doi: 10.13241/j.cnki.pmb.2019.24.023

酚妥拉明联合多巴酚丁胺与多巴胺治疗重症肺炎患儿的有效性及安全性分析*

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摘要 目的：分析和比较酚妥拉明联合多巴酚丁胺与多巴胺治疗重症肺炎患儿的有效性及安全性。**方法：**选取 2014 年 4 月至 2019 年 4 月西安交通大学附属儿童医院急诊科收治的 96 例重症肺炎患儿，根据入院单双号将其分为对照组(n=48)和研究组(n=48)。对照组接受多巴酚丁胺与小剂量多巴胺治疗，研究组在对照组的基础上联合酚妥拉明治疗。比较两组的治疗总有效率、治疗前后各血气指标与炎性因子水平变化以及不良反应的发生情况。**结果：**治疗后，研究组总有效率显著高于对照组(93.75% vs.79.17%，$P<0.05$)；两组的血气指标 PaO_2、SaO_2 均显著升高，$PaCO_2$ 显著降低，且研究组的变化比对照更加显著($P<0.05$)；两组各的炎性因子水平 IL-6、IL-8、CRP 和 TNF-α 均显著降低，且研究组显著低于对照组($P<0.05$)。两组不良反应发生率比较无统计学差异($P>0.05$)。**结论：**酚妥拉明联合多巴酚丁胺治疗重症肺炎患儿的临床疗效明显优于酚妥拉明联合多巴胺治疗，且二者安全性相当。

关键词：酚妥拉明；多巴酚丁胺；多巴胺；重症肺炎

中图分类号：R725.6 **文献标识码：**A **文章编号：**1673-6273(2019)24-4703-04

Efficacy and Safety of Phentolamine Combined with Dobutamine and Dopamine in the Treatment of Children with Severe Pneumonia*

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ABSTRACT Objective: Analysis and comparison of the efficacy and safety of phenolamine combined with dobutamine and dopamine in the treatment of children with severe pneumonia. **Methods:** 96 children with severe pneumonia admitted to the emergency department of Children's Hospital of Xi'an Jiaotong University from April 2014 to April 2019 were selected. The subjects were divided into the control group (n=48) and the study group (n=48) according to the number of single and even number of admission. The control group received dobutamine and low dose of dopamine, and the study group received combined phenolamine treatment on the basis of the control group. The total effective rate, the changes of blood gas indexes and inflammatory factor levels before and after treatment, and the incidence of adverse reactions were compared between the two groups. **Results:** After treatment, the total effective rate of treatment in the study group was significantly higher than that in the control group (93.75% vs.79.17%, $P<0.05$). The blood gas indexes PaO_2 and SaO_2 of the two groups were significantly increased, $PaCO_2$ was significantly decreased, and the change of the study group was more significant than the control group ($P<0.05$). The levels of inflammatory factors IL-6, IL-8, CRP and TNF-α were significantly lower in the two groups, and the study group was significantly lower than the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** The clinical efficacy of phentolamine combined with dobutamine in the treatment of children with severe pneumonia is significantly better than phentolamine combined with dopamine treatment, and the safety of the two is equivalent.

Key words: Phentolamine; Dobutamine; Dopamine; Severe pneumonia

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

Article ID: 1673-6273(2019)24-4703-04

前言

肺炎是儿科临床最为常见的一种呼吸道疾病，主要因细菌、病毒感染所致，以咳嗽、呼吸困难、喘息为主要临床表现，若

* 基金项目：陕西省卫生健康委科研基金项目(2018D005)

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(收稿日期：2019-07-04 接受日期：2019-07-28)

治疗不当,则会发展为重症肺炎,不仅会增加治疗难度,还可能导致患儿发生呼吸衰竭、心力衰竭等并发症,甚至威胁患儿的生命[1]。小儿身体各系统功能发育尚未完全,免疫力低下,极易受病原菌侵袭而引发感染,如何提高小儿重症肺炎的治疗效果、改善预后一直是儿科医生研究的重点[2]。目前,临床上主要通过联合用药来抑制肺炎患儿的炎性反应,改善其通气功能以控制病情发展,但其对于病情较重者治疗效果常不理想[3]。

