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孟鲁司特钠对哮喘患儿 T 淋巴细胞亚群 CD4⁺ 和 CD8⁺ 水平的影响 *

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摘要 目的:探讨孟鲁司特钠联合抗生素对哮喘患儿 T 淋巴细胞亚群 CD4⁺ 和 CD8⁺ 水平的影响。**方法:**选取我院收治的哮喘患儿 50 例,并将其随机分为两组,每组各 25 例。对照组予常规抗生素治疗,实验组在此基础上加用孟鲁司特钠治疗。观察和比较两组患儿的临床疗效、一年内复发率,以及 CD4⁺、CD8⁺ 和 CD4⁺/CD8⁺ 比值的变化情况。**结果:**两组哮喘音、咳嗽及喘憋持续时间均获得改善,实验组优于对照组,差异有统计学意义($P < 0.05$)。与同组治疗 1 天后比较,两组患儿治疗 5、10 天后的 CD4⁺、CD8⁺ 以及 CD4⁺/CD8⁺ 比值均明显升高;与同组治疗 5 天后比较,两组患儿治疗 10 天后 CD4⁺、CD8⁺ 以及 CD4⁺/CD8⁺ 比值均明显升高;实验组患儿治疗 5 天、10 天后的 CD4⁺、CD8⁺ 以及 CD4⁺/CD8⁺ 比值均明显高于对照组,差异均有统计学意义 ($P < 0.05$)。两组治疗后 CD4⁺、CD8⁺ 以及 CD4⁺/CD8⁺ 比值变化呈显著差异($P < 0.05$)。实验组 1 年复发率显著低于对照组,差异有统计学意义($P < 0.05$)。**结论:**孟鲁司特钠可能通过影响哮喘患儿 CD4⁺、CD8⁺ 及 CD4⁺/CD8⁺ 水平,改善患儿的临床症状,缩短其住院时间,值得临床推广应用。

关键词:孟鲁司特钠;哮喘;CD4⁺;CD8⁺

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Effect of Montelukast on the CD4⁺ and CD8⁺ Levels of Patients with Pediatric Asthma*

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ABSTRACT Objective: To investigate the effect of montelukast sodium combined with antibiotics on the T lymphocyte subsets CD4⁺ and CD8⁺ levels of asthmatic children. **Methods:** 50 children with asthma admitted in our hospital were selected and randomly divided into two groups with 25 cases in each group. The control group was treated with conventional antibiotics, while the experimental group was treated with the reduning on the basis of the control group. Then the clinical efficacy, recurrence rate within 1 year, and the changes of CD8⁺, CD4⁺ levels as well as ratio of CD4⁺/CD8⁺ were compared between two groups. **Results:** Wheeze, cough and asthma duration were improved, in both groups and the experimental group was better than the control group ($P < 0.05$). The CD4⁺, CD8⁺ levels and CD4⁺/CD8⁺ ratio were significantly increased after 5, 10 days' treatment compared with those on the 1st day of treatment. The CD4⁺, CD8⁺ levels and CD4⁺/CD8⁺ ratio were significantly increased after 10 days' treatment compared with those after 5 days' treatment. The CD4⁺, CD8⁺ levels and CD4⁺/CD8⁺ ratio of experimental group were significantly higher than those of the control group after 5 days' and 10 days' treatment ($P < 0.05$). Significant differences were found in CD4⁺, CD8⁺ levels and CD4⁺/CD8⁺ ratio between the two groups after treatment ($P < 0.05$). The 1 year recurrence rate of experiment group was significantly lower than that of the control group ($P < 0.05$). **Conclusions:** Montelukast could improve the CD4⁺ and CD8⁺ levels, restore the immune system function and promote the clinical effect of children with asthma.

Key words: Montelukast; Asthma; CD4⁺; CD8⁺

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前言

支气管哮喘是小儿时期常见的疾病,以反复发作、喉间痰鸣、呼吸急促、甚至呼吸困难、喘息不能平卧为特征^[1]。有资料显示,我国约有 1000-2000 万哮喘患者,以青壮年和儿童居多,成

人哮喘的发病率为 0.7%-1.5%,儿童发病率约为 0.11%-2.03%,发病季节以秋季、冬季发作为著^[2]。哮喘患儿大多在 10 岁以前发病,严重影响其生活和学习^[3]。现代医学多以糖皮质激素、支气管扩张剂以及免疫抑制剂等治疗哮喘发作,但其副作用多,安全性低,易对患儿的预后造成一定的影响。孟鲁司特钠的主

