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黄芪注射液联合布地奈德治疗支气管哮喘急性发作期患者的疗效 及对免疫功能的影响*

梅玉霞 付伟 沈毅韵 刘小敏 庄承[△]

(上海中医药大学附属第七人民医院儿科 上海 200137)

摘要 目的:探讨黄芪注射液联合布地奈德治疗支气管哮喘急性发作期患者的疗效及对免疫功能的影响,为临床用药提供依据。**方法:**选取2016年2月至2017年2月在我院接受治疗的94例支气管哮喘急性发作期患者作为研究对象,根据治疗方式将患者分为布地奈德组(n=46)与联合组(n=48)。布地奈德组患者给予布地奈德经口吸入治疗,联合组患者在此基础上联用黄芪注射液治疗,两组均治疗2周。分别于治疗前和治疗2周后测量患者第一秒用力呼气容积占预计值百分比(FEV1%)和第一秒用力呼气容积占用力肺活量百分比(FEV1/FVC),测定患者血清白细胞介素-4(IL-4)、白细胞介素-6(IL-6)、白细胞介素-8(IL-8)、白细胞介素-17(IL-17)和肿瘤坏死因子- α (TNF- α)水平,并检测所有患者的CD3⁺、CD4⁺和CD8⁺,计算CD4⁺/CD8⁺。比较两组患者治疗2周后的疗效。**结果:**治疗2周后,两组患者FEV1%、FEV1/FVC均明显上升,且联合组的FEV1%、FEV1/FVC明显高于布地奈德组(P<0.05)。治疗2周后,两组患者IL-4、IL-6、IL-8、IL-17及TNF- α 水平均明显下降,且联合组的IL-4、IL-6、IL-8、IL-17及TNF- α 水平明显低于布地奈德组(P<0.05)。治疗2周后,两组患者的CD3⁺、CD4⁺以及CD4⁺/CD8⁺均明显上升,且联合组的CD3⁺、CD4⁺以及CD4⁺/CD8⁺明显高于布地奈德组(P<0.05)。联合组总有效率为95.83%,明显高于布地奈德组的82.61%(P<0.05)。**结论:**黄芪注射液联合布地奈德对支气管哮喘急性发作期患者疗效显著,能明显改善患者肺功能和炎症指标,并能明显提高患者免疫功能,值得在临床上推广应用。

关键词:黄芪注射液;布地奈德;支气管哮喘;急性发作期;免疫功能

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Curative Effect of Astragalus Injection Combined with Budesonide in Bronchial Asthma Patients During Acute Attack Stage and its Effect on Immune Function*

MEI Yu-xia, FU Wei, SHEN Yi-yun, LIU Xiao-min, ZHUANG Cheng[△]

(Department of Pediatrics, The Seventh People's Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, 200137, China)

ABSTRACT Objective: To investigate the clinical effect of astragalus injection combined with budesonide in acute attack of bronchial asthma and its effect on immune function, in order to provide the basis for clinical medication. **Methods:** 94 cases of bronchial asthma patients during acute attack stage who were treated in our hospital from February 2016 to February 2017 were selected as subjects, and they were divided into budesonide group (n=46) and combination group (n=48) according to the treatment they received. Budesonide group was treated with budesonide oral inhalation, combination group was treated with astragalus injection on this basis, and the two groups were given treatment for two weeks. Before treatment and 2 weeks after treatment, the percentage of forced expiratory volume in the first second in predicted value (FEV1%) and the percentage of forced expiratory volume in the first second in forced vital capacity (FEV1/FVC) of all the patients were detected, the levels of serum interleukin-4 (IL-4), interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-17 (IL-17) and tumor necrosis factor- α (TNF- α) in patients were detected, CD3⁺, CD4⁺ and CD8⁺ were detected in all patients, and CD4⁺/CD8⁺ were calculated. The curative effects of two groups were compared 2 weeks after treatment. **Results:** At 2 week after treatment, the FEV1%, FEV1/FVC of the two groups were both increased significantly, and the FEV1% and FEV1/FVC of the combination group were significantly higher than that in the budesonide group (P<0.05). At 2 weeks after treatment, the levels of IL-4, IL-6, IL-8, IL-17 and TNF- α in the two groups were both decreased significantly, and the levels of IL-4, IL-6, IL-8, IL-17 and TNF- α in the combination group were significantly lower than that in the budesonide group (P<0.05). At 2 week after treatment, the CD3⁺, CD4⁺ and CD4⁺/CD8⁺ in the two groups were both increased significantly, and the CD3⁺, CD4⁺ and CD4⁺/CD8⁺ in the combination group were sig-

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作者简介:梅玉霞(1975-),女,本科,主治医师,从事儿童呼吸内科方面的研究,E-mail:kgtssg@163.com

[△] 通讯作者:庄承(1967-),男,本科,副主任医师,从事儿内科方面的研究,E-mail:otthfg@163.com

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nificantly higher than that in the budesonide group ($P < 0.05$). The total effective rate of combination group was 95.83%, which was significantly higher than 82.61% of budesonide group ($P < 0.05$). **Conclusion:** Astragalus injection combined with budesonide has a significant curative effect on bronchial asthma patients during acute attack stage, it can significantly improve the patient's lung function and inflammatory indicators, and can significantly improve the immune function of patients, which is worthy of clinical application.

