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孟鲁司特钠联合沙丁胺醇治疗重度支气管哮喘的临床效果及对患者血清 ECP、LPO、FeNO 水平及肺功能的影响 *

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摘要 目的:探讨孟鲁司特钠联合沙丁胺醇治疗重度支气管哮喘的临床效果及对患者血清嗜酸粒细胞阳离子蛋白(ECP)、过氧化脂质 / 过氧化物酶(LPO)、呼出气一氧化氮(FeNO)水平及肺功能的影响。**方法:**选择 2014 年 5 月到 2017 年 5 月我院接诊的重度支气管哮喘患者 80 例作为研究对象,以随机数表法分为观察组(n=40)和对照组(n=40)。对照组使用沙丁胺醇治疗,观察组在对照组的基础上使用孟鲁司特钠进行治疗。比较两组的临床疗效、治疗前后肺功能、血清 ECP、LPO、FeNO 水平的变化及不良反应的发生情况。**结果:**治疗后,观察组临床疗效总有效率为 92.20%,明显高于对照组(70.00%, $P < 0.05$);观察组第 1 秒用力呼气容积(FEV1)、用力肺活量(FVC)、FEV1/FVC 水平均明显高于对照组($P < 0.05$),血清 ECP、LPO、FeNO 水平均明显低于对照组($P < 0.05$)。观察组不良反应总发生率为 10.00%,显著低于对照组的 30.00%($P < 0.05$)。**结论:**孟鲁司特钠联合沙丁胺醇治疗重度支气管哮喘患者的临床效果明显优于单用沙丁胺醇治疗,其可有效改善患者的肺功能,可能与其显著降低患者血清 ECP、LPO、FeNO 水平有关。

关键词:孟鲁司特钠;沙丁胺醇;重度支气管哮喘;嗜酸粒细胞阳离子蛋白;过氧化脂质 / 过氧化物酶;呼出气一氧化氮;肺功能
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Curative Efficacy of Montelukast Sodium Combined with Albuterol in the Treatment of Severe Bronchial Asthma and Its Effects on the Serum ECP, LPO, FeNO and Lung Function*

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ABSTRACT Objective: To study the curative efficacy of montelukast sodium combined with albuterol in the treatment of severe bronchial asthma and its effects on the serum eosinophil cationic protein (ECP), lipid peroxidase (LPO), exhaled nitric oxide (FeNO) and lung function. **Methods:** 80 cases of patients with severe bronchial asthma who were diagnosed in our hospital from May 2014 to May 2017 were selected and divided into the observation group (n=40) and the control group (n=40) by the random number table. The control group was treated with salbutamol, and the observation group was treated with montelukast sodium on the basis of control group. The clinical efficacy, changes of lung function, serum ECP, LPO and FeNO levels before and after treatment and the occurrence of adverse reactions were compared between the two groups. **Results:** After treatment, the total effective rate of observation group was 92.20%, it was significantly higher than that of the control group(70.00%, $P < 0.05$). The 1-second forced expiratory volume (FEV1), forced lung volume (FVC) and FEV1/FVC levels of observation group were significantly higher than those of the control group ($P < 0.05$). The serum ECP, LPO and FeNO levels were significantly lower than those of the control group ($P < 0.05$). The total incidence of adverse reactions in observation group was 10.00%, it was significantly lower than that of the control group(30.00%, $P < 0.05$). **Conclusion:** Montelukast sodium combined with albuterol was more effective than albuterol alone in the treatment of severe bronchial asthma, it could effectively improve the lung function, which may be related to the significant reduce of serum ECP, LPO, FeNO levels.

Key words: Montelukast sodium; Albuterol; Severe bronchial asthma; The cationic protein of eosinophils; Lipid peroxidase; Exhaled nitric oxide; Lung function

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前言

支气管哮喘是一种常见、多发病,是一种气道慢性炎症疾病,包括肥大细胞、T 淋巴细胞、嗜中性粒细胞、气道上皮细胞

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和细胞成分^[1,2],其临床症状表现为哮喘、喘息、咳嗽、胸闷、夜间及清晨发作增多、反复喘息、呼吸困难等,严重影响患者的生活质量,如不及时控制甚至影响患者的生命^[3,4]。沙丁胺醇是一种短效的肾上腺素受体激动剂,能有效抑制组胺和其他致敏物质的释放,防止支气管痉挛,常用语治疗治疗支气管哮喘,但效果并不显著,容易发生恶心呕吐、心律失常等并发症,其毒性远高于其他药物^[5,6]。

孟鲁司特钠是一种医保甲类药,其不良反应少,且耐受性好,副作用轻,可与其他治疗支气管哮喘药物合用^[7,8]。为使重度支气管哮喘得到有效控制,提高患者的生活质量,本研究旨在探讨对重度支气管哮喘患者使用孟鲁司特钠联合沙丁胺醇治疗的效果,并观察其对患者血清 ECP、LPO、FeNO 水平及肺功能的影响,以期为临床提供依据,现报道如下。

