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复方丹参注射液联合阿奇霉素治疗小儿喘息性支气管炎的效果及对炎性因子的影响*

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摘要 目的：探讨复方丹参注射液联合阿奇霉素治疗小儿喘息性支气管炎的效果及对炎性因子的影响。**方法**：选取 2015 年 6 月~2018 年 6 月我院收治的喘息性支气管炎患儿 300 例，采用随机数字表法将患儿分为两组，每组各 150 例。对照组在常规治疗的基础上给予阿奇霉素注射液治疗，观察组在对照组的基础上联合应用复方丹参注射液治疗。比较两组的临床治疗效果，临床症状缓解时间及住院时间，治疗前后两组血清白介素（Interleukin, IL）-6、IL-8 和肿瘤坏死因子 -α（Tumor necrosis factor-α, TNF-α）水平的变化情况及不良反应发生情况和复发率。**结果**：治疗后，观察组治疗总有效率显著高于对照组（93.33% VS.85.33%, $P<0.05$）；观察组喘息缓解时间、咳嗽缓解时间、哮鸣音消失时间、体温恢复时间及住院时间均显著短于对照组（$P<0.05$）；两组治疗后血清 IL-6、IL-8 和 TNF-α 水平均较治疗前显著下降，且观察组更低（$P<0.05$）；两组不良反应发生率比较差异无统计学意义（$P>0.05$），观察组的复发率显著低于对照组（$P<0.05$）。**结论**：复方丹参注射液联合阿奇霉素可快速缓解喘息性支气管炎患儿的临床症状、体征并缩短住院时间，提高临床治疗效果，且复发率低，安全性较高，这可能与其可显著降低患儿血清 IL-6、IL-8 和 TNF-α 水平有关。

关键词：复方丹参注射液；阿奇霉素；小儿；喘息性支气管炎；炎性因子

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Efficacy of Compound Danshen Injection Combined with Azithromycin in the treatment of Children with Asthmatic Dronchitis and Its Effect on the Inflammatory Factors*

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ABSTRACT Objective: To investigate the effeicacy of compound Danshen injection combined with Azithromycin in the treatment of children with asthmatic bronchitis and its effect on the inflammatory factors. **Methods:** 300 children with asthmatic bronchitis admitted to our hospital from June 2015 to June 2018 were randomly divided into two groups with 150 cases in each group. The control group was treated with Azithromycin injection on the basis of conventional treatment, and the observation group was treated with compound Danshen injection on the basis of the control group. The clinical treatment effect, relief time of clinical symptom and hospitalization time, and the changes of serum IL-6, IL-8 and TNF-α before and after treatment as well as the incidence and recurrence rate of adverse reactions were compared between the two groups. **Results:** After treatment, the total effective rate of observation group was significantly higher than that of the control group (93.33% vs. 85.33%, $P<0.05$). The time of wheezing remission, cough remission, asthma disappearance, temperature recovery and hospitalization in the observation group were significantly shorter than in the control group ($P<0.05$). The levels of serum IL-6, IL-8 and TNF-α in the two groups were significantly lower than those before treatment, and the observation group was lower ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$), and the recurrence rate in the observation group was significantly lower than that in the control group ($P<0.05$). **Conclusion:** Compound Danshen injection combined with Azithromycin can rapidly relieve the clinical symptoms and signs of children with asthmatic bronchitis and shorten the hospitalization time, improve the clinical treatment effect, with a low recurrence rate and high safty, which may be related to the significantly decrease of serum IL-6, IL-8 and TNF- levels.

Key words: Compound Danshen injection; Azithromycin; Children; Asthmatic bronchitis; Inflammatory factors

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前言

喘息性支气管炎是一种小儿常见的呼吸系统疾病,又称为哮喘性支气管炎,约占临床急性下呼吸道感染的1/3,常继发于上呼吸道感染之后,由病毒、细菌、支原体、衣原体等病原体混合感染所致[1-3],临床主要表现为咳嗽、喘息、发热等,且易反复发作[4,5]。研究显示小儿支气管相对较狭窄,支气管及周围组织尚未发育完全,且免疫功能较差,受到刺激后易引起支气管痉挛,粘液分泌增多,粘膜充血水肿,并存在气道高反应性,进而引发喘息症状,且长期的喘息性支气管炎反复发作不仅影响患儿的发育,甚至可能发展为哮喘,因气道受阻引发呼吸衰竭,进而诱发心力衰竭,严重影响患儿的健康和身心发育,早期识别并进行有效干预对患儿的治疗和预后具有重要意义[6-8]。

