

doi: 10.13241/j.cnki.pmb.2017.26.032

三种方案治疗小儿重症肺炎的临床效果及安全性比较

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摘要 目的:比较三种方案治疗小儿重症肺炎的临床效果及安全性。**方法:**选取我院于2012年1月~2016年1月收治的120例重症肺炎患儿,按照不同的治疗方法随机分为观察组1(多巴胺联合多巴酚丁胺)42例,观察组2(多巴胺联合酚妥拉明)40例及对照组38例。比较三组患者临床疗效及炎症因子水平的变化。**结果:**观察组1的总有效率为90.48%,观察组2的总有效率为87.5%,均显著高于对照组的总有效率(63.16%)。观察组(1、2)的肺啰音消失时间、咳嗽症状消失时间、呼吸困难改善时间、退热时间以及住院天数均显著短于对照组($p < 0.05$)。治疗后,三组患者的血清白介素6(IL-6)、白介素8(IL-8)、C反应蛋白(CRP)以及肿瘤坏死因子(TNF- α)的水平与治疗前相比均显著降低,差异均具有统计学意义($p < 0.05$),且观察组患者以上指标的水平均显著低于对照组($p < 0.05$)。**结论:**多巴胺联合多巴酚丁胺和多巴胺联合酚妥拉明治疗小儿重症肺炎的疗效和安全性相当,二者均明显优于常规治疗。

关键词:小儿重症肺炎;多巴胺;多巴酚丁胺;酚妥拉明;炎症因子

中图分类号:R563.1 **文献标识码:**A **文章编号:**1673-6273(2017)26-5141-04

Comparison of the Clinical Effect and Safety of Three Dosage Regimens in the Treatment of Children with Severe Pneumonia

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ABSTRACT Objective: To compare the clinical effect and safety of three different regimens treating children with severe pneumonia. **Methods:** 120 cases treated in our hospital from January, 2012 to January, 2016 were randomly divided into the observation group 1 (dopamine combined with dobutamine, 42 cases), observation group 2 (dopamine combined with phentolamine, 40 cases), control group (38 cases). The clinical effect and levels of inflammatory cytokine were compared between the three groups. **Results:** The total effective rate in the observation group 1 was 90.48% and that of observation group 2 was 87.5%, which were significantly higher than that of the control group (63.16%). The disappearance time of pulmonary rales, cough, dyspnea, pyretolysis and length of stay in the observation group (both 1, 2) were significantly shorter than those of the control group ($p < 0.05$). After therapy, the level of serum IL-6, IL-8, CRP and TNF- α in all the three groups were obviously decreased compared with those of before therapy ($p < 0.05$), and those of the observation group were significantly lower than the control group ($p < 0.05$). **Conclusion:** Dopamine combined with dobutamine as well as dopamine combined with phentolamine were both effective methods in treating children with severe pneumonia, which were significantly better than conventional therapy.

Key words: Severe pneumonia; Dopamine; Dobutamine; Phentolamine; Inflammatory cytokine

Chinese Library Classification(CLC): R563.1 **Document code:** A

Article ID: 1673-6273(2017)26-5141-04

前言

重症肺炎是一种严重的肺部感染疾病,在未得到救治或者错过了最佳救治期的情况下可累及全身多个重要脏器甚至导致患者死亡^[1]。研究表明肺炎在全球范围内是造成5岁以下儿童死亡的第一大疾病。2009年,联合国通过了全球消灭儿童肺炎联盟的提议,将每年11月12日定为“世界肺炎日”,以此督

促政府加强对肺炎的防治^[2]。随着疫苗接种范围的扩大以及卫生条件的改善,我国5岁以下儿童肺炎的诊治率较以往已有较大的改善,然而重症肺炎依然是第一位死亡原因。近年来,国内外多采用常规治疗结合对心脏保护及呼吸系统改善的正性肌力药物辅助治疗小儿重症肺炎。然而,不同方案的临床疗效和安全性以及作用机制的差异鲜有报道。因此,本研究选择我院近年来收治的小儿重症肺炎患者并给予三种不同的方案进行

