺,计算CD4⁺/CD8⁺。另一管经室温下静置半小时后进行离心处理。离心参数设置为:2900 r/min的速率离心11 min,离心半径7 cm,取上清液。血清C反应蛋白(CRP)水平采用乳胶增强免疫散射比浊法检测,相关试剂盒采购自深圳迈瑞生物医疗电子股份有限公司。采用夹心化学发光免疫分析法检测降钙素原(PCT)水平,相关试剂盒采购自深圳迈瑞生物医疗电子股份有限公司。采用免疫荧光技术,双抗夹心法检测白介素-6(IL-6),相关试剂盒购自中翰盛泰生物技术股份有限公司。(3)观察两组用药安全性。

1.5 统计学方法

采用SPSS24.0软件分析数据。满足正态分布的计量资料以($\bar{x} \pm s$)描述,比较采用配对t检验(组内)或独立样本t检验(组间)。以%表示计数资料,采用卡方检验。 $\alpha=0.05$ 为检验标准。

2 结果

2.1 临床疗效对比

与对照组73.33%(22/30)比较,观察组临床总有效率93.33%(28/30)明显升高($P<0.05$),见表1。

表1 临床疗效对比[例(%)]

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

Groups	Cure	Improve	Invalid	Total effective rate
Control group(n=30)	7(23.33)	15(50.00)	8(26.67)	22(73.33)
Observation group(n=30)	10(33.33)	18(60.00)	2(6.67)	28(93.33)
χ^2				4.320
P				0.038

2.2 临床症状改善情况对比

与对照组相比,观察组热退时间、咳嗽消失时间、哮鸣音消失时间、喘息消失时间更短($P<0.05$),见表2。

2.3 T淋巴细胞亚群指标对比

治疗前两组T淋巴细胞亚群指标组间对比无差异($P>0.05$)。两组患儿治疗5 d后CD3⁺、CD4⁺、CD4⁺/CD8⁺升高,且观察

组的升高程度大于对照组($P<0.05$), $CD8^+$ 下降,且观察组下降程度较对照组大($P<0.05$),见表3。

表2 临床症状改善情况对比($\bar{x}\pm s$)Table 2 Comparison of improvement of clinical symptoms($\bar{x}\pm s$)

Groups	Wheezing sound disappearance time(d)	Heat withdrawal time(d)	Wheezing disappearance time(d)	Cough disappearance time(d)
Control group(n=30)	6.73±0.56	3.18±0.46	4.93±0.67	4.56±0.41
Observation group(n=30)	5.24±0.47	2.37±0.32	3.28±0.46	3.48±0.35
t	11.163	7.917	11.120	10.973
P	0.000	0.000	0.000	0.000

表3 T淋巴细胞亚群指标对比($\bar{x}\pm s$)Table 3 Comparison of T lymphocyte subsets($\bar{x}\pm s$)

Groups	CD3 ⁺ (%)		CD4 ⁺ (%)		CD8 ⁺ (%)		CD4 ⁺ /CD8 ⁺	
	Before treatment	5 d after treatment	Before treatment	5 d after treatment	Before treatment	5 d after treatment	Before treatment	5 d after treatment
Control group(n=30)	41.15±3.75	45.94±5.32*	33.76±4.34	39.62±5.41*	27.83±2.57	25.37±2.42*	1.21±0.28	1.56±0.36*
Observation group(n=30)	40.89±4.82	49.55±6.49*	33.59±3.47	44.58±4.86*	27.95±2.82	22.46±2.38*	1.20±0.29	1.98±0.34*
t	0.233	-2.356	0.168	-3.736	-0.172	4.696	0.136	-4.646
P	0.816	0.022	0.868	0.000	0.862	0.000	0.892	0.000

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

2.4 炎症因子水平对比

治疗前两组炎症因子水平组间对比无差异($P>0.05$)。治疗

5 d后两组患儿CRP、IL-6、PCT下降,且观察组较对照组低

($P<0.05$),见表4。

表4 炎症因子水平的对比($\bar{x}\pm s$)Table 4 Comparison of inflammatory factor levels($\bar{x}\pm s$)

Groups	CRP(mg/L)		IL-6(ng/L)		PCT(μ g/L)	
	Before treatment	5 d after treatment	Before treatment	5 d after treatment	Before treatment	5 d after treatment
Control group(n=30)	25.11±4.66	17.91±3.26*	35.73±5.25	24.69±4.81*	1.09±0.12	0.76±0.15*
Observation group(n=30)	25.63±3.73	11.76±3.35*	34.86±6.34	17.48±3.67*	1.03±0.14	0.51±0.13*
t	-0.477	7.206	0.579	6.527	1.782	6.898
P	0.635	0.000	0.565	0.000	0.080	0.000

