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布地奈德联合特布他林雾化吸入治疗对毛细支气管炎患儿潮气呼吸肺功能、T 细胞亚群及血清炎症因子的影响*

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摘要 目的:探讨布地奈德联合特布他林雾化吸入治疗对毛细支气管炎患儿潮气呼吸肺功能、T 细胞亚群及血清炎症因子的影响。**方法:**选取 2019 年 1 月~2019 年 12 月期间我院收治的毛细支气管炎患儿 98 例,采用随机数字表法分为对照组(常规方案治疗)和观察组(对照组基础上加用布地奈德联合特布他林雾化吸入治疗),各 49 例。记录两组治疗 1 周后总有效率。对比两组治疗前、治疗 1 周后的潮气呼吸肺功能指标[吸气/呼气时间比(Ti/Te)、达峰时间比(TPTEF/TE)、达峰容积比(VPEF/VE)、每千克潮气量(Vt/kg)]、T 细胞亚群[CD3⁺、CD4⁺、CD8⁺及 CD4⁺/CD8⁺]、血清炎症因子[降钙素原(PCT)、C 反应蛋白(CRP)]。比较两组不良反应发生率。**结果:**观察组治疗 1 周后的总有效率为 91.84%(45/49)高于对照组的 69.39%(34/49),差异有统计学意义($P<0.05$)。两组患儿治疗 1 周后 Ti/Te、TPTEF/TE、VPEF/VE、Vt/kg、CD3⁺、CD4⁺、CD4⁺/CD8⁺ 均高于治疗前,且观察组高于对照组($P<0.05$),PCT、CRP、CD8⁺ 均低于治疗前,且观察组低于对照组($P<0.05$)。两组患儿不良反应发生率对比无统计学差异($P>0.05$)。**结论:**雾化吸入特布他林联合布地奈德治疗毛细支气管炎患儿疗效显著,可有效改善患儿 T 细胞亚群、潮气呼吸肺功能,减轻患儿炎症反应,且安全性好。

关键词:布地奈德;特布他林;雾化吸入;毛细支气管炎;患儿;肺功能;T 细胞亚群;炎症因子

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Effects of Budesonide Combined with Terbutaline Inhalation on Tidal Breathing Pulmonary Function, T Cell Subsets and Serum Inflammatory Factors in Children with Bronchiolitis*

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ABSTRACT Objective: To investigate the effect of budesonide combined with terbutaline inhalation on tidal breathing pulmonary function, T cell subsets and serum inflammatory factors in children with bronchiolitis. **Methods:** 98 children with bronchiolitis in our hospital from January 2019 to December 2019 were selected, and they were randomly divided into control group (conventional treatment) and observation group (budesonide combined with terbutaline inhalation on the basis of the control group), 49 cases in each group. The total effective rate of the two groups 1 week after treatment was recorded. The indexes of tidal breathing pulmonary function [inspiratory/expiratory time ratio (Ti/TE), time to peak ratio (tpTEF/TE), peak volume ratio (VPEF/VE), tidal volume per kilogram (VT/kg)], T cell subsets [CD3⁺, CD4⁺, CD8⁺ and CD4⁺/CD8⁺], serum inflammatory factors [procalcitonin (PCT), C-reactive protein (CRP)] were compared between the two groups before and 1 week after treatment. The incidence of adverse reactions was compared between the two groups. **Results:** The total effective rate of the observation group was 91.84% (45/49), which was higher than 69.39% (34/49) of the control group 1 week after treatment, and the difference was statistically significant ($P<0.05$). 1 week after treatment, Ti/Te, TPTEF/TE, VPEF/VE, Vt/kg, CD3⁺, CD4⁺, CD4⁺/CD8⁺ of the two groups were higher than those before treatment, and the observation group was higher than the control group ($P<0.05$), PCT, CRP, CD8⁺ were lower than before treatment, and the observation group was lower than 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:** Budesonide combined with terbutaline aerosol inhalation in the treatment of children with bronchiolitis has significant curative effect, can play a synergistic role, improve the tidal breathing lung function effectively and T cell subsets, reduce the inflammatory reaction of children, and has good safety.

