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喜炎平注射液联合阿奇霉素序贯疗法对肺炎支气管肺炎患者血清 IL-33、IL-6 及 TNF- α 水平的影响 *

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摘要 目的:探讨喜炎平注射液联合阿奇霉素序贯疗法对肺炎支气管肺炎患者血清白介素-6(IL-6)、白介素-33(IL-33)、肿瘤坏死因子- α (TNF- α)水平的影响。**方法:**收集我院就诊或住院治疗的 840 例支气管肺炎患者,随机分为实验组和对照组,每组 420 例。对照组患者给予阿奇霉素治疗。实验组在对照组基础上给予喜炎平注射液治疗。观察并比较两组患者血清白介素-6(IL-6)、白介素-33(IL-33)、肿瘤坏死因子- α (TNF- α)水平以及临床疗效。**结果:**与治疗前相比,两组患者治疗后血清 IL-6、IL-33、TNF- α 水平均显著下降($P<0.05$);与对照组相比,实验组患者的血清 IL-6、IL-33、TNF- α 水平较低($P<0.05$),临床治疗有效率较高($P<0.05$)。**结论:**喜炎平注射液联合阿奇霉素序贯疗法能够提高肺炎支气管肺炎患者的临床疗效,可能与其降低患者血清 IL-33、IL-6 及 TNF- α 水平有关。

关键词:喜炎平注射液;阿奇霉素;序贯疗法;支气管肺炎

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Effect of Xiyanping Injection combined with Azithromycin Sequential Therapy on the Serum IL-33, IL-6 and TNF- α Levels in Patients with Bronchopneumonia*

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ABSTRACT Objective: To investigate the effect of Xiyanping injection combined with Azithromycin Sequential Therapy on the serum IL-33, IL-6 and TNF- α levels in patients with bronchopneumonia. **Methods:** 840 cases of bronchopneumonia in our hospital were selected and randomly divided into the experimental group and control group with 420 cases in each group. The control group was given azithromycin, while the experimental group was treated on the base of control group with Xiyanping. After treatment, the serum interleukin-6 (IL-6), interleukin-33 (IL-33), tumor necrosis factor- α (TNF- α) levels and clinical curative effect were detected and compared between two groups. **Results:** Compared with before treatment, the IL-6, IL-33, TNF- α levels of both groups were significantly decreased after treatment($P<0.05$). Compared with the control group, the serum IL-6, IL-33 levels of TNF- α levels of experimental group were obviously lower ($P<0.05$), the clinical effective rate was higher ($P<0.05$). **Conclusion:** Xiyanping injection combined with Azithromycin Sequential Therapy could effectively enhance the clinical curative effect of patients with bronchopneumonia, which might be related to the decrease of serum IL-33, IL-6 and TNF- α levels.

Key words: Xiyanping injection; Azithromycin; Sequential therapy; Bronchial pneumonia

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前言

支气管肺炎(bronchopneumonia)是炎症沿气管、支气管蔓延至肺泡,是小儿期最常见的肺炎类型。小儿由于气管、支气管的管腔较窄,纤毛摆动能力较差且黏液分泌较多,肺血管丰富,而肺泡数量较少,含气量较少,因此容易被黏液阻塞,易患支气管肺炎,造成呼吸困难。且一旦发生病情就较为严重,易于在肺部扩散、融合,严重时易损害小儿呼吸、循环等多系统的功能,并发心力衰竭、电解质紊乱等,严重时可能会导致患儿死亡,是小儿死亡的主要原因之一^[1-2]。临床上主要以发热、咳嗽、气急以

及肺部固定湿罗音为主要症候。目前,阿奇霉素治疗支气管肺炎的临床疗效较好,但长期使用存在副作用^[3]。喜炎平是穿心莲内酯磺化物,研究表明其对多种肺炎球菌造成的发热有较好的效果^[4]。抗生素序贯疗法是近年来提出的先静脉给药,病情稳定后改为口服的抗感染治疗方案^[5]。本实验采用序贯疗法,早期静脉滴注阿奇霉素迅速控制感染引起的发热,后改为口服,疗效较好且能避免长期使用的肝损害。本研究通过观察支气管肺炎患者血清 IL-33、IL-6 及 TNF- α 水平的变化,探讨喜炎平注射液联合阿奇霉素序贯疗法对肺炎支气管肺炎的治疗效果及其可能机制,现报道如下。

