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泛福舒胶囊联合参麦注射液治疗儿童支气管哮喘的疗效 及对血清 IL-4、hs-CRP、Ang-2 的影响 *

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摘要 目的: 研究泛福舒胶囊联合参麦注射液治疗儿童支气管哮喘的疗效及对血清 IL-4 (Interleukin -4)、hs-CRP(Hypersensitive c-reactive protein)、Ang-2(Angiotensin -2)的影响。**方法:** 选择 2015 年 3 月至 2017 年 3 月在我院接受治疗的支气管哮喘患儿 120 例,根据治疗方案不同分为观察组和对照组,对照组使用常规治疗,观察组在对照组的基础给予静脉滴注参麦注射液联合泛福舒胶囊治疗,两组患者均治疗 3 个疗程。治疗后,观察和比较两组患者的临床疗效,治疗前后 PEF(peak expiratory flow)、FEV1(forced expiratory volume)水平、T 淋巴细胞亚群水平、血清 IL-4、hs-CRP、Ang-2 水平的变化。**结果:** 治疗后,观察组总有效率(91.7%)明显高于对照组(73.3%)($P<0.05$)。与治疗前相比,两组患者治疗后血清 IL-4、hs-CRP、Ang-2 水平均明显降低,PEF、FEV1 水平明显升高($P<0.05$);与对照组相比,观察组血清 IL-4、hs-CRP、Ang-2 水平明显较低,PEF、FEV1 水平明显较高($P<0.05$)。治疗后,与对照组比较,观察组 $CD3^+$ 、 $CD4^+$ 水平显著升高, $CD8^+$ 水平及 $CD4^+/CD8^+$ 比值显著降低($P<0.05$)。**结论:** 泛福舒胶囊联合参麦注射液治疗儿童支气管哮喘可有效提高其临床疗效,改善其肺功能,可能与其显著降低患儿血清 IL-4、hs-CRP、Ang-2 水平有关。

关键词: 泛福舒胶囊;参麦注射液;支气管哮喘;白介素-4;超敏 C-反应蛋白;血管紧张素 2

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Clinical Efficacy of Bronchovaxom Capsule Unite Shenmai Injection in the Treatment of Children with Bronchial Asthma and Its Effect on the Serum Levels of IL-4, hs-CRP, Ang-2*

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ABSTRACT Objective: To study the clinical efficacy of bronchovaxom capsule unite Shenmai Injection in the treatment of children with bronchial asthma and its effect on the serum levels of IL-4, hs-CRP, Ang-2. **Methods:** 120 cases of children with bronchial asthma who were treated from March 2015 to March 2015 were selected as research objects and divided into the observation group and the control group according to different treatment. The control group was given conventional treatment, while the observation group was treated with bronchovaxom capsule combined with Shenmai injection, both groups of children were treated for three courses. After treatment, the clinical efficacy, changes of PEF, FEV1, T lymphocytic subgroup, serum IL-4, hs-CRP, and Ang-2 before and after treatment were compared between two groups. **Results:** After treatment, the total effective rate of observation group (91.7%) was significantly higher than that of the control group (73.3%) ($P<0.05$), the serum IL-4, hs-CRP, and Ang-2 levels of both groups were significantly decreased than those before treatment, while the PEF and FEV1 were obviously elevated ($P<0.05$). Compared with the control group, the serum IL-4, hs-CRP, and Ang-2 levels were significantly lower in the observation group, and the levels of PEF and FEV1 were significantly higher($P<0.05$). After treatment, the $CD3^+$, $CD4^+$ levels of observation group were significantly higher than those of the control group, whereas the $CD8^+$ level and $CD4^+/CD8^+$ ratio were significantly decreased ($P<0.05$). **Conclusion:** Bronchovaxom capsule combined with shenmai injection could effectively enhance the clinical curative effect, improve the pulmonary function in the treatment of children with bronchial asthma, which might be related to the reduce of serum IL - 4, hs CRP, Ang - 2 levels.

