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百蕊颗粒联合阿奇霉素及布地奈德雾化吸入治疗对咳嗽变异性哮喘患儿肺功能和炎症因子的影响*

李雯¹ 赵伟伟¹ 葛建敏² 吴俊峰¹ 董建芳¹ 石蔚³ 石花^{1Δ}

(1 张家口学院附属人民医院儿科 河北 张家口 075000; 2 张家口学院附属人民医院呼吸科 河北 张家口 075000;

3 河北北方学院附属第一医院儿科 河北 张家口 075061)

摘要 目的:探讨百蕊颗粒联合阿奇霉素及布地奈德雾化吸入治疗对咳嗽变异性哮喘(CVA)患儿肺功能和炎症因子的影响。**方法:**选取我院于2017年2月~2019年10月期间接收的CVA患儿97例,根据随机数字表法将患儿分为研究组(n=49)和对照组(n=48),对照组患儿予以阿奇霉素及布地奈德雾化吸入治疗,研究组在对照组的基础上联合百蕊颗粒治疗,记录两组患儿临床疗效、临床指标及不良反应发生情况,检测两组患儿炎症因子[白细胞介素-6(IL-6)、肿瘤坏死因子-α(TNF-α)、降钙素原(PCT)]水平及第1秒用力呼气容积(FEV1)、用力肺活量(FVC),计算FEV1/FVC。**结果:**研究组治疗8周后的临床总有效率为91.84%(45/49),高于对照组的75.00%(36/48)($P<0.05$)。两组不良反应发生率比较无差异($P>0.05$)。两组治疗8周后FEV1/FVC、FVC、FEV1均较治疗前升高,且研究组高于对照组($P<0.05$)。两组治疗8周后IL-6、TNF-α、PCT均下降,且研究组低于对照组($P<0.05$)。研究组咳嗽缓解时间、咳嗽消失时间均短于对照组($P<0.05$)。**结论:**百蕊颗粒联合阿奇霉素及布地奈德雾化吸入治疗CVA患儿疗效确切,可有效改善患儿肺功能及临床指标,降低炎症因子水平。

关键词:百蕊颗粒;阿奇霉素;布地奈德;咳嗽变异性哮喘;患儿;肺功能;炎症因子

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Effect of Baili Granule Combined with Azithromycin and Budesonide on Pulmonary Function and Inflammatory Factors in Children with Cough Variant Asthma*

LI Wen¹, ZHAO Wei-wei¹, GE Jian-min², WU Jun-feng¹, DONG Jian-fang¹, SHI Wei³, SHI Hua^{1Δ}

(1 Department of Pediatrics, People's Hospital Affiliated to Zhangjiakou University, Zhangjiakou, Hebei, 075000, China;

2 Department of Respiratory, People's Hospital Affiliated to Zhangjiakou University, Zhangjiakou, Hebei, 075000, China;

3 Department of Pediatrics, The First Affiliated Hospital of Hebei North University, Zhangjiakou, Hebei, 075061, China)

ABSTRACT Objective: To investigate the effect of Baili granule combined with azithromycin and budesonide on pulmonary function and inflammatory factors in children with cough variant asthma (CVA). **Methods:** 97 children with CVA who were treated in our hospital from February 2017 to October 2019 were selected, they were randomly divided into study group (n=49) and control group (n=48) according to the random number table method. Children in the control group were treated with azithromycin and budesonide atomization inhalation. The study group was treated with Baili granule on the basis of the control group, the curative effect, clinical indexes and adverse reactions of the two groups were recorded, the levels of inflammatory factors [Interleukin-6 (IL-6), tumor necrosis factor -α (TNF-α), procalcitonin (PCT)] and forced vital capacity (FVC) in the first second were measured and FEV1/FVC were calculated. **Results:** The total clinical effective rate of the study group was 91.84% (45/49), which was higher than 75.00% (36/48) of the control group ($P<0.05$). There was no difference in the incidence of adverse reactions between the two groups ($P>0.05$). FEV1/FVC, FVC and FEV1 in the two groups increased 8 weeks after treatment, and the study group were higher than those in the control group ($P<0.05$). The levels of IL-6, TNF-α and PCT in the study group were lower than those in the control group ($P<0.05$). The cough relief time and cough disappearance time in the study group were shorter than those in the control group ($P<0.05$). **Conclusion:** Baili granule combined with azithromycin and budesonide atomization inhalation is effective in the treatment of children with CVA, which can effectively improve the lung function and clinical indicators, and reduce the level of inflammatory factors.