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要成分为青蒿、金银花、栀子,具有清热、疏风、解毒之功效,为良好的抗菌、抗病毒中成药,临床上广泛用于细菌、病毒感染所致的上呼吸道感染^[4]。有研究表明^[5],孟鲁司特钠能够治疗小儿哮喘,缓解患儿痛苦,改善疗效。本研究通过观察不同时段CD4⁺/CD8⁺以及CD4⁺/CD8⁺比值变化,探讨中药联合抗生素对小儿哮喘T淋巴细胞亚群CD4⁺/CD8⁺的影响。

1 资料与方法

1.1 临床资料

选取2014年1月-2014年10月我院收治的支气管哮喘患儿50例,随机分为实验组和对照组。其中,实验组25例,包括男12例,女13例,年龄3-8岁,平均(4.7±0.6)岁;对照组25例,包括男13例,女12例;年龄4-7岁,平均(4.8±0.8)岁。两组的一般资料比较无显著差异(P>0.05),具有可比性。本研究均经过患儿家长同意并签署《知情同意书》。

1.2 诊断标准

所有入选者均符合中华医学会儿科学分会呼吸学组、《中华儿科杂志》编辑委员会儿童支气管哮喘诊断与防治指南^[6]:(1)反复发作的喘息、气促、胸闷或咳嗽,多与接触变应原、冷空气、物理或化学性刺激,病毒性上、下呼吸道感染、运动等有关;(2)发作时双肺可闻及散在或弥漫性以呼气相为主的哮鸣音,呼气相延长;(3)支气管舒张剂有显著疗效;(4)排除其他疾病所引起的喘息、气促、胸闷或咳嗽;(5)对于症状不典型、肺部闻及哮鸣音者,可采用支气管舒张试验协助诊断(15-30 min内喘息明显缓解,哮鸣音明显减少者为阳性)。

1.3 治疗方法

对照组予常规抗生素治疗,阿奇霉素10 mg/kg,加入0.9%氯化钠注射液250 mL静脉滴注,每日1次。实验组在对照组基础上,加以口服孟鲁司特钠(江苏康缘药业股份有限公司生产),0.5 mg/次/日。两组疗程均为10天。

1.4 疗效评价

(1)治愈:症状消失,体温正常,无咳嗽、咳痰,双肺部哮鸣音消失,呼吸频率正常,面色正常,精神状态佳,X线摄片正常;有效:症状减轻,咳嗽减轻,咳痰量减少,双肺部哮鸣音减少,呼吸频率减慢,面色好转,精神状态好转,X线摄片过度充气状态减轻;无效:症状无好转,或者加重。(2)观察两组住院时间、哮鸣音、咳嗽及喘憋的持续时间。(3)采用流式细胞仪(Facscalibur,美国BD公司)及其配套试剂盒测定CD4⁺和CD8⁺水平,操作均按试剂说明书进行。(4)治疗结束后对两组进行1年随访,记录复发率。

1.5 统计学方法

采用统计学软件SPSS19.0进行统计学分析,计量资料采用t检验,计数资料采用卡方检验处理,以P<0.05为有显著性差异。

2 结果

2.1 两组临床指标变化情况的比较

治疗后,实验组的住院时间、哮鸣音持续时间、咳嗽持续时间、喘憋持续时间均较对照组显著缩短,差异均有统计学意义(P<0.05)。见表1。

表1 两组患儿临床指标变化情况的比较($\bar{x} \pm s$)
Table 1 Comparison of the clinical data between two groups($\bar{x} \pm s$)

Group	Case	Hospitalization time	Wheeze duration	Cough duration	Gasp duration
Experimental group	25	9.1±1.6	6.0±1.8	7.1±1.9	7.3±1.6
Control group	25	5.7±2.1	2.4±0.7	4.7±1.4	2.4±1.7
t		3.983	4.312	3.994	4.127
P		<0.05	<0.05	<0.05	<0.05

2.2 两组CD4⁺/CD8⁺及CD4⁺/CD8⁺比值的变化情况比较

两组组内与治疗1天比较,治疗5、10天后CD4⁺/CD8⁺以及CD4⁺/CD8⁺比值均明显升高,差异均有统计学意义(P<0.05);与治疗5天比较,治疗10天后CD4⁺/CD8⁺以及