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(收稿日期:2016-12-02 接受日期:2016-12-20)

治疗,比较其临床疗效、安全性以及作用机制,以期优化重症肺炎的治疗方案提供更多的理论依据。现报道如下:

1 资料与方法

1.1 一般资料

选择2012年1月~2016年1月120例重症肺炎患者,按照不同的治疗方法将其随机分为观察组1(多巴胺联合多巴酚丁胺)42例、观察组2(多巴胺联合酚妥拉明)40例及对照组38例。其中,观察组1包含男性22例,女性20例,平均年龄(1.8 ± 1.0)岁;观察组2包含男性21例,女性19例,平均年龄(2.0 ± 0.9)岁;对照组包含男性20例,女性18例,平均年龄(1.96 ± 0.53)岁。三组患者基线资料比较差异均无统计学意义($P > 0.05$),具有可比性。纳入标准:①符合2001年美国胸科协会(ATS)提出的重症肺炎诊断标准^[3];②年龄在1~5岁;③病例资料完整,与患儿家属签署知情同意书。排除标准:①合并先天性心脏病;②合并神经系统疾病,无法配合治疗;③合并免疫系统疾病,血液病;④过敏体质。

1.2 治疗方法

对照组患者予以吸氧、吸痰、抗感染、利尿、止咳平喘、维持水电解质平衡等常规治疗。在对照组基础上,观察组1加用多巴胺联合多巴酚丁胺治疗,多巴胺(广州白云山明兴制药有限公司,国药准字H44022388, $2 \mu\text{g}/(\text{kg} \cdot \text{min}^{-1})$),多巴酚丁胺(正安医药(四川)有限公司,国药准字H20040383, $2.5 \sim 5 \mu\text{g}/(\text{kg} \cdot \text{min}^{-1})$),加入5%葡萄糖溶液用静脉输液泵匀速泵入1次/天,3~5天为一个疗程。观察组2在对照组基础上加用多巴胺联合酚妥拉

明治疗,酚妥拉明(扬州制药有限公司,国药准字H20063706, $3 \sim 5 \mu\text{g}/(\text{kg} \cdot \text{min}^{-1})$)加入5%葡萄糖溶液用静脉输液泵匀速泵入,1次/天,3~5天为一个疗程。

1.3 疗效评价及观察指标

1.3.1 疗效评价 显效:治疗3~5d后,患者呼吸困难,肺部啰音,发热,咳嗽等临床症状明显减轻;有效:治疗3~5d后,患者呼吸困难,发热,咳嗽等临床症状有一定程度减轻,肺部啰音减少;无效:治疗3~5d后患者上述症状仍无改善。治疗总有效率为显效和有效的例数之和与总例数的比值。

1.3.2 检测指标 三组患者治疗前后血清C反应蛋白(CRP)、白介素-6(IL-6)、白介素-8(IL-8)以及肿瘤坏死因子- α (TNF- α)的水平采用免疫比浊法测定(西门子公司,德国)。

1.4 不良事件的发生情况

记录三组患者的不良反应的发生情况。

1.5 统计学分析

使用SPSS17.0软件,计数资料用卡方检验对比分析,多组间计量资料用单因素方差分析,两组间比较采用t检验,以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 三组患者的临床效果比较

对照组的总有效率为63.16%,显著低于观察组1(90.48%)和观察组2(87.5%)($P < 0.05$),观察组1的总有效率稍高于观察组2,但两组无统计学差异($P > 0.05$)。

表1 三组患者的临床疗效比较[例(%)]

Table 1 Comparison of the clinical effects between three groups [n(%)]

Groups	Number	Excellent	Valid	Invalid	Total effective rate
Control group	38	7	17	14	63.16%
Observation group 1	42	22	16	4	90.48%*
Observation group 2	40	23	12	4	87.5%*