多巴酚丁胺与多巴胺均为同源性儿茶酚胺药物,可选择性的抑制β1 受体,兴奋呼吸中枢,改善患儿缺氧状态,临床上主要采用联合用药来治疗重症肺炎[4]。酚妥拉明作为一种短效的非选择性α 受体阻滞剂,可拮抗儿茶酚胺效应[5]。为提高重症肺炎患儿的治疗效果,本研究选取 2014 年 4 月至 2019 年 4 月西安交通大学附属儿童医院急诊科收治的 96 例重症肺炎患儿,探讨酚妥拉明联合多巴酚丁胺与多巴胺治疗重症肺炎患儿的有效性及安全性,具体结果报道如下。

1 资料与方法

1.1 病例资料

选取 2014 年 4 月至 2019 年 4 月西安交通大学附属儿童医院急诊科收治的 96 例重症肺炎患儿,根据入院单双号将受试者分为对照组(n=48)和研究组(n=48)。对照组中,男 26 例,女 22 例,年龄 5 个月 -3 岁,平均(1.32± 0.53)岁;病程 1-7 d,平均(3.44± 1.26)d;研究组中,男 25 例,女 23 例,年龄 6 个月 -3 岁,平均(1.62± 0.75)岁;病程 1-8 d,平均(4.03± 0.48)d。两组的一般资料比较差异无统计学意义(P>0.05),具有可比性。

1.2 纳入及排除标准

纳入标准:患儿均伴有发绀、呼吸困难、肺部啰音等症,经影像学及实验室检查确诊为重症肺炎,年龄 3 岁以内,患儿家长知情同意,自愿参与本次研究。排除标准:衣原体或支原体感染、先天性心脏病、相关药物过敏史、肝肾功能障碍及其他肺部疾病。

1.3 治疗方法

患儿入院后均给予吸氧、解痉平喘、利尿、抗感染等常规治疗,对照组在此基础上将盐酸多巴胺丁胺注射液(山东方明药业集团股份有限公司,国药准字 H20053297)采用 0.9 %生理盐水稀释后以 2-5 μg/(kg·min)静脉泵入,盐酸多巴胺注射液(陕西京西药业有限公司,国药准字 H61020258)采用 0.9 %生理盐水稀释后以 2-5 μg/(kg·min)静脉泵入,每次 3-4 h,每日 1 次,连续治疗 5 d。研究组在对照组的基础上将 20 mg 酚妥拉明注射液(上海旭东海普药业有限公司,国药准字 H31020589)加入到 0.9 %生理盐水 250 mL 中静脉滴注,每日 1 次,连续治疗 5 d。

1.4 观察指标

治疗总有效率;治疗前后血氧饱和度(Arterial oxygen saturation, SaO_2)、动脉血氧分压(Arterial oxygen pressure, PaO_2)、二氧化碳分压(Arterial partial pressure of carbon dioxide, $PaCO_2$)等血气指标;白细胞介素 -6(Interleukin-6, IL-6)、白细胞介素 -8(Interleukin-8, IL-8)、C- 反应蛋白(C-reactive protein, CRP)及肿瘤坏死因子 -α(Tumor necrosis factor α, TNF-α)等炎性因子指标;治疗过程中不良反应的发生情况。

1.5 评价标准

(1)疗效评价标准[6]:显效:治疗 5 d 内患儿症状及体征均完全消失,胸部 X 线片及病原学检查各指标基本恢复正常;有效:治疗 5 d 内患儿症状及体征均明显缓解,胸部 X 线片及病原学检查各指标明显改善;无效:治疗 5 d 后患儿症状、体征及各项检查结果均无明显好转或病情加重,总有效率为显效与有效之和的占比。(2)血气指标:抽取患儿股动脉血 4 mL,采用上海惠中公司的 MB-3100 血气分析仪检测 PaO_2、$PaCO_2$ 及 SaO_2 水平。(3)炎性因子:取患儿空腹状态下外周静脉血 5 mL,离心分离出血清后利用日立 7171 全自动生化分析仪采用酶联免疫吸附法检测 IL-6、IL-8、CRP 及 TNF-α 水平[7]。试剂盒均购买于上海酶联生物科技公司,严格按照说明书操作。