1 资料与方法

1.1 一般资料

选择 2014 年 5 月至 2017 年 5 月我院接诊的 80 例重度支气管哮喘患者进行研究,研究已获得我院伦理会批准实施。将患者通过随机数表法分为 2 组,各 40 例。观察组男 22 例,女 18 例;年龄 35~79 岁,平均(57.85±5.62)岁;病程 1~16 年,平均(9.72±2.85)年。对照组男 25 例,女 15 例;年龄 34~76 岁,平均(56.13±6.95)岁;病程 1.5~17 年,平均(9.92±2.95)年。两组性别(P=0.496)、年龄(P=0.227)等一般资料比较差异均无统计学意义(P>0.05),具有可比性。

纳入标准^[9]:(1)符合支气管哮喘防治指南诊断标准;(2)入院前 1 月内未使用介质阻滞剂者;(3)未合并肾、肺、肝等脏器重大疾病者。排除标准:(1)对本研究药物过敏者;(2)存在精神疾病、沟通障碍者;(3)不配合本次研究,依从性差者。

1.2 治疗方法

两组患者入院后均使用常规吸氧、补液、抗感染、纠正电解质紊乱等基础治疗。对照组采用沙丁胺醇(规格:28 mg;生产厂家:山东京卫制药有限公司;国药准字 H37022817)0.25 mL+2 mL 生理盐水雾化吸入治疗,每次 10~15 分钟,一天 2 次。观察组在对照组的基础上加服孟鲁司特钠治疗,孟鲁司特钠(规格:10 mg;生产厂家:Merck Sharp & Dohme Ltd;国药准字 H20120360)4 mg 一次,一天 1 次,睡前口服。两组均治疗 7 d 观察疗效。

1.3 观察指标

所有患者抽取空腹静脉血 5 mL,3000 r/min 离心 10 min,提取上层血清后置入 EP 管,并置于冷冻箱内储存以备检测,血清 ECP、LPO、FeNO 采用酶联免疫吸附法进行检测(试剂盒购于赫澎(上海)生物科技有限公司),仪器均使用 Formacs TOC/TN 分析仪。所有操作均严格按照试剂盒说明进行;肺功能采用 HI-101 肺功能检测仪测定 FEV1、FVC、FEV1/FVC 水平,仪器购于北京裕天医疗技术有限公司;疗效评定标准:显效:治疗后,喘息、呼吸困难等临床症状及肺部哮鸣音消失;有效:治疗后,喘息、呼吸困难等临床症状及肺部哮鸣音均明显减轻;无效:临床症状无明显改善甚至加重,显效+有效为总有效率。

1.4 统计学分析

本研究数据选择 SPSS22.0 软件进行统计,计量资料用均数±标准差($\bar{x} \pm s$)表示,两组间比较使用独立样本 t 检验;计数资料用[n(%)]表示,两组间比较采用 χ^2 检验,以 P<0.05 表示差异具有统计学意义。

2 结果

2.1 两组临床疗效的比较

治疗后,观察组临床疗效总有效率为 92.20%,明显高于对照组(70.00%,P<0.05),见表 1。

表 1 两组临床疗效的比较[例(%)]

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

Groups	The number of cases	Effective	Valid	Invalid	Total effective rate
Observation group	40	19(47.50)	18(45.00)	3(7.50)	37(92.20)
The control group	40	13(32.50)	15(37.50)	12(30.00)	28(70.00)
P value	40		0.033		0.010

2.2 两组患者治疗前后肺功能指标的比较

治疗前,两组患者肺功能水平比较无显著差异(P>0.05);治疗后,两组 FEV1、FVC、FEV1/FVC 水平均较治疗前显著升

高(P<0.05),且观察组 FEV1、FVC、FEV1/FVC 水平均明显高于对照组(P<0.05),见表 2。

表 2 两组患者治疗前后肺功能比较($\bar{x} \pm s$)

Table 2 Comparison of the lung function between the two groups before and after treatment($\bar{x} \pm s$)

Groups	The number of cases	FEV1(%)		FVC(%)		FEV1/FVC	
		Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment
Observation group	40	68.13±7.31	79.43±6.52	52.34±5.42	66.89±4.36	61.07±4.79	73.45±5.27
The control group	40	67.97±6.68	69.97±6.42	52.79±4.65	53.45±7.52	60.99±5.06	63.38±5.49
P value		0.919	0.000	0.691	0.000	0.942	0.000

2.3 两组患者治疗前后血清 ECP、LPO、FeNO 水平的比较

治疗前, 两组血清 ECP、LPO、FeNO 水平比较无显著差异 ($P>0.05$); 治疗后, 两组血清 ECP、LPO、FeNO 水平较治疗前均

显著降低($P<0.05$), 观察组血清 ECP、LPO、FeNO 水平明显比对照组低($P<0.05$), 见表 3。

表 3 两组患者治疗前后血清 ECP、LPO、FeNO 水平比较($\bar{x} \pm s$)Table 3 Comparison of the serum ECP, LPO and FeNO levels between twp groups before and after treatment($\bar{x} \pm s$)