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

2.2 三组患者临床症状改善时间的比较

观察组(1,2)的肺啰音消失时间、咳嗽症状消失时间、呼吸困难改善时间、退热时间以及住院天数均显著短于对照组($P <$

0.05),但观察组1和观察组2在上述症状改善方面与住院时间比较差异无明显统计学意义($P > 0.05$)。

表2 三组患者临床症状改善时间比较[$\bar{x} \pm s, \text{d}$]

Table 2 Comparison of the clinical symptoms improvement time between three groups [$\bar{x} \pm s, \text{d}$]

Groups	Number	Pulmonary rales,	Cough	Dyspnea	Pyretolysis	Length of stay
Control group	38	12.95 ± 1.46	8.83 ± 1.26	5.83 ± 1.01	6.47 ± 1.85	15.31 ± 1.72
Observation group 1	42	$7.03 \pm 0.75^*$	$5.31 \pm 1.52^*$	$4.02 \pm 0.43^*$	$4.08 \pm 0.71^*$	$10.03 \pm 2.36^*$
Observation group 2	40	$6.93 \pm 1.06^*$	$5.54 \pm 1.33^*$	$3.97 \pm 0.88^*$	$4.15 \pm 0.22^*$	$10.14 \pm 2.09^*$

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

2.3 三组患者治疗前后血清CRP、IL-6、IL-8、TNF- α 水平的比较

治疗前,三组患者血清IL-6、IL-8、CRP以及TNF- α 的水平

比较差异均无统计学意义,具有可比性。治疗后,三组患者的IL-6、IL-8、CRP以及TNF- α 的水平均较治疗前明显降低($p < 0.05$),且观察组患者血清炎性因子水平显著低于对照组($p <$

0.05)。除观察组 1 的 IL-6 水平明显低于观察组 2, 两组其余指标比较差异均无统计学意义($P>0.05$)。

表 3 三组患者治疗前后血清 CRP、IL-6、IL-8、TNF- α 水平的比较 [$\bar{x}\pm s$]

Table 3 Comparison of the serum CRP, IL-6, IL-8, TNF- α levels between three groups before and after treatment [$\bar{x}\pm s$]

Groups	Number	Before therapy				After therapy			
		IL-6 (pg/mL)	IL-8 (pg/mL)	CRP (mg/L)	TNF- α (μ g/mL)	IL-6 (pg/mL)	IL-8 (pg/mL)	CRP (mg/L)	TNF- α (μ g/mL)
Control group	38	138.64 $\pm$ 8.54	42.57 $\pm$ 6.32	59.33 $\pm$ 4.49	55.89 $\pm$ 4.98	59.72 $\pm$ 6.53 ^a	19.42 $\pm$ 5.36 ^a	22.49 $\pm$ 6.33 ^a	21.68 $\pm$ 5.47 ^a
Observation group 1	42	140.01 $\pm$ 11.60	43.38 $\pm$ 4.99	57.62 $\pm$ 7.04	53.87 $\pm$ 6.91	37.26 $\pm$ 6.37 ^{ab}	10.23 $\pm$ 2.13 ^{ab}	14.33 $\pm$ 3.14 ^{ab}	17.61 $\pm$ 3.92 ^{ab}
Observation group 2	40	137.62 $\pm$ 10.01	42.37 $\pm$ 6.04	58.47 $\pm$ 5.71	55.32 $\pm$ 7.03	45.57 $\pm$ 6.07 ^{abc}	9.55 $\pm$ 4.32 ^{ab}	15.94 $\pm$ 5.02 ^{ab}	16.03 $\pm$ 5.29 ^{ab}

Note: compared with before therapy, ^a $P<0.05$; compared with the control group after therapy, ^b $P<0.05$; compared with observation group 1 after therapy, ^c $P<0.05$.