Key words: Baisui granule; Azithromycin; Budesonide; Cough variant asthma; Children; Lung function; Inflammatory factors

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作者简介:李雯(1983-),女,本科,主治医师,研究方向:小儿呼吸系统疾病,E-mail: bobo63780330@163.com

Δ 通讯作者:石花(1976-),女,本科,副主任医师,研究方向:小儿支气管哮喘,E-mail: 15297329937@163.com

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前言

咳嗽变异性哮喘(CVA)是临床常见的慢性呼吸道疾病,该病发病率高,病情迁延不愈,随着病情的进展,可发展至典型哮喘,严重威胁患者生命健康^[1-3]。以往报道显示^[4],CVA在儿童中发病率较高,可达0.77%~5.0%。现临床针对CVA的治疗尚无统一方案,多以缓解支气管痉挛、控制气道炎症、降低气道高反应性等西药治疗为主^[5,6]。阿奇霉素及布地奈德雾化吸入治疗是治疗CVA的常用方案,但此类西药治疗存在普遍的不良反应较大、停药后易复发等不足,尚需优化治疗方案^[7,8]。百蕊颗粒是一种中成药,具有清热消炎、止咳化痰的功效,主要用于急、慢性咽喉炎等病症^[9,10]。本研究通过对我院收治的部分CVA患儿给予百蕊颗粒联合阿奇霉素及布地奈德雾化吸入治疗,疗效显著,整理报道如下。

1 资料与方法

1.1 一般资料

选取我院于2017年2月~2019年10月期间接收的CVA患儿97例,此研究已获取我院伦理学委员会批准进行。纳入标准:(1)诊断标准参考《咳嗽变异性哮喘的诊断与鉴别诊断》^[11];(2)患儿家属对本次研究知情同意;(3)患儿年龄5~14岁;(4)入院前1个月内未接受过其他治疗者;(5)完成随访者。排除标准:(1)对本次研究用药存在禁忌者;(2)精神异常、不能配合完成本次研究者;(3)未能遵从医嘱用药,中途退出治疗者;(4)因其他疾病引起的慢性咳嗽者;(5)合并心肝肾等重要脏器功能不全者。根据随机数字表法将患儿分为研究组(n=49)和对照组(n=48),其中对照组女22例,男26例,年龄5~13岁,平均(8.94±0.83)岁;病程1~13月,平均(7.28±1.16)月;体质指数13~19 kg/m²,平均(16.09±0.84)kg/m²。研究组男29例,女20例,年龄6~14岁,平均(8.71±0.72)岁;病程2~11月,平均(7.07±1.25)月;体质指数12~18 kg/m²,平均(15.95±0.73)kg/m²。两组基线资料比较无差异(P>0.05)。

1.2 方法

两组患儿入院后均给予抗炎、止咳、抗过敏等基础治疗,在

此基础上,对照组予以阿奇霉素(浙江华润三九众益制药有限公司,国药准字H20084458,规格:0.25 g)以及布地奈德(上海上药信谊药厂有限公司,国药准字H20010552,规格:200 μg)治疗,阿奇霉素剂量10 mg/kg·d,1次/d,口服,用药3 d停药4 d。布地奈德剂量1~2 mg/d,通过空气压缩泵进行雾化吸入治疗。研究组在对照组的基础上联合百蕊颗粒(安徽九华华源药业有限公司,国药准字Z20090694,规格:每1g相当于饮片2.4g)治疗,2.5 g/次,3次/d。两组疗程均为8周。

