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孟鲁司特钠联合布地奈德混悬液对哮喘急性发作患儿血清 EOS、ECP 水平和肺功能的影响

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摘要 目的: 探索孟鲁司特钠联合布地奈德混悬液对哮喘急性发作患儿血清嗜酸性粒细胞（EOS）、嗜酸性粒细胞阳离子蛋白（ECP）水平和肺功能的影响。**方法:** 选择自 2015 年 10 月至 2016 年 10 月我院收治的 200 例支气管哮喘急性发作患儿，按照随机数表法分成观察组和对照组各 100 例。对照组患儿口服孟鲁司特钠，观察组患儿在对照组基础上给予布地奈德气雾剂进行雾化治疗，两组均治疗 1 周。统计分析两组患儿的临床有效率，肺功能指标，包括第 1 秒用力呼气容积（FEV1）、用力肺活量（FVC）及 FEV1/FVC，对比治疗前后两组患儿血清中 EOS、ECP 水平的变化。**结果:** 治疗后，观察组的总有效率为 97.00%，显著高于对照组的 81.00%（P<0.05）；经治疗后两组患儿肺功能指标均较治疗前明显改善，且观察组患儿优于对照组（P<0.05）；两组患儿治疗后 EOS、ECP 水平均低于治疗前，而观察组患儿低于对照组，差异均有统计学意义（P<0.05）。**结论:** 孟鲁司特钠联合布地奈德对于小儿哮喘的急性发作具有良好的临床疗效，能显著改善患儿肺功能和血清中炎症因子的水平，减轻患儿体内的炎症反应，值得在临床上推广应用。

关键词: 孟鲁司特钠；布地奈德；儿童；哮喘；急性发作；EOS；ECP

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Effect of Montelukast Sodium Combined With Budesonide Inhalation Suspension on Serum EOS,ECP and Lung Function in Children with Acute Episoded Asthma

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ABSTRACT Objective: To explore the effect of montelukast sodium combined with budesonide inhalation suspension on serum eosinophilic cell (EOS), eosinophile cationic protein (ECP)and lung function in children with acute episoded asthma. **Methods:** Selected 200 children with acute episoded asthma who were treated in our hospital from October 2015 to October 2016, they were divided into control group and observation group according to the random number table method, with 100 patients in each group. Patients in control group were treated with montelukast sodium, while patients in observation group were treated with montelukast sodium combined with budesonide inhalation suspension, the treatment course of two groups was 1week. Statistically analyzed the clinical efficacy, pulmonary function, which including forced expiratory volume in the first second (FEV1), forced vital capacity (FVC)and FEV1/FVC, and the changes of serum EOS, ECP levels in two groups before and after treatment. **Results:** The total effective rate in observation group was 97%, which was significantly higher than control group(P<0.05). The pulmonary function indexes of two groups after treatment were significantly improved than before treatment, and the observation group were significantly better than control group (P<0.05). The serum EOS and ECP levels in two groups after treatment were significantly improved than before treatment, and the observation groups were significantly lower than control group, the differences were statistically significant (P<0.05). **Conclusion:** Montelukast sodium combined with budesonide inhalation suspension has a good clinical effect in treatment for children with acute asthma, which can significantly improve the pulmonary function and reduce the serum EOS, ECP levels, so as to relieve the inflammatory reaction of children, it is worth popularizing in clinical application.

Key words: Montelukast sodium; Budesonide; Children; Asthma; Acute episoded; EOS; ECP

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前言

支气管哮喘简称哮喘,是一类常见的呼吸系统疾病[1]。随着全球工业化的迅猛发展及生态环境的日趋恶化,日前哮喘在全世界正呈流行趋势,且哮喘患儿发病率持续上升,我国哮喘患儿患病率高达 0.12%～3.34%,形势严峻[2,3]。哮喘是多种炎性细胞(如嗜酸性粒细胞、中性粒细胞、T 淋巴细胞等)、气道结构细胞(如气道平滑肌细胞等)、细胞因子、趋化因子、黏附分子共同参与的慢性气道炎症性疾病[4,5]。吸入性糖皮质激素是临床治疗哮喘最为有效的药物,能够有效的改善哮喘患者症状,但长期使用其副作用较大,因此寻找治疗小儿哮喘更为理想的临床治疗方案已迫在眉睫[6-8]。孟鲁司特钠可用于儿童哮喘的预防及长期治疗,且患儿耐受性良好,副作用较轻微[9]。布地奈德是治疗哮喘的常用药物,临床疗效受到一致肯定[10]。但关于这两种药物联合治疗小儿哮喘急性发作还鲜有报道。本文通过分析两者药物联合治疗小儿支气管哮喘急性发作的临床疗效,以及对患儿肺功能及血清中血清嗜酸性粒细胞(Eosinophilic cell, EOS)及嗜酸性粒细胞阳离子蛋白(Eosinophile cationic protein, ECP)水平的影响,旨在为小儿支气管哮喘急性发作的治疗提供临床用药依据,具体报道如下。