Key words: Bronchovaxom capsule; Shenmai injection; Bronchial asthma; Interleukin 4; Hypersensitive c-reactive protein; Angiotensin 2

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前言

支气管哮喘的临床特征主要以气道阻塞、气道炎症、气道高反应性为主,主要表现为胸闷、咳嗽、气喘等症状,严重者极

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有可能威胁患儿的生命^[1,2]。有关文献显示^[3]炎症因子水平的增加和免疫功能紊乱在支气管哮喘的发生发展中具有重要作用。临床上通常会使用糖皮质激素作为主要药物治疗支气管哮喘,但效果不尽如人意,对改善患儿免疫水平的效果较差,从而使病情反复发作。

近年来,随着对免疫失衡在支气管哮喘发生、发展中作用研究的不断深入,人们发现免疫调节剂治疗支气管哮喘具有重要作用^[4]。泛福舒胶囊为一种糖蛋白剂型的免疫调节剂^[5],多应用于急性呼吸道感染的治疗,疗效显著,但其在儿童支气管哮喘治疗的应用较少。参麦注射液为中药免疫调节剂,内含红参、麦冬,可有效提高人体免疫机能,抑制炎症反应,有效预防及治疗支气管哮喘^[6]。因此,本研究主要探讨了泛福舒胶囊联合参麦注射液治疗儿童支气管哮喘的临床疗效及其可能机制,旨在为儿童支气管哮喘的临床治疗提供更多的参考依据,

现报道如下。

1 资料与方法

1.1 一般资料

选择 2015 年 3 月至 2017 年 3 月我院收治的 120 例支气管哮喘患儿,纳入标准:(1)检测符合儿童支气管哮喘的诊断标准^[7];(2)患儿家属对本研究知情并同意。排除标准:(1)对本研究使用药物具有过敏史;(2)在 3 个月内使用过其他相关药物治疗;(3)伴有肝、肾、心功能异常;(4)伴有全身性感染的患儿。将入选患者根据治疗方案不同分为两组,观察组 60 例,其中男 35 例,女 15 例,最小者 5 岁,最大 12 岁,体重 18~30 kg;对照组 60 例,其中男 33 例,女 17 例,最小者 6 岁,最大 11 岁,体重 17.5~31 kg。两组患者性别、年龄等一般资料相比差异均无统计学意义($P>0.05$),具有可比性,详见表 1。

表 1 两组患者的一般临床资料比较

Table 1 Comparison of the general information between two groups

Items	Observe group(n=60)	Control group(n=60)
Sex(M/F)	35/15	33/17
Age(year)	7.75± 0.87	7.96± 0.82
Weight(kg)	25.79± 3.12	25.34± 3.19
HR(beat/min)	83.45± 9.12	81.64± 8.65
SBP(mmHg)	119.21± 13.43	118.43± 12.65
DBP(mmHg)	71.75± 7.43	72.32± 7.85

1.2 治疗方法

对照组采用常规治疗,即吸氧、支气管扩张剂、补液、抗感染治疗,同时使用布地奈德 1 mg(陕西康泰莱生物医药工程有限公司,10 mg,20150119)雾化吸入,1 天 2 次。观察组以对照组为基础治疗,口服泛福舒胶囊(安徽省皖北药业股份有限公司,3.5 mg/粒,20150237),1 天 2 次,1 次 3.5 mg,同时使用参麦注射液(吉林省薪侨药业有限公司,100 mL,2014120825)10~20 mL 与 250 mL 生理盐水混合静脉滴注,1 天 1 次。两组均连续治疗 3 周。

1.3 观察指标

检测比较两组治疗前后血清白介素-4(IL-4)、超敏 C-反应蛋白(hs-CRP)、血管紧张素 2(Ang-2)、PEF、FEV1、CD3⁺、CD4⁺、CD8⁺及 CD4⁺/CD8⁺水平的变化,治疗后临床疗效及不良反应的发生情况。

于治疗前后收集两组空腹静脉血 3 mL 待检,血清 IL-4、hs-CRP、Ang-2 水平采用酶联免疫吸附法检测;使用儿童肺功

能仪检测 PEF、FEV1 水平;采用流式细胞仪检测 CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺。

疗效评价标准^[8]:(1)显效:临床症状显著改善,FEV1 增加幅度在 35%及以上;(2)有效:临床症状有所改善,FEV1 增加幅度范围在 15%~24%之间;(3)无效:临床症状及相关指标均无明显改善。