1.3 观察指标

(1)采用电子设备或门诊复查等方式随访3个月。记录两组患儿治疗8周后的临床总有效率。具体如下:总有效率=显效率+有效率,无效:咳嗽等临床症状未见改善甚至加重。有效:治疗后7 d内咳嗽等临床症状有所改善,但在治疗后1个月内症状可消失,随访期间未见复发迹象。显效:治疗后7 d内咳嗽等临床症状消失,且随访期间未见复发迹象^[12]。(2)记录两组咳嗽缓解时间和咳嗽消失时间。(3)记录两组治疗期间不良反应情况。(4)于治疗前、治疗8周后抽取两组患儿清晨空腹静脉血2 mL,经常规离心处理(离心半径16 cm,3800 r/min离心16 min),分离上清液,参考试剂盒(冷泉港生物科技股份有限公司)说明书,采用酶联免疫吸附法检测白细胞介素-6(IL-6)、肿瘤坏死因子-α(TNF-α)以及降钙素原(PCT)。(5)于治疗前、治疗8周后采用美国森迪斯公司生产的2600型肺功能仪检测两组患儿肺功能指标:第1秒用力呼气容积(FEV1)、用力肺活量(FVC),计算FEV1/FVC。

1.4 统计学方法

采用SPSS25.0进行数据分析,计数资料以率表示,行卡方检验,计量资料以均值±标准差的形式表示,行t检验。检验标准设置为α=0.05。

2 结果

2.1 临床疗效比较

研究组治疗8周后的临床总有效率为91.84%(45/49),高于对照组的75.00%(36/48)(P<0.05),详见表1。

表1 临床疗效比较例(%)

Table 1 Comparison of clinical effects n(%)

Groups	Markedly effective	Effective	Invalid	Total efficiency
Control group(n=48)	12(25.00)	24(50.00)	12(25.00)	36(75.00)
Study group(n=49)	18(36.73)	27(55.10)	4(8.16)	45(91.84)
χ^2				4.990
P				0.025

2.2 肺功能指标比较

两组治疗前FVC、FEV1/FVC、FEV1比较无差异(P>0.05);两组治疗8周后FEV1/FVC、FVC、FEV1均较治疗前升高,且研究组高于对照组(P<0.05),详见表2。

2.3 炎症因子指标比较

两组治疗前IL-6、PCT、TNF-α比较无差异(P>0.05);两组治疗8周后IL-6、PCT、TNF-α均下降,且研究组低于对照组

(P<0.05);详见表3。

2.4 临床指标比较

研究组咳嗽缓解时间、咳嗽消失时间均短于对照组(P<0.05);详见表4。

2.5 不良反应比较

对照组治疗期间出现头晕1例、恶心呕吐2例、心悸2例、肌肉痉挛1例,不良反应发生率为12.50%(6/48);研究组治疗

期间出现心悸 2 例、头晕 2 例、恶心呕吐 2 例、肌肉痉挛 1 例, 统计学差异($\chi^2=0.067, P=0.796$)。不良反应发生率为 14.29%(7/49);两组不良反应发生率比较无

表 2 肺功能指标比较($\bar{x} \pm s$)
Table 2 Comparison of lung function indexes($\bar{x} \pm s$)

Groups	FVC(L)		FEV1(L)		FEV1/FVC	
	Before treatment	8 weeks after treatment	Before treatment	8 weeks after treatment	Before treatment	8 weeks after treatment
Control group(n=48)	1.73± 0.41	2.07± 0.61*	1.56± 0.35	2.13± 0.38*	0.90± 0.13	1.03± 0.14*
Study group(n=49)	1.68± 0.47	2.39± 0.42*	1.51± 0.39	2.68± 0.36*	0.90± 0.15	1.12± 0.13*
t	0.558	3.015	0.636	7.319	0.000	3.282
P	0.578	0.003	0.526	0.000	1.000	0.001

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

表 3 炎症因子指标比较($\bar{x} \pm s$)
Table 3 Comparison of inflammatory factors($\bar{x} \pm s$)

Groups	IL-6($\mu\text{g/L}$)		TNF- α (pg/mL)		PCT(ng/mL)	
	Before treatment	8 weeks after treatment	Before treatment	8 weeks after treatment	Before treatment	8 weeks after treatment
Control group(n=48)	58.29± 7.47	21.83± 8.24*	21.13± 3.68	15.27± 3.01*	12.79± 2.24	7.51± 1.21*
Study group(n=49)	57.91± 6.52	15.32± 7.51*	20.94± 4.25	9.02± 2.29*	12.85± 2.16	4.36± 1.15*
t	0.267	4.068	0.235	11.524	0.134	13.144
P	0.790	0.000	0.815	0.000	0.893	0.000