CD4⁺/CD8⁺比值均明显升高,差异有统计学意义(P<0.05);组间比较,实验组治疗5天、10天CD4⁺/CD8⁺以及CD4⁺/CD8⁺比值均明显高于对照组,差异有统计学意义(P<0.05)。见表2。

表2 两组患儿不同时点CD4⁺/CD8⁺及CD4⁺/CD8⁺比值变化情况的比较($\bar{x} \pm s$)
Table 2 Comparison of the changes of CD4⁺/CD8⁺ and CD4⁺/CD8⁺ after treatment at different time points between two groups

Group	Time	CD4 ⁺	CD8 ⁺	CD4 ⁺ /CD8 ⁺
Experimental group	1 st day	24.76±8.43	46.36±12.15	0.63±0.31
	5 th day	25.53±8.87*▲	47.12±11.32*▲	0.68±0.26*▲
	10 th day	29.91±5.69*△▲	34.62±12.71*△▲	1.02±0.31*△▲
Control group	1 st day	23.51±9.82	47.03±11.09	0.59±0.3
	5 th day	24.43±7.02*	46.92±11.83*	0.60±0.32*
	10 th day	26.91±4.76*△	38.51±10.63*△	0.71±0.27*△

Note: *P<0.05, compared with the 1st day; △P<0.05, compared with the 5th day; ▲P<0.05, compared with control group.

2.3 两组治疗后1年复发率的比较

治疗后1年内,实验组患儿的发病率与对照组比较明显

减低,差异有统计学意义(P<0.05)。见表3。

表 3 两组治疗后 1 年复发率的比较(%)

Table 3 Comparison of the recurrence rate at one year after treatment between two groups(%)

Group	Case	patients with asthma	Asthma incidence (%)
Experimental group	25	7	28.0▲
Control group	25	11	44.0

Note: ▲P<0.05, compared with control group.

3 讨论

支气管哮喘是儿童期最常见的慢性呼吸道疾病。由于本病的诱发与呼吸道感染密切相关,故临床上常滥用抗生素,没有进行有效及时的治疗,以致贻误病情,对小儿生长发育的影响很大,严重影响学习和生活^[7]。临床实践研究认为,哮喘是一种免疫性疾病,其中 T 淋巴细胞控制着炎症反应^[8]。支气管哮喘是由多种细胞,特别是 T 淋巴细胞参与的慢性气道炎症,T 淋巴细胞主要包括 CD4⁺ 和 CD8⁺ 细胞两类细胞,辅助性 T 淋巴细胞(T helper cell, Th)两种亚型 Th1, Th2 的失衡是哮喘发病的重要机制^[15-17]。在支气管哮喘气道慢性炎症中,存在免疫功能缺陷的问题,其主要表现为 CD4⁺ 增多,同时 CD8⁺ 降低,导致 CD4⁺、CD8⁺ 细胞比例失调,免疫系统紊乱,而出现一系列现象^[18-20]。

孟鲁司特钠是一种口服白三烯受体拮抗剂,能特异性抑制气道中的半胱氨酰白三烯(CysLT1)受体,是非激素类抗炎药,具有抗菌、抗病毒、解热、抗炎、镇痛、免疫抑制作用,能够促进淋巴细胞转化率,适用于成人和 1 岁以上儿童哮喘的预防和长期治疗及过敏性鼻炎的治疗,有助于改善气道炎症,有效控制哮喘症状^[9-13]。本研究结果显示,患儿经孟鲁司特钠配合抗生素治疗后,CD4⁺ 细胞减少,CD8⁺ 细胞增多,CD4⁺/CD8⁺ 比值显著降低,表明孟鲁司特钠配合抗生素可能通过减少 CD4⁺ 细胞,增加 CD8⁺ 细胞,从而抑制气道炎症,调节紊乱的免疫系统,缓解哮喘急性发作。此外,经孟鲁司特钠配合抗生素治疗的患儿的临床疗效较常规治疗显著提高,而且患儿 1 年内哮喘发作明显减少,表明孟鲁司特钠配合抗生素治疗哮喘可取得很好的临床疗效,可降低哮喘的再发率。

综上所述,孟鲁司特钠可能通过影响哮喘患儿 CD4⁺、CD8⁺ 及 CD4⁺/CD8⁺ 水平,改善患儿的临床症状,缩短其住院时间,值得临床推广应用。

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