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·临床研究·

孟鲁司特钠联合左卡巴斯汀鼻喷剂治疗小儿过敏性鼻炎的疗效评价及对血清ECP、EOS及CRP水平的影响*

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摘要 目的：探讨孟鲁司特钠联合左卡巴斯汀鼻喷剂治疗小儿过敏性鼻炎的疗效及对血清嗜酸性粒细胞阳离子蛋白（ECP）、嗜酸性粒细胞（EOS）及C反应蛋白（CRP）水平的影响。**方法：**选择我院2016年7月~2018年7月收治的151例过敏性鼻炎患儿，按随机数字表法分为69例对照组和82例观察组，对照组采用左卡巴斯汀鼻喷剂治疗，观察组在对照组基础上联合孟鲁司特钠治疗，比较两组临床疗效，治疗前后症状及体征评分，生活质量评分，血清ECP、EOS及CRP、总免疫球蛋白E（TIgE）和特异性免疫球蛋白E（SigE）水平，和不良反应发生情况。**结果：**观察组总有效率高于对照组，差异有统计学意义（$P<0.05$）。治疗前，两组症状及体征评分，生活质量评分，血清ECP、EOS及CRP、总免疫球蛋白E（TIgE）和特异性免疫球蛋白E（SigE）水平比较差异无统计学意义（$P>0.05$）；治疗后，两组以上指标均下降，观察组低于对照组，差异均有统计学意义（均$P<0.05$）。两组均有胃肠道反应、口干、头痛发生，组间总不良反应发生率比较无统计学差异（$P>0.05$）。**结论：**孟鲁司特钠联合左卡巴斯汀鼻喷剂治疗小儿过敏性鼻炎安全有效，能够降低血清ECP、EOS及CRP水平，促进患儿恢复。

关键词：小儿过敏性鼻炎；孟鲁司特钠；左卡巴斯汀鼻喷剂；嗜酸性粒细胞阳离子蛋白；嗜酸性粒细胞；C反应蛋白

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Efficacy Evaluation of Montelukast Sodium Combined with Levorabastine Nasal Spray in the Treatment of Allergic Rhinitis in Children and its Effects on Serum Levels of ECP, EOS and CRP*

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ABSTRACT Objective: To explore the efficacy of monclulast sodium combined with levorabastine nasal spray in the treatment of allergic rhinitis in children and the effects on serum levels of eosinophil cationic protein (ECP), eosinophil (EOS) and c-reactive protein (CRP). **Methods:** 151 cases of children with allergic rhinitis who treated from July 2016 to July 2018 in our hospital, according to random number table method thoese childre were divided into 69 control groups and 82 observation groups, the control group was treated with levocarbastine nasal spray, and the observation group was treated with montelukast sodium on the basis of the control group.then clinical curative effect, the symptoms and signs scores, the quality of life score, serum levels of ECP, EOS and CRP, total immunoglobulin E (TIgE) and specific immunoglobulin E (SIgE) before and after the treatment, and adverse reactions occur in both group were compared. **Results:** The total effective rate in the observation group was higher than that in the control group, and the difference was statistically significant ($P<0.05$). Before treatment, the scores of symptoms and signs, quality of life, serum levels of ECP, EOS and CRP, total immunoglobulin E (TIgE) and specific immunoglobulin E (SIgE) showed no significant difference between the two groups ($P>0.05$). After treatment, the above indicators in both groups were decreased, and the observation group was lower than the control group, and the difference was statistically significant (all $P<0.05$). Both groups had gastrointestinal reactions, dry mouth, and headache, and there was no statistical difference in the incidence of total adverse reactions between the two groups ($P>0.05$). **Conclusion:** Montelukast sodium combined with levorabastine nasal spray is safe and effective in the treatment of allergic rhinitis in children, which can reduce serum levels of ECP, EOS and CRP and promote the recovery of children.

Key words: Children allergic rhinitis; Montelukast sodium; Left carbastine nasal spray; Eosinophilic cationic protein; Eosinophils; C-reactive protein

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前言

小儿过敏性鼻炎为耳鼻喉科的常见病，以阵法性鼻塞、鼻痒、喷嚏、清水样鼻涕为典型症状，长期反复可导致慢性咽炎、鼻窦炎等并发症，且可导致患儿面 - 口 - 颌骨骼发育畸形，明显影响患儿的生活质量[1,2]。相关研究报道[3,4]，过敏性鼻炎为慢性炎症病变，可有多种细胞因子参与，能够在疾病发生发展中起到重要作用。目前药物是缓解小儿过敏性鼻炎症状的有效手段之一，其中抗组胺药物是其首选药物，左卡巴斯汀鼻喷剂为长效、强效具有高度选择性的组胺 H1 受体拮抗剂，能够和组胺竞争 H1 受体，抑制组胺的生物学作用，从而控制此类疾病的症状[5]。但有研究发现[6]，过敏性鼻炎患儿多合并不同程度的伴发疾病，因此可辅助全身药物治疗。孟鲁司特钠能够改善白三烯产生的刺激症状，减轻机体对于激素所致的依赖性，临床上已得到广泛应用[7]。但目前缺乏二者联合应用的全面报道，本研究旨在评价孟鲁司特钠联合左卡巴斯汀鼻喷剂治疗小儿过敏性鼻炎的疗效及对血清相关细胞因子水平的影响。