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

2.5 不良反应发生率对比

在治疗过程中两组患儿均未出现明显的药物不良反应。

3 讨论

小儿喘息性支气管炎的发病机制是病原侵入呼吸道后,由于小儿各项脏器发育不完全,免疫力较低,病原向下蔓延至支气管、毛细支气管及肺泡,进而导致黏膜炎症水肿,炎症渗出物积聚于肺泡腔,由此妨碍了通气和换气功能,最终表现为发热、喘息、咳嗽、出气吸气不畅、咳嗽等状况^[8-10]。儿科临床常规治疗多给予抗生素、平喘、抗病毒、止咳、解热药、化痰等对症治疗,其中糖皮质激素为首选的药物,布地奈德是具有高效局部抗炎

作用的糖皮质激素,其雾化吸入治疗抗炎作用显著,可使气道炎症快速缓解;且避免经口服用药物的肝脏首过效应,不会影响患儿的生长发育^[11,12]。但西药使用疗效不稳定,停药后易反复发作,仍需进一步优化治疗方案。小儿肺热咳喘口服液是在白虎汤、麻杏石甘汤、银翘散等三方基础上加减组成,其主要成分包括鱼腥草、麻黄、连翘、知母、黄芩、金银花、麦冬、苦杏仁、石膏等11味中药,具有宣肺化痰、清热解毒功效,常用于热邪犯于肺卫所致微恶风寒、咳嗽、痰黄、发热、汗出,或兼喘息、口干而渴^[13,14]。

本次研究结果显示,与单用布地奈德雾化吸入治疗相比,布地奈德雾化吸入、小儿肺热咳喘口服液联合治疗小儿喘息性

支气管炎,可缩短哮鸣音消失时间、热退时间、喘息消失时间、咳嗽消失时间,提高临床治疗效果。这可能是因为布地奈德具有抗炎、抗病毒作用,而在这基础上,小儿肺热咳喘口服液具有广谱抗菌、抗病毒作用,能抑制病毒和细菌生长^[15,16];同时小儿肺热咳喘口服液还具有较强的祛痰作用,能明显稀释痰液,加强排痰^[17]。此外,其还可抑制延脑咳嗽中枢,阻止过敏递质释放,松弛支气管平滑肌,达到平喘的目的^[18]。小儿肺热咳喘口服液联合布地奈德雾化吸入治疗可发挥协调增效作用,共同促进疗效提高。本研究显示,CRP、IL-6、PCT在喘息性支气管炎患儿体内水平异常升高。CRP是一种急性时相反应蛋白,当机体遭受感染时,其水平会急剧升高,提示存在炎症反应^[19]。IL-6是一种在感染炎症发生过程中的重要细胞因子,在炎症反应中诱导急性反应蛋白生成,促进细胞炎性作用^[20,21]。PCT可反映机体炎症反应程度,小儿喘息性支气管炎呼吸道炎症越重表现为PCT水平越高^[22]。本次研究发现,小儿肺热咳喘口服液联合布地奈德雾化吸入治疗可更好的控制小儿喘息性支气管炎的炎性反应,考虑可能是与小儿肺热咳喘口服液中的金银花、鱼腥草、连翘具有抑制病毒细菌生长,减轻炎症反应有关^[23];同时麻黄与黄芩配伍能抑制气管炎性刺激,松弛支气管平滑肌^[24]。作为人体重要的免疫细胞群,T淋巴细胞既是免疫调节细胞,又是效应细胞^[25-27]。本次研究发现,小儿肺热咳喘口服液联合布地奈德雾化吸入治疗可有效改善小儿喘息性支气管炎的免疫功能。药理研究证实:麦冬养阴润肺并通过调节T淋巴细胞亚群水平,改善患儿免疫功能^[28]。另在治疗过程中,两组患儿均未出现明显的药物不良反应。可见联合用药安全性较好,小儿肺热咳喘口服液对机体生理影响小,对人体比较安全,能够在有效抗炎、抗菌的基础上保持良好的安全性^[29]。

综上所述,小儿喘息性支气管炎采用小儿肺热咳喘口服液联合布地奈德雾化吸入治疗,可缩短症状缓解时间,降低患儿炎症因子水平,提高其免疫力。

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