

doi: 10.13241/j.cnki.pmb.2017.13.023

盐酸氨溴索雾化吸入联合阿奇霉素静滴对支气管哮喘小儿急性发作期血清 IL-10 及 INF- γ 水平的影响 *

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摘要 目的:探讨盐酸氨溴索雾化吸入联合阿奇霉素静滴对支气管哮喘小儿急性发作期血清 IL-10 及 INF- γ 水平的影响。**方法:**收集我院住院治疗的 100 例小儿支气管哮喘急性发作期患者,随机分为实验组和对照组,每组 50 例。对照组患者给予阿奇霉素 10 mg/kg + 5% 葡萄糖注射液 250 mL 静脉滴注,1 次/d。实验组则在对照组基础上给予盐酸氨溴索 3 mg/kg + 5 mL 生理盐水,使用超声雾化器雾化吸入,15 min/次,3 次/d。治疗均 5 d 为 1 个疗程,共治疗 2 个疗程。治疗后,对患者热退时间、咳嗽消失时间、肺部啰音消失时间、白介素 -10、干扰素 - γ 以及临床疗效进行检测并比较。**结果:**与治疗前相比,两组患者治疗后的血清 IL-10、INF- γ 水平均升高($P < 0.05$);与对照组相比,实验组患者 IL-10、INF- γ 较高,热退时间、咳嗽消失时间、啰音消失时间较短,临床总有效率较高($P < 0.05$)。两组患者治疗效果相比,实验组(100.0%)的治疗总有效率与对照组(96.0%)相比较,但差异无统计学意义($P > 0.05$)。**结论:**盐酸氨溴索雾化吸入联合阿奇霉素静滴能够提高支气管哮喘小儿急性发作期的临床效果,可能与其升高血清 IL-10 及 INF- γ 水平有关。

关键词:盐酸氨溴索;阿奇霉素;支气管哮喘;白介素 -10;干扰素 - γ

中图分类号:R725.6 **文献标识码:**A **文章编号:**1673-6273(2017)13-2491-04

Effect of Aerosol Inhalation of Ambroxol Hydrochloride Combined with Azithromycin on the Serum IL-10 and INF- γ Levels of Children with Acute Onset of Asthma*

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ABSTRACT Objective: To investigate the effect of aerosol inhalation of ambroxol hydrochloride combined with azithromycin on the serum IL-10 and INF- γ levels of children with acute onset of asthma. **Methods:** 100 cases of children with bronchial asthma in our hospital were selected and randomly divided into the experimental group and control group, with 50 cases in each group. The control group was given azithromycin 10 mg + 5% glucose 250 ml by intravenous drip, 1 time daily. The experimental group was given ambroxol hydrochloride 3 mg + 5 mL saline group on the basis of control group, using the ultrasonic nebulizer inhalation, 15 minutes per time, 3 times daily. A total of two courses of treatment with 5 days for each course has been provided. After treatment, the pyretolysis time, disappearance time of cough and pulmonary rales, serum IL-10, interferon gamma levels and clinical curative effect were detected and compared between two groups. **Results:** The serum IL-10 and INF- γ levels of both groups were increased after treatment than those before treatment($P < 0.05$); compared with the control group, the serum IL-10 and INF- γ levels in the experimental group were higher after treatment($P < 0.05$), the pyretolysis time, disappearance time of cough and pulmonary rales were shorter($P < 0.05$), the total clinical efficacy rate was higher ($P < 0.05$). **Conclusions:** Ambroxol hydrochloride combined with azithromycin atomization inhalation could enhance the clinical effect of acute attack of asthma in children, it might be correlated with the increase of serum IL-10 and INF- γ levels.