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1 资料与方法

1.1 临床资料

收集 2014 年 3 月~2015 年 3 月于我院就诊或住院治疗的 840 例支气管炎患者,随机分为实验组 and 对照组,每组 420 例。实验组内患者平均年龄(8.12 ± 1.01)岁;对照组内患者平均年龄(7.78 ± 1.13)岁。所有患者符合《实用儿科学》中关于支气管炎的诊断标准,所有患者年龄在 3~12 岁,所有患者状态良好,无其他肺部以及支气管疾病,无先天性疾病,患者无免疫系统疾病;患者无感染性疾病;患者在实验前未接受过激素以及支气管舒张剂治疗,实验前未使用过实验相关药物,对实验药物无过敏,由家长签署知情同意书同意进行实验。两组患者一般资料比较无明显差异($P < 0.05$)。

1.2 治疗方法

两组患者入院后均给予相应的治疗措施。接受包括吸氧、抗感染、维持水、电解质平衡等基础治疗,对照组患者给予阿奇霉素(东北制药集团沈阳第一制药有限公司国药准字 H20000426)10 mg/(kg·d)+5%葡萄糖溶液 250 mL 中静脉滴注,1 次/d,连续 5 d 后间歇 4 d 为 1 个疗程,治疗 1 个疗程,以后给予阿奇霉素颗粒(辉瑞制药有限公司国药准字 H10360167)口服 10 mg/(kg·d),1 次/d,连续 3 d 后间歇 4 d 为 1 个疗程,连续 2 个疗程;实验组则在对照组基础上给予喜炎平(国药准字 Z20026249 江西青峰药业有限公司)200mg+5%葡萄糖溶液 250 mL 中静脉滴注,1 次/d,连续 1 周。治疗期间根据患者情况及时调整药量。

1.3 血清 IL-6、IL-33、TNF- α 水平检测

取所有患者治疗前后外周静脉血 2 mL,离心取上清,于 -80℃ 条件下保存待检,采用双抗体夹心 ELISA 法,严格按照试剂盒说明书,检测患者血清白介素 -6(IL-6)、白介素 -33(IL-33)、肿瘤坏死因子 - α (TNF- α)水平。

1.4 临床疗效评价

治疗后对患者的临床疗效进行评价,患者治疗后临床症状和体征消失,血象正常,患者症状评分减少在 80%以上为痊愈;患者治疗后临床症状和体征明显改善,血象接近正常,症状评分减少超过 50%为显效;患者治疗后主要症状和体征以及血象结果有改善,症状评分减少超过 20%为有效;患者病情无改善,甚至加重,症状评分减少低于 20%为无效,对患者的治疗总有效率进行统计。

1.5 统计学分析

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

2 结果

2.1 两组患者治疗前后血清 IL-6 水平的比较

与治疗前相比,两组患者治疗后的血清 IL-6 水平均下降($P < 0.05$);与对照组相比,实验组患者的血清 IL-6 水平较低($P < 0.05$),见表 1。

2.2 两组患者治疗前后血清 IL-33 水平比较

治疗后,两组患者血清 IL-33 水平与治疗前相比均下降,

表 1 两组患者治疗前后血清 IL-6 水平比较(pg/mL, $\bar{x} \pm s$)

Table 1 Comparison of the serum IL-6 levels between two groups before and after treatment(pg/mL, $\bar{x} \pm s$)

Groups	Before treatment	After treatment
Experimental group	71.28 $\pm$ 7.22	10.15 $\pm$ 3.12**
Control group	69.01 $\pm$ 6.89	24.33 $\pm$ 2.99*

Note: Compared with before treatment, * $P < 0.05$; compared with the control group, ** $P < 0.05$.

差异具有统计学意义($P < 0.05$);与对照组相比,实验组患者血清 IL-33 水平较低,差异具有统计学意义($P < 0.05$),见表 2。

表 2 两组患者治疗前后血清 IL-33 水平比较(pg/mL, $\bar{x} \pm s$)

Table 2 Comparison of the serum IL-33level between two groups before and after treatment(pg/mL, $\bar{x} \pm s$)

Groups	Before treatment	After treatment
Experimental group	78.01 $\pm$ 5.12	7.03 $\pm$ 2.29**
Control group	81.15 $\pm$ 4.06	21.28 $\pm$ 2.01*

Note: Compared with before treatment, * $P < 0.05$; compared with the control group, ** $P < 0.05$.