1.4 统计学分析

本研究数据统计采用 spss18.0 进行,计量资料比较采用 t 检验,计数资料比较采用 χ^2 检验,当 $P<0.05$ 时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,观察组的总有效率为 91.7%,显著高于对照组(73.3%),差异具有统计学意义($P<0.05$),详见表 2。

表 2 两组患儿临床疗效的比较[例(%)]

Table 2 Comparison of the clinical efficacy between two groups[n (%)]

Groups	n	Excellent	Progress	Invalid	Total effective rate
Observation group	60	31(51.7)	24(40.0)	5(8.3)	55(91.7) ^a
Control group	60	23(38.3)	21(35.0)	16(26.7)	44(73.3)

Note: Compared with control group, ^a $P<0.05$.

2.2 两组治疗前后肺功能的比较

治疗前, 两组 PEF、FEV1 水平比较差异均无统计学意义(P>0.05); 经治疗后, 患儿的 PEF、FEV1 水平均较治疗前显著提

升(P<0.05), 且观察组 PEF、FEV1 水平均明显高于对照组(P<0.05), 详见表 3。

表 3 两组治疗前后肺功能的比较($\bar{x} \pm s$)

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

Groups	n	Time	PEF(L/s)	FEV1(L)
Observation group	62	Before treatment	2.41± 0.29	1.26± 0.15
		After treatment	3.44± 0.36 ^{ab}	1.63± 0.19 ^{ab}
Control group	62	Before treatment	2.43± 0.33	1.28± 0.17
		After treatment	3.05± 0.35 ^b	1.47± 0.21 ^b

Note: Compared with control group, ^aP<0.05; Compared with before, ^bP<0.05.

2.3 两组治疗前后血清 IL-4、hs-CRP、Ang-2 水平的比较

治疗前, 两组血清 IL-4、hs-CRP、Ang-2 水平比较差异均无统计学意义(P>0.05); 经治疗后, 两组患儿血清 IL-4、hs-CRP、

Ang-2 水平均较治疗前显著降低(P<0.05); 且观察组血清 IL-4、hs-CRP、Ang-2 水平明显低于对照组(P<0.05), 详见表 4。

表 4 两组治疗前后血清 IL-4、hs-CRP、Ang-2 水平的比较($\bar{x} \pm s$)

Table 4 Comparison of the serum levels of IL-4, hs-CRP and Ang-2 levels between two groups before and after treatment($\bar{x} \pm s$)

Groups	n	Time	IL-4(ng/mL)	hs-CRP(mL/L)	Ang-2(pg/mL)
Observation group	62	Before treatment	52.28± 5.75	4.58± 0.52	142.86± 18.86
		After treatment	26.47± 2.97 ^{ab}	1.34± 0.17 ^{ab}	75.21± 7.32 ^{ab}
Control group	62	Before treatment	52.16± 6.04	4.62± 0.52	142.94± 18.12
		After treatment	17.85± 2.06 ^b	1.96± 2.04 ^b	102.34± 12.36 ^b

Note: Compared with control group, ^aP<0.05; Compared with before, ^bP<0.05.

2.4 T 两组治疗前后淋巴细胞亚群水平的比较

治疗前, 两组患儿 CD3⁺、CD4⁺、CD8⁺ 水平及 CD4⁺/CD8⁺ 比值比较差异均无统计学意义(P>0.05); 治疗后, 观察组患儿

CD3⁺、CD4⁺ 水平较对照组显著升高, CD8⁺ 水平及 CD4⁺/CD8⁺ 比值较对照组显著降低(P<0.05), 详见表 5。

表 5 两组治疗前后外周血 T 淋巴细胞亚群水平的比较($\bar{x} \pm s$)

Table 5 Comparison of T lymphocyte subgroups levels in the peripheral blood between the two groups before and after treatment($\bar{x} \pm s$)

Groups	n	Time	CD3 ⁺ (%)	CD4 ⁺ (%)	CD8 ⁺ (%)	CD4 ⁺ /CD8 ⁺
Observation group	62	Before treatment	58.18± 6.45	31.28± 3.97	30.23± 3.21	1.31± 0.17
		After treatment	64.21± 6.83 ^{ab}	36.84± 3.76 ^{ab}	26.12± 2.86 ^{ab}	1.76± 0.21 ^{ab}
Control group	62	Before treatment	58.16± 6.32	30.94± 3.32	30.12± 3.96	1.32± 0.17
		After treatment	59.15± 6.06	31.25± 3.27	30.42± 3.65	1.35± 0.18

Note: Compared with the control group, ^aP<0.05; Compared with before the operation, ^bP<0.05.