Key words: Astragalus injection; Budesonide; Bronchial asthma; Acute attack stage; Immune function

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前言

支气管哮喘是一种病情反复发作、疾病周期长的慢性呼吸道类疾病,根据病情可将其分为缓解期和急性发作期^[1,2]。患者处于支气管哮喘急性发作期时,呼吸困难、气促、剧烈咳嗽、胸闷等症状突然出现,同时患者机体多项功能紊乱,使其身体、心理受到严重影响,若抢救不及时,可能导致呼吸衰竭、肺不张、酸中毒等疾病的发生,甚至导致患者死亡^[3-5]。快速缓解患者临床症状是治疗急性发作期支气管哮喘的主要目的,布地奈德作为一种高效糖皮质激素,能有效地缓解患者临床症状,控制支气管哮喘的进一步发展,但长期使用治疗时效果降低,且不良反应较多^[6-8]。随着临床上对支气管哮喘认识的深入,患者机体的T细胞亚群失衡也越来越受到重视^[9]。黄芪注射液因其具有良好的免疫调节功能,对免疫功能紊乱治疗效果较好而逐渐开始被用于支气管哮喘的治疗中^[10]。本研究对急性发作期的支气管哮喘患者采用黄芪注射液联合布地奈德吸入治疗,观察其疗效和对患者免疫功能的影响,以期临床用药提供依据,现做如下报告。

1 资料与方法

1.1 一般资料

选取2016年2月至2017年2月在我院接受治疗的94例支气管哮喘急性发作期患者作为研究对象,纳入标准:①所有病例均符合2008年中华医学会儿科学会呼吸学组所制定的《儿童支气管哮喘诊断和防治指南》中的标准^[11];②就诊时患者均伴不同程度的咳嗽、气促、呼吸困难、胸闷等急性发作期症状;③肺部听诊存在弥散性或散在哮鸣音。排除标准:①严重心、肝、肾功能损害者;②合并严重肺部感染和其它肺部疾病者;③近一个月内接受过糖皮质激素治疗的患者。根据治疗方式将患者分为布地奈德组与联合组。布地奈德组患者46例,其中男28例,女18例,年龄3~14岁,平均(8.78±3.42)岁,病程6个月~7年,平均(4.32±1.77)年,轻度8例,中度29例,重度9例;联合组患者48例,其中男30例,女18例,年龄3~13岁,平均(8.62±3.13)岁,病程8个月~6年,平均(4.59±1.04)年,轻度9例,中度31例,重度8例。两组一般资料间比较无统计学差异($P > 0.05$)。所有患者对本研究知情同意,且本研究经医院伦理委员会批准进行。

1.2 治疗方法

所有患者均给予抗过敏、抗感染、止咳平喘、吸氧等常规治疗,并保持患者呼吸道畅通。布地奈德组患者给予布地奈德(AstraZeneca AB,批号:20151123,规格:1 mg/支)1 mg/次加入2 mL生理盐水稀释后置入空气压缩泵经口吸入治疗,2次

/d,0.3 mg/次。联合组患者采用黄芪注射液联合布地奈德进行治疗,其中布地奈德用法用量与布地奈德组相同,在此基础上将30 mL黄芪注射液(正大青春宝药业有限公司,国药准字Z33020179,规格:10 mL/支)0.5~1.0 mL/kg(最大剂量30 mL)加入100 mL~250 mL生理盐水中静脉滴注,1次/d。两组患者治疗时间均为2周。

1.3 观察指标

分别于治疗前和治疗2周后采用日本福田ST-150型肺功能仪测量患者第一秒用力呼气容积占预计值百分比(FEV1%)和第一秒用力呼气容积占用力肺活量百分比(FEV1/FVC)。分别于治疗前和治疗2周后清晨采集患者空腹状态下静脉血3 mL,分离血清(2000 r/min,离心15 min)后在-70℃下冻存待用;采用酶联免疫法测定患者血清白细胞介素-4(IL-4)、白细胞介素-6(IL-6)、白细胞介素-8(IL-8)、白细胞介素-17(IL-17)和肿瘤坏死因子- α (TNF- α)水平,试剂盒购自上海酶联生物科技有限公司,严格按照说明书进行操作。采用流式细胞仪通过荧光标记法分别于治疗前和治疗2周后检测所有患者的外周血T细胞亚群,包括CD3⁺、CD4⁺和CD8⁺,并计算CD4⁺/CD8⁺。治疗2周后比较两组患者的治疗效果。

