doi: 10.13241/j.cnki.pmb.2018.23.035

孟鲁司特联合信必可治疗支气管哮喘的疗效及对患者肺功能和血嗜酸细胞、C反应蛋白水平的影响*

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摘要 目的:探讨孟鲁司特联合信必可治疗支气管哮喘的疗效及对患者肺功能和血嗜酸细胞(EOS)、C反应蛋白(CRP)水平的影响。**方法:**选取我院2016年1月~2017年4月收治的136例支气管哮喘患者,按照随机数字表法均分为两组。对照组(68例)采取信必可治疗,观察组(68例)在此基础上加用孟鲁司特治疗。治疗12周后,评价两组的临床疗效,对比两组治疗前后哮喘症状评分、肺功能、外周血EOS计数及血清CRP水平变化的情况。**结果:**经12周治疗后,观察组总有效率为95.59%(65/68),与对照组[79.41%(54/68)]相比显著上升(P<0.01)。与治疗前对比,两组治疗12周后日间与夜间哮喘评分、外周血EOS计数、血清CRP水平均显著下降(P<0.01),且观察组以上指标均显著低于对照组(P<0.01)。与治疗前相比,两组治疗12周后肺功能指标FVC、FEV1、PEF值均有明显升高(P<0.01);且观察组以上指标均显著高于对照组(P<0.01)。**结论:**孟鲁司特联合信必可治疗支气管哮喘可有效改善患者的肺功能,减轻气道炎症反应,促进哮喘症状缓解,疗效确切。

关键词:孟鲁司特;信必可;支气管哮喘;肺功能;炎症反应

中图分类号:R562.25 **文献标识码:**A **文章编号:**1673-6273(2018)23-4548-04

Clinical Efficacy of Montelukast Combined with Symbicort in the Treatment of Bronchial Asthma and Its Effect on the Lung Function and Blood Eosinophils, C-reactive Protein Levels*

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ABSTRACT Objective: To explore clinical effect of montelukast combined with symbicort in the treatment of bronchial asthma and its effect on lung function and blood eosinophils, c-reactive protein. **Methods:** 136 cases with bronchial asthma who treated from January 2016 to April 2017 in our hospital, all were divided into two groups according to the random number table method.The control group (68 cases) was treated with symbicort, and the observation group(68 cases) was treated with montelukast based on the control group. After 12 weeks of treatment, the clinical efficacy, and the changes of asthma symptom score, lung function, peripheral blood EOS count and serum CRP level before and after treatment in both group were compared. **Results:** After 12 weeks of treatment, the total effective rate of the observation group was 95.59%(65/68), which was significantly higher than the control group [79.41%(54/68)](P<0.01). Compared with before treatment, the asthma score, peripheral blood EOS count, and serum CRP level in both groups were significantly decreased at 12 weeks after treatment (P<0.01), and the above indexes of the observation group were significantly lower than those of the control group (P<0.01). Compared with before treatment, the pulmonary function indexes FVC, FEV1 and PEF were significantly increased in both groups after 12 weeks of treatment (P<0.01). The above indexes in the observation group were significantly higher than those in the control group (P<0.01). **Conclusion:** montelukast combined with cimb can effectively improve the lung function of patients with bronchial asthma, reduce airway inflammation and promote the relief of asthma symptoms.

Key words: Montelukast; Symbicort; Bronchial asthma; Lung function; Inflammation

Chinese Library Classification(CLC): R562.25 Document code: A

Article ID: 1673-6273(2018)23-4548-04

前言

支气管哮喘为临床常见慢性呼吸道疾病,可致咳嗽及呼吸困难等症状反复发作,严重影响患者正常的工作及学习,造成生活质量显著下降[1]。流行病学调查显示[2]支气管哮喘在全球范围内的发病率有明显升高趋势,因此积极采取有效的防治措施

* 基金项目:陕西省自然科学基础研究计划项目(2014JM4186)

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(收稿日期:2018-08-06 接受日期:2018-08-30)