1.6 统计学方法

采用 SPSS19.0 分析研究数据,以($\bar{x}$± s)示计量资料,以(%)示计数资料,分别行 t 检验及 x^2 检验,以 P<0.05 为差异具有统计学意义。

2 结果

2.1 两组治疗总有效率的比较

治疗后,研究组治疗总有效率显著高于对照组(93.75% vs. 79.17%,P<0.05),见表 1。

表 1 两组治疗总有效率的比较(例,%)

Table 1 Comparison of the total effective rate between two groups(n, %)

Groups	n	Excellent	Effective	Invalid	Total effective rate
Study Group	48	29(60.42)	16(33.33)	3(6.25)	46(93.75)*
Control group	48	24(50.00)	14(29.17)	10(20.83)	38(79.17)

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

2.2 两组治疗前后血气指标变化的比较

与治疗前相比,治疗后两组的血气指标 PaO_2、SaO_2 均显著升高,$PaCO_2$ 显著降低,且研究组变化比对照组显著(P<0.05),见表 2。

2.3 两组治疗前后血清炎性因子水平变化的比较

与治疗前相比,治疗后两组的炎性因子水平 IL-6、IL-8、CRP 和 TNF-α 均显著降低,且研究组变化比对照组更显著(P<0.05),见表 3。

2.4 两组不良反应发生情况的比较

两组药物不良反应的发生情况比较差异无统计学意义(P>0.05),见表 4。

3 讨论

肺炎主要因细菌、病毒、真菌、非典型病原体感染或环境因素引起,小儿肺炎早期症状常不明显,以轻微咳嗽为主,易被家长忽视[8]。小儿时期免疫功能低下,气管壁较薄软,淋巴细胞间

隙较大,肺泡数量不足,常无法抵御病原体的侵入,早期炎症常存在于肺部,给予对症治疗后多可痊愈,随着病原菌继续入侵其他组织,则可出现肺泡弥散障碍或肺泡通气不足,引发重症肺炎[9-11]。重症肺炎除了呼吸系统改变外,还可引发消化、神经及循环系统病变,部分患儿可发生脑水肿,进而出现意识障碍、警觉、光敏感消失,甚至呼吸停止[11]。

表 2 两组治疗前后各血气指标变化($\bar{x}\pm s$)

Table 2 Comparison of the changes of blood gas indexes between two groups before and after treatment($\bar{x}\pm s$)

Groups	Time	PaO_2(mmHg)	$PaCO_2$(mmHg)	SaO_2(%)
Study Group(n=48)	Before treatment	43.63± 5.38	52.33± 5.17	55.21± 5.43
	After treatment	84.15± 7.22*#	40.18± 2.54*#	94.27± 4.52*#
Control group(n=48)	Before treatment	43.27± 5.29	53.06± 5.48	56.03± 5.68
	After treatment	69.58± 7.04*	46.73± 3.22*	73.88± 5.43*

Note: compared with pre-treatment and the control group, *$P<0.05$, #$P<0.05$.

表 3 两组炎性因子水平变化($\bar{x}\pm s$)

Table 3 Changes in the levels of inflammatory factors in the two groups($\bar{x}\pm s$)

Groups	Time	IL-6(pg/mL)	IL-8(pg/mL)	CRP(mg/mL)	TNF-α(mg/L)
Study Group(n=48)	Before treatment	146.88± 13.45	40.36± 4.35	42.18± 8.43	57.24± 5.84
	After treatment	31.24± 5.22*#	9.33± 1.25*#	10.21± 3.32*#	14.32± 4.27*#
Control group(n=48)	Before treatment	146.32± 12.26	41.03± 5.26	42.22± 7.41	56.66± 5.77
	After treatment	60.28± 6.57*	20.48± 3.25*	18.67± 4.37*	23.72± 4.56*