1.4 疗效评价标准^[12]

根据《支气管哮喘防治指南》,疗效评价分为四个等级:①无效:患者FEV1%测定结果以及患者临床症状均无明显改善,甚至加重;②有效:患者FEV1%测定结果得到15~24%的增加,临床症状有所减轻;③显效:患者治疗后的FEV1%得到25~35%的增加,且其值在60~79%之间,同时患者症状明显改善;④临床控制:患者治疗后的FEV1%达到80%或增加超过35%,同时临床症状完全缓解,无需继续进行药物治疗。总有效=有效+显效+临床控制。

1.5 统计学方法

本研究所有数据均采用SPSS17.0软件处理分析,其中计数资料以(%)表示,采用 χ^2 检验,计量资料以($\bar{x} \pm s$)表示,采用双侧t检验。检验标准为 $\alpha = 0.05$ 。

2 结果

2.1 两组患者FEV1%、FEV1/FVC比较

两组患者治疗前的FEV1%、FEV1/FVC比较均无统计学差异($P > 0.05$)。治疗2周后,两组患者FEV1%、FEV1/FVC均明显上升,且联合组的FEV1%、FEV1/FVC均明显高于布地奈德组($P < 0.05$)。见表1。

2.2 两组患者炎症因子水平比较

两组患者治疗前的IL-4、IL-6、IL-8、IL-17及TNF- α 水平比较均无统计学差异($P > 0.05$)。治疗2周后,两组患者IL-4、IL-6、

IL-8、IL-17 及 TNF-α 水平均明显下降,且联合组的 IL-4、IL-6、 表 2。

IL-8、IL-17 及 TNF-α 水平均明显低于布地奈德组(P<0.05)。见

表 1 两组患者 FEV1%、FEV1/FVC 比较($\bar{x} \pm s$)

Table 1 Comparison of FEV1% and FEV1/FVC of patients in two groups ($\bar{x} \pm s$)

Groups	FEV1%		FEV1/FVC(%)	
	Before treatment	2 weeks aftertreatment	Before treatment	2 weeks aftertreatment
Budesonide group(n=46)	52.67± 6.68	69.87± 8.45*	55.79± 5.74	71.34± 7.54*
Combined group(n=48)	52.18± 7.03	81.89± 9.23*	56.21± 6.11	79.85± 8.09*
t	0.346	6.577	0.343	4.651
P	0.730	0.000	0.732	0.000

Note: compared with before treatment, *P<0.05.

表 2 两组患者炎症因子水平比较($\bar{x} \pm s$, pg/mL)

Table 2 Comparison of the levels of inflammatory factors in the two groups($\bar{x} \pm s$, pg/mL)

Groups	Time	IL-4	IL-6	IL-8	IL-17	TNF-α
Budesonide group (n=46)	Before treatment	216.49± 45.92	130.74± 16.32	0.72± 0.13	22.37± 3.12	236.31± 56.32
	2 weeks aftertreatment	137.36± 29.78 [#]	107.21± 17.64 [#]	0.58± 0.11 [#]	18.92± 3.35 [#]	168.45± 37.91 [#]
Combined group (n=48)	Before treatment	219.74± 43.67	128.95± 16.83	0.70± 0.11	22.63± 3.56	234.53± 58.67
	2 weeks aftertreatment	111.32± 26.69 ^{**}	89.63± 14.59 ^{**}	0.29± 0.04 ^{**}	14.31± 2.04 ^{**}	132.82± 34.78 ^{**}

Note: compared with budesonide group, *P<0.05, compared with before treatment, [#]P<0.05.

2.3 两组患者外周血 T 细胞亚群检测结果比较

两组患者治疗前的 CD3⁺、CD4⁺、CD8⁺ 以及 CD4⁺/CD8⁺ 比较差异均无统计学意义 (P>0.05)。治疗 2 周后, 两组患者的

CD3⁺、CD4⁺ 以及 CD4⁺/CD8⁺ 均明显上升, 且联合组的 CD3⁺、CD4⁺ 以及 CD4⁺/CD8⁺ 均明显高于布地奈德组(P<0.05)。两组患者治疗前后的 CD8⁺ 无明显变化(P>0.05)。见表 3。

表 3 两组患者外周血 T 细胞亚群检测结果比较($\bar{x} \pm s$)

Table 3 Comparison of detection results of T lymphocyte subsets in peripheral blood of patients in two groups ($\bar{x} \pm s$)

Groups	Time	CD3 ⁺ (%)	CD4 ⁺ (%)	CD8 ⁺ (%)	CD4 ⁺ /CD8 ⁺
Budesonide group (n=46)	Before treatment	53.23± 7.41	31.68± 4.32	28.58± 5.98	1.09± 0.31
	2 weeks aftertreatment	59.02± 6.92 [#]	36.93± 3.72 [#]	27.49± 6.12	1.41± 0.37 [#]
Combined group (n=48)	Before treatment	52.98± 7.09	32.09± 4.51	27.87± 6.31	1.11± 0.33
	2 weeks aftertreatment	63.96± 5.87 ^{**}	41.81± 3.69 ^{**}	27.36± 6.10	1.63± 0.41 ^{**}

Note: compared with budesonide group, *P<0.05, compared with before treatment, [#]P<0.05.