目前,临床对于喘息性支气管炎主要采用糖皮质激素进行抗炎治疗,但治疗周期较长,疗效不佳,且不良反应较多,依从性较差[9-11]。随着祖国传统医学的发展,中医中药在小儿呼吸系统疾病的治疗中得到了广泛的应用[12-14]。有研究显示[15]复方丹参注射液对喘息性支气管炎具有一定的保护作用。本研究在阿奇霉素治疗的基础上联合复方丹参注射液治疗小儿喘息性支气管炎,探讨了其临床治疗效果及可能机制。

1 资料与方法

1.1 一般资料

选取2015年6月~2018年6月我院收治的患儿300例,均为喘息性支气管炎。纳入标准:① 符合相关诊断标准;② 临床主要表现为刺激性干咳、喘息、肺部有哮鸣音,发热等;③ 胸部X线检查显示正常或支气管周围炎性病变,或肺部粗纹理增加;④ 年龄3~6岁;⑤ 患儿家属知情同意。排除标准:① 支气管狭窄、异物及肺门淋巴结核者;② 合并心、肝、肾等重要器官功能异常者;③ 合并免疫功能缺陷及先天性心脏病者;④ 入组前已服用抗哮喘药物、抗生素者。随机将患儿分为两组,对照组150例,男85例,女65例;年龄3~5岁,平均4.12± 1.03岁;病程1~6 d,平均3.45± 0.85 d。观察组150例,男83例,女67例;年龄3~6岁,平均4.52± 1.34岁;病程1~5 d,平均3.08± 0.73 d。两组一般资料比较差异均无统计学意义(P>0.05),具有可比性。

1.2 治疗方法

均给予吸氧、镇静、解痉平喘、祛痰止咳、补液、并保持呼吸道通畅等常规治疗。对照组在此基础上给予阿奇霉素注射液(江苏吴中医药集团有限公司苏州制药厂,国药准字H20020342)治疗,5~10 mg/kg加入50 mL 5 %葡萄糖溶液中筋脉滴注,1次/d,连续治疗7 d。观察组在对照组的基础上给予复方丹参注射液(辅仁药业集团河南同源制药,国药准字Z20073091)治疗,0.1~1 mL/kg·d,加入50 mL 10 %葡萄糖溶液中静脉滴注,持续治疗7 d。

1.3 观察指标

① 总有效率;② 临床症状缓解时间;③ 炎性因子相关指标,分别于治疗前后抽取两组的空腹静脉血2 mL,采用酶联免疫吸附法测定IL-6、IL-8和TNF-α水平,试剂盒购买于上海酶联生物科技有限公司,严格按照说明书操作;④ 不良反应及复发率。

1.4 临床疗效评定标准

显效:治疗48 h内喘息消失或者显著减轻,呼吸平稳,肺哮鸣音消失或显著减少;有效:治疗72 h内患儿的症状体征得到明显改善。无效:未达到以上标准。

1.5 统计学方法

数据采用SPSS16.0软件进行统计学分析,定性资料以%表示,组间比较行卡方检验,定量资料以($\bar{x}\pm s$)表示,组间比较行t检验,以P<0.05为差异有统计学意义。

2 结果

2.1 两组治疗总有效率的比较

治疗后,观察组总有效率为93.33%,显著高于对照组(85.33%,P<0.05),见表1。

表1 两组临床治疗效果的比较[例(%)]

Table 1 Comparison of the clinical therapeutic effect between the two groups[n(%)]

Groups	Cases	Excellent	Valid	Invalidity	Total effective rate
Control group	150	82(54.67)	46(30.67)	22(14.67)	128(85.33)
Observation group	150	119(79.33)	31(20.67)	10(6.67)	140(93.33)
x^2					5.037
P					0.025

2.2 两组临床症状缓解时间及住院时间的比较

观察组各临床症状缓解时间及住院时间均显著短于对照组(P<0.05),见表2。

表2 两组患儿的临床症状缓解时间及住院时间比较($\bar{x}\pm s$,d)

Table 2 Comparison of the ease time of clinical symptom and hospital stay between the two groups($\bar{x}\pm s$,d)

Groups	Cases	Ease time of wheeze	Ease time of cough	Extinction time of wheeze	Temperature recovery time	Hospital stays
Control group	150	3.97± 0.84	5.16± 1.23	5.67± 1.14	4.98± 1.23	7.33± 2.01
Observation group	150	3.05± 0.67	4.08± 0.95	4.12± 0.86	3.14± 0.76	6.14± 1.76
t	-	10.487	8.511	13.294	15.586	5.455
P	-	<0.001	<0.001	<0.001	<0.001	<0.001