Key words: Ambroxol hydrochloride; Azithromycin; Asthma; IL-10; INF- γ

Chinese Library Classification(CLC): R725.6 **Document code:** A

Article ID: 1673-6273(2017)13-2491-04

前言

支气管哮喘(bronchial asthma)是小儿时期慢性呼吸系统疾病之一,是一种反复发作的痰鸣气喘疾病,并以此作为辩证和诊断治疗的依据^[1]。寒湿失调、接触异物、过食生冷咸酸是其发

病的外在诱发因素^[2]。现代医学认为^[3]支气管哮喘是由多种炎性细胞和细胞组分合成与释放,与受体结合后共同参与的气道慢性炎症性疾病,可以导致强烈持久的气道收缩、唾液分泌和血管通透性增高^[4,5],临床上主要表现为反复发作性的喘息、气促、咳嗽,常在夜间或清晨发作,而感染是支气管哮喘发作常见诱

* 基金项目:广东省自然科学基金项目(06021299)

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(收稿日期:2016-08-01 接受日期:2016-08-27)

因,目前临床对于支气管哮喘的治疗以激素、解痉药物、抗生素为主。盐酸氨溴索是一种粘液溶解剂,具有抗氧化作用,同时还可以有效减少粘液腺分泌,降低痰液粘度,促进肺表面活性物质分泌,使痰液易于咳出,从而增强激素、解痉药物、抗生素疗效^[6]。本实验观察盐酸氨溴索雾化吸入联合阿奇霉素静滴对支气管哮喘急性发作期患儿血清 IL-10 及 INF- γ 水平的影响,探讨盐酸氨溴索雾化吸入联合阿奇霉素静滴对小儿支气管哮喘急性发作期的治疗作用及其可能机制,现报道如下。

1 资料与方法

1.1 临床资料

收集 2015 年 1 月~2016 年 6 月于我院住院治疗的 100 例小儿感染诱发的支气管哮喘急性发作期患者,随机分为实验组和对照组,每组 50 例。实验组内患者平均年龄(8.32 ± 1.23)岁;对照组内患者平均年龄(7.35 ± 1.51)岁。所有患者均符合参照 2003 年中华医学会儿科学分会呼吸学组修订《儿童支气管哮喘防治常规试行》中有关小儿支气管哮喘的诊断标准。所有患者符合支气管哮喘的诊断标准,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;患者在实验前未接受过激素以及支气管舒张剂治疗,所有患者实验前未使用过实验相关药物,对实验药物无过敏,无其他先天性疾病,无肝肾功能不全等。两组患者一般资料具有可比性($P>0.05$)。

1.2 方法

1.2.1 治疗方法 两组患者入院后均给予相应的治疗措施。接受包括镇静、吸氧、抗感染、维持水、电解质以及酸碱平衡等基础治疗,对照组患者给予阿奇霉素(亚宝药业集团股份有限公司 国药准字 H20010554)10 mg/kg +5%葡萄糖注射液 250 mL 中静脉滴注,1 次/d。实验组则在对照组基础上给予盐酸氨溴

索(上海勃林格殷格翰药业 国药准字 J20080031)3 mg/kg+5 mL 生理盐水,使用超声雾化器雾化吸入,15 min/次,3 次/d。治疗均 5 d 为 1 个疗程,共治疗 2 个疗程。

1.2.2 热退时间、咳嗽消失时间、啰音消失时间检测 对两组患者治疗时的热退时间、咳嗽消失时间、啰音消失时间进行检测。

1.2.3 治疗前后白介素 -10(IL-10)水平检测 取所有患者治疗前后清晨空腹外周静脉血 2 mL,离心取血清,于 -80℃ 条件下保存待检,采用酶联免疫吸附法(ELISA),严格按照试剂盒说明书,对患者血清白介素 -10(IL-10)水平进行检测。

1.2.4 治疗前后干扰素 - γ (INF- γ)水平检测 取所有患者治疗前后清晨空腹外周静脉血 2 mL,离心取血清,于 -80℃ 条件下保存待检,采用酶联免疫吸附法(ELISA),严格按照试剂盒说明书,对患者血清干扰素 - γ (INF- γ)水平进行检测。

1.2.5 临床疗效评价 治疗后对患者的临床疗效进行评价:患者咳嗽、胸闷、喘息及肺部哮鸣音等症状均消失,偶尔发作但无需用药即可缓解缓解为临床控制;患者哮喘症状显著减轻,但发作时仍需要用药缓解为显效;患者哮喘症状均有一定程度改善,肺部哮鸣音减轻为有效;患者哮喘症状无明显改善,甚至加重为无效。计算患者的治疗总有效率。