2.3 两组患者治疗前后血清 TNF- α 水平比较

治疗后,两组患者的血清 TNF- α 水平与治疗前相比均下降($P < 0.05$);与对照组相比,实验组患者的血清 TNF- α 水平较低($P < 0.05$),见表 3。

表 3 两组患者治疗前后血清 TNF- α 水平比较(pg/mL, $\bar{x} \pm s$)

Table 3 Comparison of the serum TNF- α level between two groups before and after treatment(pg/mL, $\bar{x} \pm s$)

Groups	Before treatment	After treatment
Experimental group	51.23 $\pm$ 6.43	12.23 $\pm$ 3.53**
Control group	49.27 $\pm$ 7.87	23.48 $\pm$ 4.02*

Note: Compared with before treatment, * $P < 0.05$; compared with the control group, ** $P < 0.05$.

2.4 两组患者临床效果比较

治疗后,实验组的治疗总有效率与对照组相比比较高($P < 0.05$),见表 4。

3 讨论

支气管炎一年四季均可发病,尤多发于冬、春季。据统计,我国儿科住院患者中 25%~65%为肺炎患儿,小儿支气管炎的发病率及病死率为小儿疾病的第一位^[6]。本研究选用的喜炎平静脉注射具有较好的清热解毒功效^[7],联合采用序贯疗法治疗后,患者临床疗效有效提高。现代研究证实^[8,9]喜炎平对多种流感病毒、呼吸道合胞病毒均具有灭活作用;同时具有抗革兰氏阳性细菌具有杀菌和抑菌作用作用;此外,喜炎平的解热消炎作用,还能够舒张气管、支气管平滑肌,增强患者机体免疫功能,对于支气管肺炎就较好的治疗作用^[10]。

白介素 -6(IL-6)具有复杂生物学特性,是一种多细胞来源的细胞因子。研究证实 IL-6 水平的变化能够反应炎症反应的

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(% , $\bar{x} \pm s$)

Groups	Recovery	Excellence	Effective	Invalid	Total effective rate
Experimental group	217(51.67)	96(22.86)	88(20.95)	19(4.52)	401(95.48)*
Control group	147(35.0)	108(25.71)	104(24.76)	61(14.52)	359(85.48)

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

严重程度^[11]。IL-6 可介导 T 细胞的增殖,在正常情况下具有调节免疫应答的作用。在病理状态下,IL-6 分泌明显增加,水平过高会引起机体的病理损伤^[12]。有研究证实^[13]肺炎的咳嗽等症状可能与 IL-6 促进了炎症介质的释放有关。肿瘤坏死因子- α (TNF- α)是炎症早期突出的细胞因子,具有双重生生物学特性,一方面可以对机体产生抗病毒以及防护作用,另一方面能够介导机体的免疫损伤^[14]。低浓度的 TNF- α 发挥白细胞的旁分泌和自分泌作用,高浓度的 TNF- α 则产生内分泌作用,造成机体的免疫损伤,诱发炎症反应^[15-16]。有研究证实肺炎急性期感染可导致 TNF- α 水平上升。白介素-33(IL-33)是 IL-1 家族成员,在炎症以及自身免疫性疾病的过程中具有重要作用^[18]。IL-33 具有促炎作用,在 Ig E 的调节下,肥大细胞产生 IL-33,IL-33 又能激活肥大细胞,产生细胞因子,加重气道炎症^[19]。近年来的研究表明 IL-33 还可能介导炎症基因的表达,起到促炎作用^[20]。

提示本实验的治疗措施具有较好的抗炎作用,实验组患者的血清 IL-33 水平较对照组低,表明应用喜炎平注射液联合阿奇霉素序贯疗法的抗炎的效果优于单独使用阿奇霉素,治疗效果较好。本实验结果显示支气管肺炎患者经治疗后血清 IL-6、IL-33 及 TNF- α 水平下降,提示患者的感染情况好转,可能减轻其对免疫细胞的损害。

总之,喜炎平注射液联合阿奇霉素序贯疗法能够提高肺炎支气管肺炎患者的临床疗效,可能与其降低患者血清 IL-33、IL-6 及 TNF- α 水平有关。

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