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

表 4 临床指标比较($\bar{x} \pm s, d$)
Table 4 Comparison of clinical indicators($\bar{x} \pm s, d$)

Groups	Cough relief time	Disappearance time of cough
Control group(n=48)	4.86± 0.52	7.72± 0.47
Study group(n=49)	2.75± 0.63	4.31± 0.40
t	11.970	38.509
P	0.000	0.000

3 讨论

CVA 是一种气道持续性炎症反应,对外界刺激反应性高。现临床有关 CVA 的具体发病机制仍不够清楚,多数学者认可的是 CVA 是由多种炎性细胞共同参与的气道慢性变态反应性炎症^[13-15]。IL-6、TNF- α 、PCT 均是临床常见的反应炎症严重程度的指标,当上述指标水平升高可引起患儿气道的炎症反应,而当气道仅具备高反应性,却不发生狭窄、痉挛或轻微变化时,临床上可表现出持续咳嗽而未出现典型哮喘的喘息^[16-18]。现临床针对 CVA 患儿的治疗方案尚未完全统一,由于该病本质上与哮喘相同,故其基本治疗与哮喘治疗方案相似,均以糖皮质激素、支气管扩张剂、抗变态反应药物等为主^[19,20]。阿奇霉素是第 3 代大环内酯类抗生素,具有明显的抑制黏液分泌的作用,可减少支气管扩张、哮喘等患者的脓液^[21]。布地奈德是糖皮质激素类药,能抑制过敏性细胞对过敏介质的释放,改善毛细血管通透性,从而有效阻止 CVA 疾病进展^[22]。由于 CVA 发病机制

复杂,难以治愈,单纯的西药治疗无法彻底阻止患儿肺功能进行性的下降。百蕊颗粒主要组分为百蕊草,具有止咳化痰、清热消炎的功效^[23]。

本次研究结果显示,相比于阿奇霉素及布地奈德雾化吸入治疗 CVA 患儿,联合百蕊颗粒治疗的有效率更高,可进一步提高治疗效果。分析其原因,阿奇霉素的组织渗透性较高,经血液循环被传送至各感染部位,发挥较好的治疗效果^[24]。布地奈德可通过能抑制气道局部免疫球蛋白 E 的合成及减少免疫球蛋白 E 活性。此外,布地奈德通过雾化吸入治疗进入人体,可以使药物直接局部作用于气道,最大程度的发挥药效^[25]。百蕊颗粒的主要组分为百蕊草,而百蕊草所含的山柰酚有止咳、祛痰作用;百蕊草素、山柰酚及其 3-葡萄糖鼠李糖甙、琥珀酸在体外具广谱抗菌活性;D-甘露醇、琥珀酸有平喘作用^[26]。上述药物从不同的作用机制出发,发挥协同作用,共同促进疗效提升。IL-6 作为炎症因子的一种,可促进机体炎症反应扩大级联化;PCT 是诊断和评估感染性疾病的一种新型的炎症标记物。TNF- α 是促

炎因子的一种,在机体发生炎症反生中发挥启动因子的作用^[27]。既往研究已证实^[28],大部分 CVA 患儿都存在不同程度的肺功能损害, 本研究中两组患儿肺功能和炎症因子均有所改善,且百蕊颗粒联合阿奇霉素及布地奈德雾化吸入治疗者的改善效果更佳,这可能与百蕊颗粒具有以下几个药理特性有关:百蕊颗粒可以通过结合病毒核酸或者壳体蛋白,进而阻止病毒复制。百蕊颗粒被认为是广谱抗菌药,同时具有显著的抗炎作用;百蕊颗粒可以减少咳嗽的频率,提高气管的排痰能力,进而改善患儿肺功能^[29,30]。另两组不良反应发生率比较无差异,可见本研究联合治疗安全性较好,这可能是因为百蕊颗粒主要成分为中药类,符合中药类药物一贯的低毒副作用特性,安全可靠。

综上所述,百蕊颗粒联合阿奇霉素及布地奈德雾化吸入治疗 CVA 患儿,疗效显著,可有效改善患儿肺功能和炎症因子水平,且安全性较好。

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