1 资料与方法

1.1 一般资料

选择我院 2016 年 7 月 ~2018 年 7 月收治的 151 例过敏性鼻炎患儿，纳入标准：符合过敏性鼻炎诊断标准[8]；轻度、持续性过敏性鼻炎；年龄 5~14 岁，患儿可清楚表达个人意愿及感受；近期未接受抗组胺等相关治疗。排除标准：哮喘发作期；合并严重慢性鼻窦炎、鼻息肉、鼻中隔偏曲等鼻腔病变，或接受过鼻部手术；外感喷嚏、流涕及鼻塞；心、脑、肾、造血等严重原发性疾病。所有患儿按随机数字表法分为 69 例对照组和 82 例观察组，对照组男 39 例，女 30 例；年龄 5~14 岁，平均（10.43± 1.69）岁；病程 3 个月 ~4 年，平均病程（1.65± 0.41）个月。观察组男 42 例，女 40 例；年龄 5~14 岁，平均（10.85± 1.51）岁；病程 5 个月 ~4 年，平均病程（1.61± 0.45）个月。两组一般资料比较无统计学差异（P>0.05）。

1.2 方法

对照组采用左卡巴斯汀鼻喷剂（厂家：上海强生制药有限公司，规格：5 mg/mL/ 瓶，批号：20160115）治疗，每鼻孔 1 喷，每天 2 次，持续治疗 2 周，患儿喷鼻前需擤净鼻涕。观察组在对照组基础上联合孟鲁司特钠（厂家：杭州默沙东制药有限公司，规格：4 mg/ 片，批号：20151105）治疗，口服 5 mg，每天 1 次，持续治疗 2 周。两组治疗期间均勿接触过敏原，停药随访 3 个月后进行疗效评价，记录不良反应发生情况。

1.3 观察指标

1.3.1 临床疗效 临床体征、症状基本消失，症状及体征积分减少 >95%为痊愈；临床体征、症状显著改善，症状及体征积分减少 >65%为有效；临床体征、症状有所好转，症状及体征积分减少 26%~65%为有效；临床体征、症状加重或者无明显改善，症状及体征积分减少 <25%为无效。痊愈率 + 显效率 + 有效率为总有效率[8]。

1.3.2 观察症状及体征积分 于治疗前及停药随访 3 个月后时进行，症状积分：包含鼻塞、鼻痒、喷嚏、流涕，按症状严重程度分为 0、1、2、3 分；体征积分：按严重程度分为 1、2、3 分[8]。

1.3.3 生活质量评分 于治疗前及停药随访 3 个月后时进行，包含鼻部症状（鼻塞、喷嚏、流涕、鼻后滴漏），眼部症状（眼肿、眼痛、流泪、眼痒），非鼻或者眼症状（精疲力竭、头痛、注意力不集中、厌烦、创造力降低、口渴、疲倦），情感（被症状烦恼、易激惹及不耐烦、无助、沮丧）、睡眠（睡眠质量差、睡中觉醒、入睡困难）、日常生活方面（反复擤鼻或吸鼻、揉鼻或眼、进餐使用纸巾）[8]。

1.3.4 血清指标 于治疗前及停药随访 3 个月后时进行，采集患儿空腹外周静脉血，常规分离血清后保存在 -70℃低温箱中待检。采用分光光度计比色法检测血清嗜酸性粒细胞阳离子蛋白（ECP）水平，采用全自动生化分析仪检测血清 EOS（嗜酸性粒细胞），采用酶联免疫双抗体夹心法检测 C 反应蛋白（CRP）、总免疫球蛋白 E（TIgE）和特异性免疫球蛋白 E（SigE）浓度。

1.4 统计学分析

数据处理选用 SPSS18.0 软件包，计量资料用（$\bar{x}\pm s$）表示，选用独立样本 t 检验，计数资料用[（例）%]表示，用 x^2 检验比较，P<0.05 表示差异有统计学意义。

2 结果

2.1 两组临床疗效比较

观察组总有效率高于对照组（P<0.05），见表 1。

表 1 两组临床疗效比较[（例）%]

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

Groups	n	Heal	Significant Effect	Effective	Invalid	Total effective rate
Control group	69	20(28.99)	17(24.64)	18(26.09)	14(20.28)	55(79.71)
Observation group	82	40(48.78)	26(31.71)	10(12.19)	6(7.32)	76(92.68)#

Note: Compared with the control group #P<0.05.