1 资料与方法

1.1 一般资料

选择 2015 年 10 月～2016 年 10 月我院收治的支气管哮喘急性发作患儿 200 例为研究对象。纳入标准:① 符合中华医学会制定的儿童支气管哮喘诊断标准中关于急性发作期哮喘的定义[11];② 首次接受诊断的患儿;③ 家属均签知情同意书。排除标准:① 鼻窦炎、肺结核、咳嗽变异性哮喘、嗜酸性细胞支气管炎患儿;② 对本实验药物过敏患儿;③ 不能坚持服药患儿。经随机数表法分为观察组与对照组,每组 100 例。观察组男 56 例,女 44 例;年龄 6 个月 ~12 岁,平均(5.2± 3.3)岁;病程 1 ~2 个月,平均(1.6± 0.4)个月;对照组男 55 例,女 45 例;年龄 7 个月 ~12 岁,平均(5.1± 3.2)岁;病程 1 ~3 个月,平均(1.3± 0.6)个月。两组临床基本情况比较,差异无统计学意义(P>0.05),满足组间比较条件。本研究经我院伦理委员会批准进行。

1.2 方法

所有患儿入院后均实施维持水电解质平衡、常规吸氧、止咳化痰以及解痉平喘等对症基础治疗。在此基础上给予对照组患者口服孟鲁司特钠(四川大冢制药有限公司,国药准字 H20064370;规格:10 mg/ 片),每次一片(10 mg),每天一次。观察组在对照组的治疗基础上给予雾化吸入布地奈德悬浮液(普米克令舒)(澳大利亚 AstraZeneca Pty Ltd;注册证号:H20140475;规格:2 mL:1 mg)治疗,一次 0.5～1 mg,一天二次。两组疗程均为 1 周。

1.3 疗效判定

临床疗效分为显效、有效、无效,具体判定标准如下:有效:胸闷、呼吸困难、气喘等症状完全缓解,肺功能指标恢复至正常范围,EOS、ECP 水平均明显下降;胸闷、呼吸困难、气喘等症状有所减轻,肺功能指标及 EOS、ECP 水平均有改善;无效:胸闷、呼吸困难、气喘等症状、肺功能指标及 EOS、ECP 水平均无改善[12]。临床总有效率 =(显效 + 有效)/ 总例数× 100%。

1.4 观察指标

(1)EOS 和 ECP 水平。所有患儿于入院后第二天清晨空腹取外周静脉血 4 mL,4000 rpm 离心 20 min 提取血清,存于 -80℃冰箱中待检,此外出院时同样操作留下样品,并采用 ELISA 法测定 ECP 水平。ECP 试剂盒购自上海拜力生物科技有限公司,检测步骤均严格按试剂盒操作进行。EOS 采用乙二胺四二酸抗凝血清后,伊红染色后,在显微镜下进行计数。

(2)肺功能。采用 MSA-99 检测仪(购自上海欧启电子科技有限公司)测定各组第 1 秒呼吸气体的容积(FEV1)、用力呼吸的肺活量(FVC)以及 FVC 占预计值百分比(FVC%)。

1.5 统计学方法

采用 SPSS20.0 软件对数据进行处理,临床疗效、并发症发生率、复发率等计数资料经由 n(%)表示,两组数据比较采用 x^2 检验,肺功能指标、血清 EOS、ECP 水平等计量资料经由($\bar{x}\pm s$)表示,两组比较采用 t 检验;检验标准设置为 α=0.05。

2 结果

2.1 两组患儿的临床疗效对比分析

观察组患儿总有效率为 97.00%(97/100),明显高于对照组的 81.00%(81/100),差异具有统计学意义(P<0.05)。具体见表 1。

表 1 两组患儿的临床疗效对比分析表[n(%)]

Table 1 Clinical efficacy of two groups of children, comparative analysis table [n (%)]

Groups	Excellence	Effective	Invalid	Total effective rate
Control group(n=100)	47(47.00)	50(50.00)	3(3.00)	97(97.00)
Observation group(n=100)	28(28.00)	53(53.00)	19(19.00)	81(81.00)
x^2				7.747
P				0.000

2.2 两组患儿治疗前后肺功能对比

治疗前两组患儿 FEV1、FVC 以及 FEV1/FVC 均无统计学差异(P>0.05),治疗后两组患儿 FEV1、FVC 以及 FEV1/FVC 均改善,且观察组患儿 FEV1、FVC 以及 FEV1/FVC 显著优于对照组(P<0.05)。具体见表 2。

2.3 两组患儿治疗前后血清中 EOS、ECP 水平对比

治疗前两组患儿血清 EOS、ECP 水平均无统计学差异(P>0.05),经过治疗后两组患儿血清 EOS、ECP 水平均明显下降,且观察组患儿显著低于对照组,差异有统计学意义(P<0.05)。具体见表 3。