Key words: Budesonide; Terbutaline; Aerosol inhalation; Bronchiolitis; Children; Lung function; T cell subsets; Inflammatory factors

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前言

毛细支气管炎是指病变部位位于肺部的细小支气管,此类细小支气管受分泌物阻塞或者炎性肿胀,引起人体通气功能异常的一类疾病^[1,2]。小儿肺部和支气管由于处于生长发育阶段,抵抗力相对成年群体较低,易受到外来微生物的刺激,诱发毛细支气管炎^[3,4]。据相关数据显示^[5],该病是3岁以下儿童最常见的疾病之一,以1岁内患儿最为常见,约占所有发病人数的80%。该病的主要症状包括气喘、咳嗽、发热、反复感染等,若得不到有效的治疗,症状反复,可导致机体内多器官功能衰竭^[6,7]。目前,毛细支气管炎的治疗尚无特效方案,以控制感染等常规对症治疗为主,疗效存在局限性^[8]。布地奈德是糖皮质激素类药物,具有良好的局部抗炎作用;特布他林是选择性 β 受体激动剂,主要功能为缓解气道痉挛,既往常用于支气管哮喘的治疗中^[9,10]。本研究通过探讨雾化吸入特布他林联合布地奈德治疗对毛细支气管炎患儿的临床效果,以期临床该病的治疗提供数据支持。

1 资料与方法

1.1 研究对象

根据临床症状、生命体征和胸部X线片检查情况确诊。本次研究已通过我院伦理学委员会批准进行。选取2019年1月~2019年12月间我院接收的98例毛细支气管炎患儿,上述患儿采用随机数字表法分为对照组和观察组,其中对照组49例,女28例,男21例,病程1~3d,平均 (2.13 ± 0.47) d;年龄4~24月,平均 (12.58 ± 2.21) 月。观察组49例,女30例,男19例,病程0.6~3d,平均 (1.98 ± 0.22) d;年龄6~23月,平均 (12.29 ± 2.35) 月。两组一般资料均衡可比($P > 0.05$)。

1.2 纳入、排除标准

纳入标准:(1)参考《诸福棠实用儿科学》^[11];临床表现为反复感染、气喘、咳嗽、发热、四肢酸痛等;(2)年龄 ≤ 24 月;(3)入院前3d内未接受过 β 受体激动剂和糖皮质激素类药物治疗;(4)对本次研究用药无禁忌症。排除标准:(1)合并心、脑、肾等重要脏器功能不全;(2)意识障碍无法配合治疗;(3)既往有哮喘史;(4)支气管发育不良;(5)存在免疫缺陷;(6)合并先天性

心脏病、肺结核、佝偻病者。

1.3 治疗方法

两组均给予常规对症治疗,包括降温、体位引流、补液、吸痰、纠正水电解质和酸碱平衡、解痉平喘、氧疗、利尿等。在此基础上,观察组加用布地奈德(国药准字H20030987,鲁南贝特制药有限公司,规格:每瓶含布地奈德20mg,每瓶200滴,每滴含布地奈德0.1mg)联合特布他林(国药准字H20203158,四川美大康华康药业有限公司,规格:2mL:5mg)治疗,雾化吸入,布地奈德1mL,特布他林0.5mL,上述药物加入生理盐水2mL混匀,10min/次,2次/d。两组均治疗1周。

1.4 疗效判定

总有效率=显效率+有效率,治疗后48h内,气喘、咳嗽症状显著改善,治疗后72h内气喘症状完全消失,治疗后1周内肺部啰音、肺炎咳嗽症状消失为显效。治疗后72h内咳嗽、气喘减轻,治疗后1周内症状完全消失为有效。治疗后临床症状未改善甚至加重为无效^[12]。

1.5 观察指标

(1)采集2mL患儿治疗前、治疗1周后空腹静脉血,经4100r/min离心20min后取上清液保存待测。采用酶联免疫吸附试验检测降钙素原(PCT)、C反应蛋白(CRP)。采用FACScount自动化流式细胞仪(Becton Dickinson公司)检测T细胞亚群:CD3⁺、CD4⁺、CD8⁺,并计算CD4⁺/CD8⁺值。试剂盒由北京方程生物科技有限公司提供。(2)治疗前、治疗1周后采用肺功能仪(日本杰斯特公司)评估患儿潮气呼吸肺功能指标:吸气/呼气时间比(Ti/Te)、达峰时间比(TPTEF/TE)、达峰容积比(VPEF/VE)、每千克潮气量(Vt/kg)。(3)记录不良反应发生情况。