具有重要意义。

支气管哮喘的病理过程涉及到多种炎性细胞因子及炎症介质，目前糖皮质激素和长效β2受体激动剂吸入治疗已成为该病治疗的主要方法[3]。信必可是糖皮质激素和β2受体激动剂的复合制剂，由布地奈德与福莫特罗组成。在支气管哮喘的发病机制中，白三烯起着重要作用，通过使用白三烯受体拮抗剂有助于促进病情缓解，孟鲁司特则是目前最常使用的白三烯受体拮抗剂之一[4]。为进一步探讨信必可与孟鲁司特联合使用在支气管哮喘中的应用价值，本研究对在我院接受治疗的136例支气管哮喘患者分别给予了孟鲁司特联合信必可治疗以及单用信必可治疗，现做如下报道。

1 资料与方法

1.1 一般资料

研究对象选自我院2016年1月~2017年4月收治的136例支气管哮喘患者，依据随机数字表分成观察组与对照组2组，每组68例。观察组中，男36例，女32例；年龄18~74岁，平均(47.2± 6.4)岁；病程2~15年，平均(8.5± 1.9)年；病情严重程度：轻度21例，中度35例，重度12例。对照组中，男38例，女30例；年龄19~73岁，平均(46.5± 6.8)岁；病程2~14年，平均(8.1± 1.6)年；病情严重程度：轻度24例，中度34例，重度10例。统计学分析显示两组一般资料比较无明显差异(P>0.05)，具备可比性。

1.2 病例纳入、排除标准

纳入标准：(1) 符合支气管哮喘防治指南2016年版的诊断标准；(2)年龄18~75岁；(3)签订知情同意书。排除标准：(1)合并恶性肿瘤、其他自身免疫性疾病；(2)心肝肾功能障碍；(3)合并其他严重基础性疾病，如严重高血压、糖尿病等；(4)合并肾炎、肝炎等感染性疾病；(5)合并肺结核、慢性阻塞性肺疾病、支气管扩张等其他肺部疾病；(6)合并呼吸衰竭等严重并发症；(7)近1个月内使用过类似白三烯受体拮抗剂、糖皮质激素、β2受体激动剂等；(8)对研究药物过敏，或过敏体质；(9)精神障碍；(10)儿童、妊娠及哺乳期妇女。

1.3 治疗方法

两组患者均采取常规对症支持治疗，包括抗感染、吸氧、镇静、补液、维持酸碱平衡等。在此基础上，观察组给予孟鲁司特(Merck Sharp & amp，批号151205)+ 信必可(AstraZeneca AB，批号151123)治疗，其中孟鲁司特每次10 mg，每晚1次口服治疗；信必可(布地奈德/福莫特罗：160 μg/4.5 μg/吸)每次1吸，每日2次，吸后漱口。对照组仅给予信必可吸入治疗，用法用量同观察组。两组均连续治疗12周。

1.4 观察指标

(1)哮喘症状评分[5]：包括日间哮喘症状评分与夜间哮喘症状评分，其中日间哮喘症状评分：无症状计0分；出现1次短暂症状计1分；出现至少2次短暂症状计2分；多数时间有症状，但不影响日常生活计3分；多数时间有症状，影响日常生活计4分；症状严重，无法进行日常活动及工作计5分。夜间哮喘症状评分：无症状计0分；夜间憋醒1次或早晨憋醒计1分；夜间憋醒至少2次，包括早晨憋醒计2分；夜间多次憋醒，多数时间无法入睡计3分；症状严重，无法入睡计4分。(2)肺功能：分别于治疗前后检测用力肺活量 (FVC)、第1秒钟用力呼气容积(FEV1)以及呼气峰值流速(PEF)。(3)炎性指标：分别于治疗前后抽取患者的外周静脉血，检测外周血嗜酸性粒细胞(EOS)计数、血清C反应蛋白(CRP)水平。

1.5 疗效评定标准

临床控制：咳嗽、喘息、肺部哮鸣音完全消失，PEF或FEV1增加>35%，；显效：咳嗽、喘息、肺部哮鸣音显著好转，PEF或FEV1增加25%~35%；有效：咳嗽、喘息、肺部哮鸣音有所好转，PEF或FEV1增加15%~24%；无效：咳嗽、喘息、肺部哮鸣音无明显改善，PEF或FEV1增加<15%，或病情加重。以临床控制、显效、有效为总有效。