Groups	The number of cases	ECP(pg/L)		LPO(nmol/L)		FeNO(ppb)	
		Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment
Observation group	40	20.36 $\pm$ 2.27	6.02 $\pm$ 0.84	18.31 $\pm$ 2.08	7.01 $\pm$ 0.57	39.27 $\pm$ 5.87	15.46 $\pm$ 2.32
The control group	40	20.38 $\pm$ 2.25	10.16 $\pm$ 1.23	18.22 $\pm$ 2.04	10.26 $\pm$ 1.15	39.31 $\pm$ 5.57	21.29 $\pm$ 2.89
P value		0.969	0.000	0.846	0.000	0.975	0.000

2.4 两组患者不良反应发生情况的比较

观察组不良反应总发生率为 10.00%, 显著低于对照组

(30.00%, $P<0.05$), 见表 4。

表 4 两组患者不良反应发生情况的比较[例(%)]

Table 4 Comparison of the incidence of adverse reactions between the two groups[n(%)]

Groups	The number of cases	Nausea and vomiting	Arrhythmia	Insomnia	The total incidence of
Observation group	40	2(5.00)	1(2.50)	1(2.50)	4(10.00)
The control group	40	5(12.50)	3(7.50)	4(10.00)	12(30.00)
P value		0.235	0.305	0.166	0.025

3 讨论

支气管哮喘是呼吸内科常见疾病之一, 是一种复杂的气道炎症性疾病, 气道的副交感神经张力是主要诱发因素, 如不及时治疗可能发展为呼吸衰竭, 且严重导致患者的肺功能下降^[10,11]。因此, 治疗必须尽快消除支气管平滑肌痉挛, 减少和消除气道黏液水肿, 尽早纠正低氧血症, 恢复肺功能, 确保正常的通气和通气功能, 以降低支气管哮喘的死亡率^[12,13]。

沙丁胺醇是一种选择性短效 β_2 受体激动剂, 在消化道内不容易被硫酸酯酶和组织中的儿茶酚氧位甲基转移酶破坏, 雾化吸入仅在 5 min 内发生, 并持续很长时间^[14,15]。孟鲁司特钠是一种强效选择性的半胱氨酰白三烯 D4 受体拮抗剂, 可在气道平滑肌活性的控制中选择性的白三烯多肽, 与白三烯受体相竞争, 可预防因抗原, 如冷空气吸入诱导气道^[16,17]。本研究结果显示使用孟鲁司特钠联合沙丁胺醇治疗的患者的总有效率为 92.2%, 明显高于使用沙丁胺醇治疗的患者, 分析是因为孟鲁司特钠抑制肽素生长因子对嗜碱性粒细胞的促成熟作用, 降低了患者血液内的嗜碱性粒细胞, 达到了临床控制的目的。此外, 孟鲁司特钠联合沙丁胺醇治疗的患者治疗后 FEV1、FVC、FEV1/FVC 水平明显高于使用沙丁胺醇治疗的患者, 提示联合用药可以有效改善患者的肺功能。

ECP 可诱导嗜酸性粒细胞和肥大细胞释放组胺, 并导致气道平滑肌痉挛, 引起气道黏膜水肿, 同时引起肺和气管上皮组织损伤, 形成黏液栓塞或脱落的上皮细胞, 是诱发支气管哮喘的主要炎症因子^[18,19]。LPO 是通过脂质过氧化、膜脂过氧化、膜结构和各种疾病引起的细胞功能损伤, 在人体膜结构中加入更多不饱和脂肪酸^[20,21]。由气道细胞产生的 FeNO, 其浓度与高度

炎症细胞的数量有关, 如气道炎性生物标志物, 可用于检测哮喘控制, 简单有效的反射气道嗜酸性粒细胞炎症水平。正常人群血清中 ECP、LPO、FeNO 表达较低, 而在重度支气管哮喘患者血清中均存在着高表达的 ECP、LPO、FeNO, 不仅有利于鉴别疾病, 且可判断支气管哮喘的严重程度^[22,23]。孟鲁司特钠是一种口服有效的选择性白三烯受体拮抗剂, 能特异性抑制半胱氨酰白三烯受体。本研究结果显示使用孟鲁司特钠联合沙丁胺醇治疗的患者血清 ECP、LPO、FeNO 水平明显比使用沙丁胺醇治疗的患者低。此外, 使用孟鲁司特钠联合沙丁胺醇治疗的患者不良反应总发生率为 10%, 明显低于使用沙丁胺醇治疗的 30%, 分析是因为孟鲁司特钠能抑制肺纤维化和基底膜增厚方面有较好的疗效, 减少 β_2 受体激动剂的用量, 进而降低多种并发症的发生。

综上所述, 孟鲁司特钠联合沙丁胺醇治疗重度支气管哮喘患者的临床效果明显优于单用沙丁胺醇治疗, 其可有效改善患者的肺功能, 可能与其显著降低患者血清 ECP、LPO、FeNO 水平有关。

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