1.6 统计学分析

采用SPSS23.0统计学软件对研究数据进行处理。计数资料以[n(%)]表示,行 χ^2 检验。计量资料以 $(\bar{x} \pm s)$ 表示,行t检验。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组临床疗效比较

治疗1周后,对照组的总有效率为69.39%(34/49),观察组为91.84%(45/49),观察组的较对照组的高($P < 0.05$),详见表1。

表1 两组临床疗效比较例(%)

Table 1 Comparison of clinical efficacy between the two groups n(%)

Groups	Remarkable effect	Effective	Invalid	Total effective rate
Control group(n=49)	11(22.45)	23(46.94)	15(30.61)	34(69.39)
Observation group(n=49)	16(32.65)	29(59.18)	4(8.16)	45(91.84)
χ^2				7.900
P				0.005

2.2 两组T细胞亚群比较

两组治疗前CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺比较无显著性差异($P > 0.05$),两组治疗1周后CD8⁺低于治疗前,观察组较对照组低($P < 0.05$),CD3⁺、CD4⁺、CD4⁺/CD8⁺均高于治疗前,观察组较对照组高($P < 0.05$),详见表2。

2.3 两组炎症因子比较

两组患儿治疗前PCT、CRP比较无显著性差异($P > 0.05$),两组患儿治疗1周后PCT、CRP均低于治疗前,且观察组低于对照组($P < 0.05$),详见表3。

表 2 两组 T 淋巴细胞亚群比较($\bar{x} \pm s$)

Table 2 Comparison of T lymphocyte subsets between the two groups($\bar{x} \pm s$)

Groups	CD3 ⁺ (%)		CD4 ⁺ (%)		CD8 ⁺ (%)		CD4 ⁺ /CD8 ⁺	
	Before treatment	1 week after treatment	Before treatment	1 week after treatment	Before treatment	1 week after treatment	Before treatment	1 week after treatment
Control group (n=49)	38.06± 5.26	43.98± 7.36 ^a	33.41± 6.05	38.87± 5.79 ^a	29.09± 4.84	26.32± 3.75 ^a	1.15± 0.19	1.48± 0.18 ^a
Observation group(n=49)	38.13± 6.23	48.31± 6.57 ^a	33.19± 5.91	43.23± 6.28 ^a	29.34± 4.38	23.67± 4.53 ^a	1.13± 0.17	1.83± 0.21 ^a
t	0.060	3.072	0.182	3.573	0.268	3.154	0.549	8.858
P	0.952	0.003	0.856	0.001	0.789	0.002	0.854	0.000

Note: compared with before treatment, ^aP<0.05.

表 3 两组炎症因子比较($\bar{x} \pm s$)

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

Groups	PCT(ng/mL)		CRP(mg/L)	
	Before treatment	1 week after treatment	Before treatment	1 week after treatment
Control group(n=49)	0.97± 0.21	0.68± 0.17 ^a	58.64± 6.57	39.63± 5.38 ^a
Observation group(n=49)	0.92± 0.23	0.42± 0.15 ^a	58.22± 7.54	23.76± 5.74 ^a
t	1.124	8.028	0.294	14.121
P	0.264	0.000	0.769	0.000

2.4 两组潮气肺功能指标比较

TPTEF/TE、VPEF/VE、Vt/kg 均高于治疗前,且观察组高于对照

两组患儿治疗前 Ti/Te、TPTEF/TE、VPEF/VE、Vt/kg 比较 (P<0.05),详见表 4。

无显著性差异 (P>0.05), 两组患儿治疗 1 周后 Ti/Te、

表 4 两组潮气肺功能指标比较($\bar{x} \pm s$)

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

Groups	Ti/Te		TPTEF/TE(%)		VPEF/VE(%)		Vt/kg(mL/kg)	
	Before treatment	1 week after treatment	Before treatment	1 week after treatment	Before treatment	1 week after treatment	Before treatment	1 week after treatment
Control group (n=49)	0.66± 0.07	0.72± 0.06 ^a	16.56± 1.39	18.91± 1.32 ^a	20.88± 2.17	22.98± 2.09 ^a	6.69± 0.74	7.32± 0.65 ^a
Observation group(n=49)	0.67± 0.08	0.76± 0.05 ^a	16.61± 1.35	20.75± 1.35 ^a	20.94± 2.06	24.87± 2.28 ^a	6.73± 0.51	8.13± 1.19 ^a
t	0.659	3.585	0.181	6.882	0.140	4.277	0.312	4.182
P	0.512	0.001	0.857	0.000	0.889	0.000	0.756	0.000

Note: compared with before treatment, ^aP<0.05.