1.6 统计学分析

统计软件采用SPSS19.0，计数资料以%表示，组间及采取x^2检验，计量资料以($\bar{x}$± s)表示，组间比较采取t检验。以P<0.05为差异有统计学意义。

2 结果

2.1 两组疗效对比

观察组总有效率为95.59%(65/68)，与对照组[79.41%(54/68)]相比显著上升(P<0.01)，见表1。

表1 两组疗效对比[例(%)]

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

Groups	n	Clinical control	Significant effect	Effective	Invalid	Total effective rate
Observation group	68	49	12	4	3	65(95.59)#
Control group	68	32	18	4	14	54(79.41)

Note: Compared with control group #P<0.05.

2.2 两组治疗前后哮喘症状评分比较

与治疗前比较，两组治疗12周后日间与夜间哮喘评分均明显降低(P<0.01)，且观察组两项哮喘症状评分明显低于对照组(P<0.01)，见表2。

2.3 两组治疗前后肺功能比较

与治疗前相比，两组治疗12周后肺功能指标FVC、FEV1、PEF值均显著升高(P<0.01)；且观察组以上指标明显高于对照组(P<0.01)，见表3。

2.4 两组治疗前后EOS计数、CRP水平比较

两组经治疗12周后后外周血EOS计数、血清CRP水平均明显低于治疗前 (P<0.01)，观察组外周血EOS计数、血清CRP水平明显低于对照组(P<0.01)，见表4。

3 讨论

支气管哮喘属于呼吸内科常见病及多发病，以发作性喘息、咳嗽、胸闷、咳白色泡沫痰等为主要临床表现[6,7]。支气管哮

表 2 两组治疗前后哮喘症状评分比较($\bar{x}\pm s$,分)

Table 2 Comparison the asthma symptom score between two groups before and after treatment($\bar{x}\pm s$, points)

Groups	n	Time	Daytime symptom score	Nocturnal symptom score
Observation group	68	After treatment	4.28± 0.32	2.62± 0.22
		Before treatment	0.13± 0.42*#	0.12± 0.16*#
Control group	68	After treatment	4.23± 0.29	2.59± 0.26
		Before treatment	0.62± 0.57*	0.12± 0.16*

Note: Compared with control group #P<0.05; compared with before treatment *P<0.05.

表 3 两组治疗前后肺功能比较($\bar{x}\pm s$)

Table 3 Comparison of the pulmonary function before treatment and after treatment between two groups($\bar{x}\pm s$)

Groups	n	Time	FVC(L)	FEV1(L)	PEF(mL/s)
Observation group	68	After treatment	2.51± 0.82	1.70± 0.65	218.45± 37.45
		Before treatment	3.63± 0.92*#	2.93± 0.72*#	312.24± 58.23*#
Control group	68	After treatment	2.53± 0.87	1.72± 0.73	220.35± 42.12
		Before treatment	3.08± 0.83*	2.49± 0.82*	258.35± 60.35*

Note: Compared with control group #P<0.05; compared with before treatment *P<0.05.

表 4 两组治疗前后外周血 EOS 计数、血清 CRP 水平比较($\bar{x}\pm s$)

Table 4 Comparison of the peripheral blood EOS count, serum CRP before treatment and after treatment between two groups($\bar{x}\pm s$)

Groups	n	Time	EOS(× 10^9/L)	CRP(μg/mL)
Observation group	68	After treatment	0.51± 0.15	34.24± 5.32
		Before treatment	0.13± 0.10*#	6.57± 2.32*#
Control group	68	After treatment	0.50± 0.14	35.52± 5.94
		Before treatment	0.31± 0.12*	14.38± 4.26*

Note: Compared with control group #P<0.05; compared with before treatment *P<0.05.