2.5 两组患儿不良反应发生情况的比较

治疗中, 两组均未发生严重的不良反应。

3 讨论

支气管哮喘为临床多见病, 特征以呼吸道高反应性为主, 好发于儿童, 发病率可达 3% 左右, 且近年来有上升趋势^[9,10]。研究表明^[11-13], 多种炎症因子以及细胞因子参与支气管哮喘的发生发展, 各种类型炎症因子的释放与不同气道炎症细胞的浸润是此疾病共同的病理学特征^[14]。

糖皮质激素是临床常用的抗炎反应药物, 可有效改善患者局部的炎症反应, 可通过减少微血管的渗漏达到改善气道阻塞

症状的目的^[15], 本研究结果显示: 患儿经常规治疗后其临床总有效率仅为 73% 左右, 且糖皮质激素无法改善患儿免疫功能, 并存在一定的不良反应, 患儿的 T 淋巴细胞水平并无明显改善。泛福舒胶囊由多种细菌溶解产物组成的一种免疫调节剂, 对 Th1/Th2 的失衡状态具有显著的改善效果, 利于支气管哮喘的治疗^[16]; 此外可通过诱导机体产生自主性的免疫应答, 发挥免疫保护、改善免疫机能的作用^[17]。据国外相关文献报道^[18,19], 细菌溶解产物可有效改善儿童支气管哮喘的免疫水平。参麦注射液中所含的人参麦冬可提高机体器官抗应激能力以及免疫功能^[20]。研究表明参麦注射液可通过调理 T 淋巴细胞增殖从而增加机体免疫功能^[21]。本研究结果显示患儿经泛福舒胶囊联合

参麦注射液治疗后总有效率显著提高。

在支气管哮喘发作时, Th1/Th2 比例出现失衡^[22]。IL-4 是 Th2 细胞产生的一种多效应细胞因子, 在支气管哮喘患者中其水平明显增高, 有关研究报道^[23]血清 IL-4 与血清中嗜酸粒细胞存在正比关系, 与气道高反应性等炎症反应有关; 此外, IL-4 可促进 IgE 的合成, 而 IgE 可影响机体免疫应答及变态反应^[24], 说明 IL-4 水平的升高可能是发生气道重塑的重要机制。患儿通过联合治疗后血清 IL-4 水平显著降低, 与国外相关文献结论一致^[25], 提示泛福舒胶囊与参麦注射液均可有效改善机体 Th1/Th2 失衡。对于支气管哮喘患者而言, 不仅存在局部的炎症, 同时伴随全身的炎症反应。hs-CRP 是一种典型的系统性炎症标准物, 在正常情况下呈低水平表达, 一旦机体出现急性炎症、创伤、肿瘤等情况时其水平会迅速增加^[26]。本结果显示: 患儿在联合治疗后其血清 hs-CRP 水平明显降低, 基本趋于正常水平, 同时 CD3⁺、CD4⁺ 水平显著升高, CD8⁺ 水平及 CD4⁺/CD8⁺ 比值显著降低, 说明泛福舒胶囊与参麦注射液可有效改善患者炎症反应。

Ang-2 是肾素-血管紧张素系统的主要活性物质, 可有效控制血压以及调节水盐代谢, 同时具有促进细胞增殖和局部组织纤维化的作用, 参与机体炎症相关疾病的发生发展^[27]。研究表明 Ang-2 在支气管哮喘患者中其血清水平显著升高^[28]; Kim M 等研究发现使用 Ang-2 拮抗剂可抑制哮喘气道重塑, 减低气管道高反应^[29]。本研究结果显示, 患儿治疗后血清 Ang-2 水平显著降低, 我们认为泛福舒胶囊与参麦注射液可能通过调节 Th1/Th2 平衡从而发挥其作用。

综上所述, 泛福舒胶囊联合参麦注射液治疗儿童支气管哮喘可有效提高其临床疗效, 改善其肺功能, 可能与其显著降低患儿血清 IL-4、hs-CRP、Ang-2 水平有关。

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