2.4 两组不良反应比较

观察组出现皮疹 1 例、胃肠道不适 2 例,不良反应发生率为 6.12%(3/49);对照组出现皮疹 1 例、胃肠道不适 1 例,不良反应发生率为 4.08%(2/49); 两组患儿不良反应发生率对比无统计学差异($\chi^2=0.211$, P=0.646)。

3 讨论

婴幼儿的支气管解剖学结构特殊,气流速度慢,细小支气管管腔结构薄弱,病原微生物易滞留,一旦发生病原微生物感染,即可引起毛细支气管上皮细胞脱落、坏死,黏液分泌增加,管腔狭窄甚至堵塞,进而引起肺气肿、肺不张,表现出类似于肺炎的临床症状,尤以喘憋最为明显^[13-15]。近年来有关毛细支气管

炎的发病机制的探讨均证实毛细支气管炎是由免疫细胞介导的气道炎症反应所引起^[16,17]。毛细支气管炎的病原体主要为呼吸道合胞病毒,病毒入侵人体后可刺激患儿产生免疫反应,诱导局部炎症反应,而局部炎症反应可破坏气道黏膜的完整并引起平滑肌痉挛,导致黏液栓大量形成;同时,婴幼儿呼吸肌发育尚不完善,气道的狭窄和阻塞可引起患儿呼气功能障碍,进一步引起缺氧、二氧化碳潴留、酸中毒等,增加呼吸衰竭发生风险^[18-20]。因此,应重视婴幼儿毛细支气管炎的治疗。目前国内外对小儿毛细支气管炎的治疗尚无统一的标准方案,多采用常规对症处理的方法,虽可短期内缓解患儿症状,但极易复发,且会增加病原体耐药率,远期疗效有限^[21]。

雾化吸入是治疗小儿毛细支气管炎的首选治疗方式,通过

雾化吸入可增加药物作用范围,发挥局部抗炎优势^[22,23]。布地奈德是一种可吸入糖皮质激素,通过雾化吸入,到达下呼吸道并长时间在肺部维持较高浓度,可有效稀释支气管内痰液,减少抗体合成,抑制免疫反应,发挥高效局部抗炎作用^[24]。特布他林可增强支气管黏膜上皮细胞的纤毛运动,减少体内致密物质的合成和释放,帮助稀释和消除黏液^[25]。本研究中布地奈德联合特布他林雾化吸入治疗毛细支气管炎患儿,可提高有效率,同时还可有效提高机体免疫功能,减轻炎症反应。PCT、CRP是临床常见的炎症因子,当机体内出现任何炎症或损伤时,其水平迅速上升^[26]。既往有研究表明,毛细支气管炎患儿体内T淋巴细胞亚群处于紊乱状态^[27]。药理学研究发现^[28],布地奈德与特布他林有较好的协同作用,布地奈德压缩雾化吸入可直接到达患儿呼吸道,在发挥扩张气道作用的同时发挥抗炎作用,同时其还能避免 β 受体激动性下调,增强特布他林松弛气道平滑肌的作用。同时特布他林可促进药物向气道转运,并增强布地奈德祛除呼吸道内炎症反应产物的作用,提高患儿免疫力为控制患儿气道炎症提供良好基础,进一步改善临床疗效。潮气呼吸肺功能检测可直观地反映婴幼儿呼吸功能,可有效观察患儿治疗效果^[29]。本次研究结果中,雾化吸入特布他林联合布地奈德治疗可较好的恢复患儿呼吸道通畅,利于其肺功能改善。这可能与两种药物对气道炎症和气道高反应性的协同抑制,可有效控制机体喘息、咳嗽、缺氧等症状,进而减少肺功能损伤有关^[30]。另两组患儿不良反应发生率对比无统计学差异,分析原因是因为布地奈德、特布他林主要沉积和停留在肺部,在体内可被迅速且充分代谢,全身绝对生物利用度低,故基本不产生全身性作用,发生急性中毒的可能性极低,不良反应轻微。

综上所述,雾化吸入特布他林联合布地奈德治疗毛细支气管炎患儿疗效显著,可有效减轻患儿炎症反应,改善患儿T淋巴细胞亚群、潮气呼吸肺功能,且安全性好。

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