2.4 三组患者治疗期间不良反应发生情况比较

治疗期间, 对照组 3 例发生恶心呕吐, 观察组 1 有 2 例发生恶心呕吐, 1 例心率过快, 观察组 2 有 1 例鼻塞, 三组不良事件发生情况比较差异无统计学意义($P>0.05$)

3 讨论

肺炎是儿童时期常见的呼吸道感染疾病, 由微生物入侵、免疫损伤、过敏等一系列原因造成的肺部感染性疾病。由于儿童的抵抗力较弱, 加之儿童鼻、咽、喉的长度较成人相对短一些, 气管表面附着的纤毛数量有限, 细菌和病毒更加容易入侵到气管造成肺部感染^[9]。炎症反应导致的分泌物增多, 会堵塞肺气道, 引起气体交换功能障碍, 早期会出现呼吸困难、气喘等症状, 重症肺炎会加重循环障碍, 促进多器官衰竭^[9], 甚至危及儿童生命。

小儿重症肺炎通常给予吸氧、抗病毒以及抗生素药物治疗, 必要时加用激素药物。然而, 常规治疗的疗效并不理想, 且对于损伤器官的保护作用有限^[6,7]。因此, 现阶段医者倾向于在常规治疗的基础上辅以其他药物治疗。多巴胺是一种具有正性肌力的神经递质, 可增强心肌收缩能力、每搏输出量, 积极改善血流状态。同时, 多巴胺还可兴奋 α 受体, 增加肾脏血流量, 降低肺泡张力, 改善患者通气状态^[8,9]。多巴酚丁胺是一种儿茶酚胺类药物, 其作用于 β_1 受体, 减轻心脏负荷, 改善肺气体交换功能^[10,11]。酚妥拉明是一种短效肾上腺素能受体阻滞剂(α 受体阻滞剂和 β -受体阻滞剂), 具有扩张血管的作用, 可明显降低肺动脉压及血管阻力, 增强心肌收缩力, 改善肾、胃肠、肝脏、心脏的血液微循环, 肺换气功能^[12,13]。既往研究表明多巴胺联合多巴酚丁胺^[14,15], 多巴胺联合酚妥拉明^[16]能有效治疗小儿重症肺炎, 但关于这两种给药方式的临床疗效、作用机制的差异鲜有报道。本研究采用多巴胺分别联合多巴酚丁胺、酚妥拉明与常规治疗小儿重症肺炎, 结果显示: 观察组 1(多巴胺联合多巴酚丁胺)、观察组 2(多巴胺联合酚妥拉明)的总有效率均显著高于对照组(常规治疗); 观察组(1, 2)的肺啰音消失时间、咳嗽症状消失时间、呼吸困难改善时间、退热时间以及住院天数均显著短

于对照组($p<0.05$), 且观察组 1 和观察组 2 在上述症状改善方面与住院时间上无明显差异。这表明多巴胺联合多巴酚丁胺的临床疗效与多巴胺联合酚妥拉明相当。治疗期间, 两种给药方式均存在不良反应发生情况, 多巴胺联合多巴酚丁胺组主要为恶心呕吐、心率过快, 多巴胺联合酚妥拉明组主要为腹泻, 提示在用药时一定要注意用法和剂量。

重症肺炎的一大特点就是全身炎症状态, 大量产生和释放的炎症因子可激活 NF- κ B 途径, 使炎症反应进一步扩大, 加重病情^[17-19]。白海波^[20]研究表明重症肺炎的临床症状消失时间与炎症因子的水平呈正相关, 说明血清指标的改善与患儿病情良好转归密切相关。本研究中, 三组患者血 IL-6、IL-8、CRP 以及 TNF- α 的水平均有效降低, 且观察组患者血清炎症因子水平显著低于对照组, 表明多巴胺联合多巴酚丁胺和多巴胺联合酚妥拉明均能有效控制小儿重症肺炎的炎症反应。

综上所述, 多巴胺联合多巴酚丁胺和多巴胺联合酚妥拉明治疗小儿重症肺炎的疗效和安全性相当, 二者均明显优于常规治疗。

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