喘的临床治疗目前尚缺乏特效药,抗感染、吸氧、镇静、补液等常规治疗措施多难取得满意疗效[8]。糖皮质激素联合长效 β2受体激动剂吸入治疗目前被广泛应用于支气管哮喘的治疗中,这两类药物联合治疗可有效促进呼吸道黏膜水肿的缓解,减少炎症介质的释放,抑制平滑肌痉挛或增生,缓解气道炎症反应以及平滑肌功能异常[9,10]。信必可是由糖皮质激素、长效 β2 受体激动剂组成的复合制剂,可发挥抗炎、速效缓解与长效控制三重功效,既可用做缓解用药,也可用做维持用药[11,12]。信必可中布地奈德是目前临床应用最为广泛的抗炎药物之一,其可减少循环中 T 淋巴细胞、嗜碱性粒细胞、嗜酸性粒细胞等的数量,调节细胞因子与炎性介质的释放,降低微血管通透性,减少微血管渗漏,降低气道高反应性,促进气道炎症缓解[13,14]。通过吸入给药的方式可使药物直接作用在气道黏膜上,从而增强局部抗炎作用。福莫特罗为 β2 肾上腺素受体激动剂,具有有效的支气管扩张作用,可使支气管平滑肌舒张,缓解支气管痉挛[15]。布地奈德与福莫特罗两种药物联合使用在减轻哮喘症状、缓解气道高反应性、改善肺功能方面具有较好的协同作用[16]。

白三烯为花生四烯酸代谢生成的产物,可引起气道平滑肌痉挛,导致炎性细胞活化,增加黏液分泌等,因此其在支气管哮喘炎症反应过程中起着重要作用[17]。而采用信必可治疗时,对于白三烯的合成与释放无法起到有效的抑制作用,对由白三烯造成的气道微血管通透性增加、黏液分泌以及气道嗜酸性细胞渗出等作用有限[18]。孟鲁司特属于高选择性半胱氨酸白三烯受体拮抗剂,可竞争性地结合半胱氨酰白三烯受体,使受体与白三烯结合被抑制,进而改善血管通透性,抑制气道嗜酸性粒细胞浸润,避免气道重塑,缓解支气管痉挛,使气道高反应性降低,缓解哮喘症状,减少急性发作次数,促进肺功能的改善[19,20]。孟鲁司特是除吸入糖皮质激素外唯一能单独使用的一种长效控制药,能显著缓解气道炎症反应[21]。

本研究结果显示采用孟鲁司特联合信必可治疗后的支气管哮喘患者总有效率达 95.59%,显著高于单用信必可治疗,且期在哮喘症状评分方面改善效果更优。可见,孟鲁司特与信必可联用可起到良好的协同增效的作用[22]。在评价支气管哮喘的疗效方面,根据哮喘的临床症状表现有时并不能客观反映出哮喘患者的气道阻塞情况,若仅依靠症状体征判断病情、评估疗效可能会出现失误。而通过检测肺功能则能更加客观、敏感地反映出气道阻塞情况[23]。本研究通过检测肺功能对不同临床用药方案的疗效进行评估,发现采用孟鲁司特联合信必可治疗相对于单用信必可治疗对肺功能的改善效果更明显。此外,采用孟鲁司特联合信必可治疗的患者外周血 EOS 计数、血清 CRP 水平降低更明显。这可能与孟鲁司特治疗支气管哮喘的作用机制有关,孟鲁司特对嗜酸性粒细胞具有抑制作用,可使其浸润减少,从而减少炎症介质的释放,缓解炎症反应。

在用药方法上，吸入治疗方式尽管能提高局部药物浓度，但吸入方法掌握是否正确直接关系到治疗效果，吸入方法掌握不佳，治疗依从性差，可使达到气道的有效药物剂量减少，从而影响疗效。而孟鲁司特属于非糖皮质激素类抗炎药物，不仅适用于各种程度的支气管哮喘以及过敏性鼻炎等的治疗中，其在与吸入性糖皮质激素联合使用时，还可减少糖皮质激素的使用剂量，并有利于提高患者治疗的依从性，因此疗效较好[24,25]。

综上所述，孟鲁司特联合信必可在支气管哮喘的治疗上可发挥良好的协同作用，与单用信必可治疗相比，孟鲁司特联合信必可的用药方案能进一步加快哮喘症状的改善，促进炎症反应的缓解，促使肺功能明显改善，疗效确切。

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