2.2 两组治疗前后症状及体征积分比较

治疗前，两组症状及体征积分比较无统计学差异（P>0.05）；治疗后，两组症状及体征积分均下降，观察组低于对照组，差异有统计学意义（P<0.05），见表 2。

2.3 两组治疗前后生活质量评分比较

治疗前，两组生活质量评分比较无统计学差异（P>0.05）；治疗后，两组生活质量评分均下降，观察组低于对照组（P<0.05），见表 3。

2.4 两组治疗前后血清 ECP、EOS 及 CRP 水平比较

治疗前，两组血清 ECP、EOS 及 CRP 水平比较无统计学差异（P>0.05）；治疗后，两组血清 ECP、EOS 及 CRP 水平均下降，观察组低于对照组（P<0.05），见表 4。

表 2 两组治疗前后症状及体征积分比较($\bar{x}\pm s$,分)

Table 2 Comparison of symptoms and signs before and after treatment in both groups($\bar{x}\pm s$, points)

Groups	n	Time	Nasal congestion	Nasal itching	Runny nose	Sneeze	Signs
Control group	69	Before treatment	2.15± 0.25	2.21± 0.24	2.45± 0.27	2.79± 0.22	1.68± 0.25
		After treatment	1.07± 0.12△	1.03± 0.10△	1.15± 0.13△	1.27± 0.12△	0.96± 0.13△
Observation group	82	Before treatment	2.18± 0.21	2.24± 0.20	2.41± 0.31	2.74± 0.31	1.72± 0.22
		After treatment	0.38± 0.08△#	0.55± 0.07△#	0.62± 0.07△#	0.62± 0.08△#	0.48± 0.05△#

Note: Compared with the control group #P<0.05; Compared with the same group before treatment △ P<0.05.

表 3 两组治疗前后生活质量评分比较($\bar{x}\pm s$,分)

Table 3 Comparison of quality of life score before and after treatment in both groups($\bar{x}\pm s$, points)

Groups	n	Time	RQLQ
Control group	69	Before treatment	26.49± 3.25
		After treatment	14.65± 1.75△
Observation group	82	Before treatment	25.83± 3.71
		After treatment	11.04± 1.24

Note: Compared with the control group #*P*<0.05; Compared with the same group before treatment △ *P*<0.05.

表 4 两组治疗前后血清 ECP、EOS 及 CRP 水平比较($\bar{x}\pm s$)

Table 4 Comparison of serum levels of ECP, EOS and CRP before and after treatment in both groups($\bar{x}\pm s$)

Groups	n	Time	ECP(μg/L)	EOS(×10^6)	CRP(mg/L)
Control group	69	Before treatment	25.73± 3.71	29.85± 4.72	23.06± 3.02
		After treatment	14.36± 1.82△	12.90± 1.85△	9.72± 1.39△
Observation group	82	Before treatment	25.02± 3.96	30.41± 4.14	22.51± 3.75
		After treatment	10.61± 1.31△#	10.23± 1.39△#	5.83± 0.75△#

Note: Compared with the control group #*P*<0.05; Compared with the same group before treatment △ *P*<0.05.

2.5 两组治疗前后血清 SIgE、TIgE 水平比较

治疗前，两组血清 SIgE、TIgE 水平比较无统计学差异（*P*>0.05）；治疗后，两组血清 SIgE、TIgE 水平均下降，观察组低于对照组（*P*<0.05），见表 5。

表 5 两组治疗前后血清 SIgE、TIgE 水平比较($\bar{x}\pm s$)

Table 5 Comparison of serum levels of SigE,TIgE before and after treatment in both groups($\bar{x}\pm s$)

Groups	n	Time	SIgE(kU/L)	TIgE(kU/L)
Control group	69	Before treatment	28.75± 4.03	463.09± 64.12
		After treatment	14.27± 1.83△	317.86± 43.27△
Observation group	82	Before treatment	29.49± 3.75	458.74± 69.03
		After treatment	12.30± 1.40△#	245.11± 35.11△#

Note: Compared with the control group #*P*<0.05; Compared with the same group before treatment △ *P*<0.05.