2.3 两组治疗前后血清 IL-6、IL-8 和 TNF-α 水平的比较

治疗后，两组血清 IL-6、IL-8 和 TNF-α 水平均较治疗前显著下降，且观察组以上指标均显著低于对照组($P<0.05$)，见表3。

表 3 两组患儿治疗前后的血清 IL-6、IL-8 和 TNF-α 水平的比较($\bar{x}\pm s$，ng/L)

Table 3 Comparison the levels of serum inflammatory factor between two groups before and after treatment($\bar{x}\pm s$, ng/L)

Groups	IL-6		IL-8		TNF-α	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	371.54± 85.34	315.08± 56.37*	109.65± 28.64	88.79± 21.64*	522.68± 103.27	465.37± 91.25*
Observation group	375.21± 86.75	255.64± 35.69*	108.75± 27.31	70.34± 18.47*	531.08± 105.61	357.84± 81.54*
x^2	-0.369	-10.911	0.279	-7.942	-0.698	-10.762
P	0.712	＜0.001	0.780	＜0.001	0.487	＜0.001

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

2.4 两组不良反应的发生情况及复发情况的比较

对照组发生心悸 1 例，恶心 2 例，头晕 1 例，观察组发生心悸 1 例，恶心 1 例，两组不良反应的发生率比较无统计学差异($P>0.05$)。治疗 6 个月后，对照组复发 11 例，观察组复发 3 例，观察组的复发率显著低于对照组($P<0.05$)。

3 讨论

近年来，在多种因素的综合作用下，小儿喘息性支气管炎的发病率呈居高不下的态势[16]。小儿的支气管、气管相对比较狭窄，粘膜娇嫩，血管丰富，且缺乏弹力组织，支撑作用较差，又由于粘液分泌不足使得呼吸道较干燥，纤毛的运动能力较差使得清除能力不足，故而极易发生呼吸道感染，进而继发喘息性支气管炎[17-19]。该病好发于春秋季节，且以剧烈喘息为特点，起病急，进展快，迅速缓解患儿喘息等临床症状是治疗的关键[20,21]。西医主要以雾化吸入、静脉或口服激素、解痉药、化痰平喘药等治疗药物为主[22,23]。中医认为该病属于哮喘的范畴，治疗包括内服和外治，包括针灸、穴位注射、敷帖等[23]。复方丹参注射液由丹参和降香提取精制而成，具有通经活络、活血化瘀的功效[24]。有研究显示[25]复方丹参注射液可改善微循环，缓解喘息症状。因此，本研究主要探讨了复方丹参注射液联合阿奇霉素治疗小儿喘息性支气管炎的效果，结果显示复方丹参注射液联合阿奇霉素治疗的患儿的临床症状缓解时间显著短于对照组，临床治疗总有效率显著高于对照组，说明复方丹参注射液联合阿奇霉素可快速改善喘息性支气管炎患儿的临床症状并提高治疗效果。

研究表明炎性反应在喘息性支气管炎的发生和发展过程中具有重要作用，其病理表现为支气管粘膜充血水肿，纤毛上皮细胞脱落，并伴有大量中性粒细胞和淋巴细胞浸润[26,27]。TNF-α 是一种单核巨噬细胞分泌的炎性因子，与其他细胞因子共同维持机体内环境的稳定，并介导致病因子、感染、创伤以及免疫应答反应[28]。IL-6 在炎性反应过程中具有关键作用，可促进 B 细胞的增殖与分化，促使机体释放内源性致热源，加速炎性反应[29]。IL-8 出现在组织损伤的早期，可介导并趋化中性粒细胞浸润 [30]。本研究结果显示观察组患儿治疗后的血清 TNF-α、IL-6 和 IL-8 水平较治疗前显著降低，且显著低于对照组，说明复方丹参注射液联合阿奇霉素可显著改善喘息性支气管炎患儿的炎性因子水平。阿奇霉素是大环内酯类广谱抗生素，对革兰氏阳性菌及支原体等具有较强的抑制作用。复方丹参注射液可改善微循环，改变血流动力学，提高动脉氧分压，扩张血管，减轻支气管组织的水肿与损伤，加快肺泡内炎性因子的渗出，进而起到抗炎作用。两者联合应用对患儿炎性水平的控制效果更佳[30]。复方丹参注射液有效成为主要为丹参酮、丹参素和儿茶酚胺等，不仅具有较好的抗炎作用，还能够解除痉挛，从而迅速改善临床症状，提高治疗效果。在安全性方面，阿奇霉素联合应用复方丹参注射液不会增加患儿不良反应的发生率，安全性较高。

综上所述，复方丹参注射液联合阿奇霉素可快速缓解喘息性支气管炎患儿的临床症状、体征并缩短住院时间，提高临床治疗效果，且复发率低，安全性较高，这可能与其可显著降低患儿血清 IL-6、IL-8 和 TNF-α 水平有关。

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