1.3 统计学分析

采用 SPSS 19.0 统计软件进行分析。计量数据采用 t 检验,以均数 $\pm$ 标准差($\bar{x} \pm s$)表示;计数资料采用卡方检验,用%表示。以 $P<0.05$ 认为差异有统计学意义。

2 结果

2.1 两组患者热退时间、咳嗽消失时间、啰音消失时间比较

与对照组相比,实验组患者的热退时间、咳嗽消失时间以及啰音消失时间较短($P<0.05$),具体见表 1。

表 1 两组患者热退时间、咳嗽消失时间、啰音消失时间比较($d, \bar{x} \pm s$)

Table 1 Comparison of the pyretolysis time, disappearance time of cough and pulmonary rales between two groups ($d, \bar{x} \pm s$)

	Pyretolysis time	Disappearance time of cough	Disappearance time of cough pulmonary rales
Experimental group	$2.63 \pm 0.87^*$	$6.65 \pm 2.17^*$	$6.98 \pm 2.03^*$
Control group	4.31 ± 1.21	8.03 ± 2.41	9.07 ± 2.79

Note: Compared with the control group, $*P<0.05$.

2.2 两组患者治疗前后血清白介素 -10(IL-10)水平比较

治疗后,两组患者的血清白介素 -10(IL-10)水平与治疗前

相比均显著升高($P<0.05$),与对照组相比,实验组患者血清白介素 -10(IL-10)水平较高($P<0.05$),具体见表 2。

表 2 两组患者治疗前后血清 IL-10 水平比较($pg/mL, \bar{x} \pm s$)

Table 2 Comparison of the serum IL-10 level between two groups before and after treatment($pg/mL, \bar{x} \pm s$)

	Before treatment	After treatment	t	P
Experimental group	10.83 ± 2.01	18.62 ± 3.67	3.262	0.001
Control group	11.01 ± 3.24	14.51 ± 3.69	2.922	0.003
t	1.304	-	-	-
P	0.097	0.008	-	-

2.3 两组患者治疗前后血清干扰素 - γ (INF- γ)水平比较

治疗后,两组患者的血清干扰素 - γ (INF- γ)水平与治疗前相比均显著升高($P<0.05$),与对照组相比,实验组患者血清干扰素 - γ (INF- γ)水平较高($P<0.05$),具体见表 3。

2.4 两组患者临床效果比较

治疗后,两组患者治疗效果相比,实验组(100.0%)的治疗总有效率与对照组(96.0%)相比较,但差异无统计学意义($P>0.05$),具体见表 4。

表 3 两组患者治疗前后血清 INF- γ 水平比较(ng/L, $\bar{x} \pm s$)Table 3 Comparison of the serum INF- γ level between two groups before and after treatment(ng/L, $\bar{x} \pm s$)

	Before treatment	After treatment	t	P
Experimental group	47.26 $\pm$ 15.76	66.38 $\pm$ 18.89	2.735	0.004
Control group	46.21 $\pm$ 21.06	60.74 $\pm$ 18.07	2.921	0.003
t	1.423	3.263	-	-
P	0.083	0.001	-	-

表 4 两组患者临床疗效比较(% , $\bar{x} \pm s$)Table 4 Comparison of the clinical curative effect between two groups(% , $\bar{x} \pm s$)

	Clinical control	Excellent	Effective	Invalid	Total effective rate
Experimental group	22(44.0)	19(39.0)	9(18.0)	0(0)	50(100.0)*
Control group	19(38.0)	20(40.0)	9(18.0)	2(4.0)	48(96.0)

Note: Compared with the control group, *P<0.05.