表 2 两组患儿肺功能改善情况对比分析表($\bar{x}\pm s$)

Table 2 Comparison of lung function improvement in two groups($\bar{x}\pm s$)

Groups	FEV1 (% forecast)		FVC (% forecast)		FEV1/FVC	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=100)	67.99± 6.37	69.97± 6.32*	52.13± 5.32	52.35± 7.57*	60.99± 5.03	61.36± 5.43*
Observation group (n=100)	68.13± 7.33	78.43± 6.52*	52.12± 4.72	66.82± 4.33*	61.02± 4.77	72.42± 5.32*
t	0.147	9.326	0.014	16.596	0.044	14.549
P	0.384	0.000	0.842	0.000	0.803	0.000

Note: compared with before treatment, *P<0.05.

表 3 两组患儿治疗前后血清中 EOS、ECP 水平对比分析表($\bar{x}\pm s$)

Table 3 Comparison of serum EOS and ECP levels in the two groups before and after treatment($\bar{x}\pm s$)

Groups	EOS(%)		ECP(μg/L)	
	Before treatment	After treatment	Before treatment	After treatment
Control group(n=100)	0.19± 0.07	0.13± 0.06*	39.03± 12.89	22.53± 5.38*
Observation group(n=100)	0.18± 0.06	0.08± 0.01*	39.22± 12.26	15.37± 4.27*
t	1.082	8.227	0.113	10.425
P	0.093	0.000	0.421	0.000

Note: compared with before treatment, *P<0.05.

3 讨论

小儿哮喘急性发作可引发气道阻塞,发生气促、胸闷、呼吸困难等临床症状,如不及时处理,会有意识模糊、昏迷等危重症状,严重时甚至危及患儿生命[13,14]。哮喘的发病机理主要与支气管平滑肌的收缩、粘膜水肿、粘液分泌增多及炎症细胞浸润,而其中气道炎症则通常被认为是引发哮喘的根本所在[15-17]。哮喘相关的慢性气道炎症反应主要有各种炎性细胞(比如 EOS、肥大细胞、气道上皮细胞等)以及多种炎症介质譬如组胺、血小板激活因子、ECP、白三烯等等[18-20]。目前,哮喘急性发作期患儿,临床上一般采用解痉、平喘、抗感染、糖皮质激素、吸氧等临床对症治疗,糖皮质激素是目前相对疗效最好的的抗炎药物,但长期服用副作用较大[21-23]。白三烯为诱发哮喘的重要炎性介质,而白三烯受体拮抗剂作为新型治疗哮喘的药物备受关注[24]。近年来诸多研究也表明,EOS 是导致气道高反应性的关键细胞,在介导气道炎症反应及哮喘发病过程中起重要作用[25,26]。所以有效控制气道的慢性炎症便是治疗支气管哮喘发作的关键所在。

孟鲁司特钠是目前拮抗能力最强的特异性半胱氨酸白三烯受体拮抗剂,是新型非糖皮质激素抗感染药之一[27]。布地奈德混悬液是一种吸入性糖皮质激素,可有效维持平滑肌细胞与内皮细胞的生理功能,缓解哮喘症状[28]。本研究尝试将这两种哮喘治疗药物联用用于哮喘急性发作患儿的临床治疗。结果显示,联合用药的总有效率高于单用孟鲁司特钠,差异有统计学意义(P<0.05)。说明二者联合用药具有协同作用,孟鲁司特钠是通过阻碍半胱氨酸白三烯与白三烯受体的结合,使其丧失生物学活性,通过抑制血管通透性的增强,缓解支气管的痉挛,而联合布地奈德则能够在气道炎症患儿的支气管沉积,有效维持血药浓度,缓解咳嗽症状[29]。此外,本研究发现,观察组患儿治疗后各项肺功能指标 FEV1、FVC 以及 FEV1/FVC 水平均显著优于对照组,提示孟鲁司特钠和布地奈德联合用药对改善患儿肺功能效果优于孟鲁司特钠单独用药。分析原因,布地奈德为糖皮质激素,可有效减轻气道高反应性,缓解呼吸道炎症反应,扩张支气管,且布地奈德雾化后吸入能够直接作用于病灶部位,减轻呼吸道阻力,缓解高气道反应,最终改善肺功能。对两组患儿治疗后 EOS、ECP 水平进行比较,结果显示孟鲁司特钠和布地奈德联合用药的观察组患儿 EOS、ECP 水平显著优于单独用孟鲁司特钠的对照组患儿,提示联合用药在改善 EOS、ECP 水平方面的效果相较于单独应用孟鲁司特钠更具优势,这可能与二者相互作用后阻止炎性因子释放的能力增强有关[30]。

总之,孟鲁司特钠联合布地奈德可改善患儿临床症状及肺功能,提高临床治愈率,同时可显著降低患儿血清中的 EOS、ECP 水平,对于临床用药具有一定指导意义,值得临床推广和应用。

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