2.4 两组患者临床疗效比较

布地奈德组临床控制 11 例, 显效 14 例, 有效 13 例, 无效 8 例, 总有效率为 82.61%(38/46)。联合组临床控制 16 例, 显效 17 例, 有效 13 例, 无效 2 例, 总有效率为 95.83%(46/48)。联合组总有效率明显高于布地奈德组($\chi^2=4.321, P=0.038$)。

3 讨论

支气管哮喘是儿科呼吸系统最常见疾病之一, 由于近年来空气质量下降、空气污染加重, 其发病率呈现出逐年上升的趋势^[13,14]。支气管哮喘被定义为一种由多种炎症细胞参与的慢性气道炎症性疾病, 西医认为上皮细胞等结构细胞和炎性细胞所释放的趋化因子以及细胞因子所导致的机体内细胞因子网络调控失衡被认为是支气管哮喘反复发作的主要原因, 因此支气

管哮喘治疗的核心环节是控制气道炎症^[15,16]。布地奈德作为一种高效的糖皮质激素, 已被广泛应用于支气管哮喘的治疗中, 其可有效减轻患者气道炎性反应、修复气道。但也有研究认为^[17,18], 布地奈德虽然起效快, 但支气管哮喘患者的整体症状并未得到真正的改善。中医认为痰是支气管哮喘发病的潜在 " 夙根 ", 其因人体津液不归正化凝聚而成, 于肺中伏藏可导致支气管哮喘的反复发作^[19], 因此, 在治疗支气管哮喘的过程中, 恢复患者的肺功能和调节免疫功能具有重要意义。有报道表明^[20], 黄芪注射液能有效改善患者肺功能, 同时能纠正机体免疫系统紊乱。

本研究中联合组患者采用黄芪注射液联合布地奈德进行治疗, 治疗 2 周后肺功能指标 FEV1%和 FEV1/FVC 明显上升, 炎性因子 IL-4、IL-6、IL-8、IL-17 及 TNF-α 水平均明显下降, 同时联合组的上述指标均优于布地奈德组。提示联合组患者肺功

能恢复更为明显,且抗炎效果更好。推测其原因为布地奈德对参与支气管哮喘患者气道炎症反应的多种细胞有抑制作用,包括抑制嗜酸性粒细胞的趋化与活化、抑制细胞因子在免疫活性细胞中的合成等,同时布地奈德可直接与气道内的激素受体相结合,减少腺体分泌,从而快速减轻患者气道炎症反应,并对气道有一定的修复作用^[21-23];而黄芪注射液中含有黄芪多糖、皂苷、黄酮、生物碱等多种成分,能有效改善患者血流动力学并可促进患者痰液排出,舒张气管,同时具有利尿消肿的功能,对支气管粘膜的炎性水肿有明显的改善效果,从而有利于患者气道炎症反应的减轻^[24-26]。同时本研究对两组患者外周血 T 细胞亚群的检测结果显示,治疗 2 周后,两组患者的 CD3⁺、CD4⁺ 以及 CD4⁺/CD8⁺ 均明显上升,且联合组的 CD3⁺、CD4⁺ 以及 CD4⁺/CD8⁺ 均明显高于布地奈德组,提示黄芪注射液联合布地奈德对患者免疫功能恢复效果更好。推测与黄芪注射液对淋巴细胞的增殖的促进作用有关,其能促进 T 淋巴细胞的转换,促进抗体形成,从而纠正 T 细胞亚群的紊乱状态,并能对网状内皮系统的吞噬功能有加强的效果,从而刺激机体免疫功能的恢复^[27-29]。同时黄芪注射液中还含有多种可提高机体免疫功能的微量元素,但其作用机制尚需进一步的研究。本研究中联合组总有效率为 95.83%,明显高于布地奈德组的 82.61%,李蓉^[30]的研究中采用黄芪注射液联合布地奈德进行治疗的有效率高达 97.90%,与本研究结果基本一致,提示黄芪注射液联合布地奈德能有效改善支气管哮喘急性发作期患者的治疗效果。

综上所述,黄芪注射液联合布地奈德对支气管哮喘急性发作期患者疗效显著,能明显改善患者肺功能和炎症指标,并能明显提高患者免疫功能,值得在临床上推广应用。

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