3 讨论

据统计,目前世界范围内哮喘患者已达 3 亿,并且这一数字还在呈上升趋势^[7]。在我国,随着空气污染的加重,支气管哮喘的发病率日趋升高,支气管哮喘是小儿时期的常见肺系疾病,目前已经是一种全球性的儿科慢性疾病,我国儿童哮喘的患病率在 0.11%~2.03%,严重危害了小儿的身心健康^[8]。祖国医学目前公认小儿支气管哮喘的发病内因责之于“伏痰”,哮指声响,喘指气息,哮必兼喘,故统称哮喘^[9]。现代医学认为^[10,11]哮喘是一种慢性气道炎症性疾病,其发病机制繁杂,目前仍无法完全明确,其病因病机可以交互重叠,目前主要存在有气道炎症学说、气道神经调节机制、病毒感染学说、神经信号转导机制以及气道重构等多种学说。

阿奇霉素在临床治疗支气管哮喘的疗效已经得到认可,阿奇霉素属于第二代大环内酯类抗生素,可以通过细胞壁的直接吸收而到达各个感染部位,尤其是在支气管、肺内等部位药物浓度最高,对支气管哮喘具有较好的疗效^[12,13]。其独特的药代动力学,消除半衰期长,且胃肠耐受性好,组织渗透性高,肝脏损害小等优势,逐渐受到人们的重视。而近年来的研究显示,阿奇霉素除抗感染的作用外,治疗哮喘等气道炎症性疾病的效果也较好。其能够通过抑制炎症介质的释放,进而降低气道的高反应性,减轻气道水肿,发挥抗炎平喘的作用。盐酸氨溴索是一种黏液溶解药物,具有多种生物学效应,能对浆液以及黏液性液体的分泌产生调节作用,因此能够对粘稠的痰液加以稀释,同时加强气管纤毛的摆动,使分泌物易于排出体外,保持呼吸道通畅。同时氨溴索的抗氧化作用,能够抑制炎症介质释放,减少有害物质的产生,抑制肺泡上皮细胞受到损伤,减轻支气管水肿的严重程度^[14],改善患者的肺通气状态^[15]。氨溴索与抗生素合用会提高抗生素在肺组织的浓度。

哮喘患儿不仅存在通气功能的异常,血清中与炎症反应有关的指标也会发生变化,因此对于相关指标的检测是衡量临床治疗效果的重要标志。白细胞介素-10(interleukin-10, IL-10)由单核巨噬细胞和 T 细胞分泌,能对中性粒细胞和巨噬细胞分泌炎症细胞产生抑制,促进中性粒细胞凋亡,加强肺部炎症清除,拮抗过敏性炎症^[16,17]。同时,IL-10 能够抑制 Th1 型免疫应答,抑

制 Th1 细胞的增殖以及白细胞介素-2(IL-2)、干扰素- γ (Interferon- γ , IFN- γ)、粒细胞-巨噬细胞集落刺激因子(colony stimulating factor, CSF)等细胞因子的产生,使单核细胞提呈抗原能力下降,抑制自然杀伤细胞的活性,抑制反应性氮氧化物产生;还能够促进 B 细胞的增殖、分化与抗体的产生;具有增强细胞毒 T 细胞的发育的作用^[18]。已有研究表明^[19]哮喘的严重程度与 IL-10 水平呈负相关,其原因可能是哮喘患者的 IL-10 水平降低,不能对炎症反应产生抑制作用。INF- γ (Interferon- γ , IFN- γ)属于 Th1 型细胞因子,能够抑制 Th2 细胞分化,对 IgE 的生成产生抑制作用,对 Th1/Th2 免疫应答失衡具有重要意义。因此 INF- γ 水平的下降就会导致 IgE 的生成过多,导致哮喘发生^[20]。因此在支气管哮喘患者中,血清中的 IFN- γ 降低。

本研究结果显示:治疗后,两组患者的血清 IL-10 水平、IFN- γ 水平均升高,实验组患者的血清 IL-10 水平、IFN- γ 水平较高。这提示盐酸氨溴索雾化吸入联合阿奇霉素静滴可能通过调控血清 IL-10、IFN- γ 水平调控炎症和过敏反应,进而减轻哮喘的临床症状。

综上所述,盐酸氨溴索雾化吸入联合阿奇霉素静滴能够提高支气管哮喘小儿急性发作期的临床效果,可能与其升高血清 IL-10 及 INF- γ 水平有关。

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