2.6 两组不良反应发生情况比较

两组均有胃肠道反应、口干、头痛发生，组间总不良反应发生率比较无统计学差异（*P*>0.05），见表 6。

表 6 两组不良反应发生情况比较[例(%)]

Table 6 Comparison of adverse reaction between the two groups[(n)%]

Groups	n	Gastrointestinal reaction	Dry Mouth	Headache	Total Adverse Reaction Rate
Control group	69	4(5.78)	5(7.24)	4(5.78)	13(18.84)
Observation group	82	7(8.53)	5(6.09)	8(9.75)	20(24.39)

3 讨论

小儿过敏性鼻炎为最常见的慢性疾病之一，临床发生率相对较高，容易引起多种体征及症状，且病情迁延，易反复发作[9,10]。目前小儿过敏性鼻炎需长时间辅助药物治疗，组胺在小儿过敏性鼻炎发生的多个环节中有重要作用，是导致此类疾病

症状的主要炎症介质之一[11]。过敏性鼻炎患儿受到变应原激发后可刺激组胺释放,激动分布在鼻粘膜的 H1 受体,导致喷嚏、鼻痒症状,又可扩张微血管,增加血管通透性,导致组织水肿,诱导腺体分泌亢进[12,13]。H1 受体阻滞剂能够竞争性地结合 H1 受体,阻断 H1 受体和组胺的作用,抑制组织发挥生物学作用,发挥抗过敏效应[14,15]。

左卡巴斯汀鼻喷剂为第三代抗组胺药,对组胺 H1 受体的拮抗作用较高,鼻腔黏膜吸收快速,在局部应用后可快速起效,可竞争性的和 H1 受体结合,阻断组胺的生物学效应,抑制局部组织中白三烯及前列腺素的释放,抑制变态反应,减轻局部充血水肿,从而减轻过敏性鼻炎的症状[16,17]。鼻内给药有较多优势,高浓度药物能够直接作用于鼻部,减少或避免全身副作用,但有研究报道[18],抗组胺药物对控制持续抗原暴露所致的鼻塞症状较差,并有研究发现,药物需作用于不同靶器官,鼻内给药并非最佳选择,建议全身药物治疗。

抗白三烯药在儿童哮喘中的效果已得到临床认可,近年来有研究发现,抗白三烯药对过敏性鼻炎有一定效果[19]。孟鲁司特钠为选择性白三烯受体拮抗药, 可阻断白三烯和其受体结合,抑制其炎性作用,降低气道和周围血中刺激物质的浓度,减轻炎症反应[20]。本研究结果显示,孟鲁司特钠联合左卡巴斯汀鼻喷剂组总有效率较左卡巴斯汀鼻喷剂组高,说明二者联合治疗可提高疗效,可能与孟鲁司特钠能够阻断白三烯受体,从而减轻其诱导的血管通透性改变,促进患儿恢复。过敏性鼻炎患儿因症状较为典型,因此可明显影响患儿生活质量,通过评估其生活质量改变能够一定程度的反映疗效。本研究发现,联合治疗组治疗后症状及体征积分、生活质量评分改善更为明显,进一步说明二者联合治疗更能有效减轻患儿症状,改善生活质量,证实二者联合作用的效果。

随着医学技术的不断发展,临床对过敏性鼻炎的发病机制有更全面、深层次的了解,大量研究发现,通过抑制相关细胞因子的作用可有效控制过敏性鼻炎患儿的症状[21,22]。ECP 及 EOS 浸润是过敏性鼻炎的重要特征, 其中 ECP 为最主要的嗜酸性粒细胞活性及转归的重要标记, 可刺激嗜碱性粒细胞释放组胺,增加粘膜粘液分泌,参与相关的变态反应疾病[23]U。EOS 可导致鼻粘膜受损,增加鼻粘膜的敏感性,且可破坏小血管壁,增加局部通透性,导致组织水肿及血浆外渗,加重鼻部症状[24,25]。近年来,血清 ECP、EOS 水平和过敏性结膜炎、鼻炎等疾病的发生及预后关系已被临床研究证实,在疾病诊治及疗效评价中有重要作用[26]。CRP 为急性相蛋白,当机体受到损伤时可快速上升,其浓度和小儿过敏性鼻炎鼻塞、鼻痒等症状有明显关系,较高浓度的 CRP 能够间接反映病情程度[27]。本研究结果显示,治疗后患者血清 ECP、EOS 及 CRP 水平均下降,且联合治疗组降低更明显, 说明二者联合治疗更能有效减轻局部过敏反应,控制炎症反应,从而促进疾病恢复,在这些方面肯定了其疗效。血清 SIgE、TIgE 是确诊过敏性鼻炎的依据,治疗后联合治疗组血清 SIgE、TIgE 水平相对较低,证实联合治疗的效果[28,29]。

综上所述,孟鲁司特钠联合左卡巴斯汀鼻喷剂治疗小儿过敏性鼻炎安全有效, 能够降低血清 ECP、EOS 及 CRP 水平,促进患儿恢复。

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