表 4 两组不良反应发生情况的比较(例,%)

Table 4 Comparison of the incidence of adverse reactions between two groups(n, %)

Groups	NNT	diarrhea	nausea	vomiting	Total effective rate
Study Group	48	1(2.08)	3(6.25)	2(4.17)	6(12.50)*
Control group	48	2(4.17)	1(2.08)	1(2.08)	4(8.33)

针对小儿重症肺炎临床上常通过胸部 X 线、实验室检查等判断病情严重程度,以为临床确立治疗方案提供参考。目前临床上常通过吸氧、解痉平喘、利尿、抗感染、扩血管等常规治疗来缓解重症肺炎患儿的临床症状,控制病情进展,但临床实践证实,常规治疗长无法抑制病情凶险患儿疾病发展,且易造成脏器功能损害,因此还应辅助相关药物来进一步保证治疗效果,控制病情发展[12-15]。

抑制机体炎性反应、改善患儿通气功能是重症肺炎治疗中的关键环节。多巴胺为脑垂体腺及下丘脑神经传导递质,可激发心肌 β 受体促进去甲肾上腺素的释放, 增加心肌收缩力,发挥正性肌力作用[22-24]。另外还可抑制大脑皮层网状结构,兴奋呼吸中枢,增大心排血量,降低心脏负荷,改善呼吸衰竭及心力衰竭症状[25]。多巴胺丁胺为 β 受体激动剂,可扩张外周血管,提高心肌收缩力,降低肺循环阻力,增高肺动脉压,促进肺部炎症吸收。在小儿重症肺炎治疗中可有效增强肺部换气功能,减少心脏负荷,与多巴胺联合应用可协同性的增强患儿心脏功能及肺功能,缓解临床症状[26-28]。酚妥拉明可有效缓解支气管痉挛,舒张血管,减少肺动脉压力,改善患儿肺部通气功能,促进肾脏新陈代谢,降低药物不良反应,在多巴胺与多巴胺丁胺的基础上联合应用能够增效减毒[29,30]。

IL-6 具有多重炎性作用,可对多类细胞分化与生长、机体免疫应答进行调节,还可诱导并释放血管内皮生长因子,促进炎性细胞渗出,其水平的异常表达与疾病的严重程度有密切关系[16-18]。IL-6 作为炎性疾病的重要介质,在抗感染反应及免疫应答中具有重要作用[19]。TNF-α 作为一种经典的促炎因子,可破坏内皮细胞的完整性,参与正常的炎性反应及免疫反应[20]。CRP 作为急性时相反应蛋白, 在炎性反应中其水平可异常增高[21]。PaO_2、$PaCO_2$ 及 SaO_2 常被作为肺通气功能的重要指标用于评价病情严重程度及治疗效果。本研究结果显示研究组治疗总有效率显著高于对照组,治疗后两组的血气指标 PaO_2、SaO_2 均显著升高,$PaCO_2$ 显著降低,且研究组的变化比对照更加显著,两组各的炎性因子水平 IL-6、IL-8、CRP 和 TNF-α 均显著降低,且研究组显著低于对照组,提示酚妥拉明联合多巴酚丁胺与多巴胺可协同性的改善患儿临床症状与体征,提高治疗效果。此外酚妥拉明联合多巴酚丁胺与多巴胺可协同性的减少肺泡张力,降低肺循环阻力,促进肺部炎症吸收,有效改善患儿的通气功能。而两组药物不良反应发生率比较无统计学差异,进一步说明酚妥拉明联合多巴酚丁胺与多巴胺不仅有助于提高治疗效果,且安全性高。

综上所述,酚妥拉明联合多巴酚丁胺治疗重症肺炎患儿的临床疗效明显优于酚妥拉明联合多巴胺治疗,且二者安全性相当,对促进重症肺炎患儿病情康复具有积极意义。

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