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婴幼儿重症肺炎潮气呼吸肺功能、D-二聚体水平的变化 及盐酸氨溴索的干预效果研究*

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摘要 目的: 探讨婴幼儿重症肺炎潮气呼吸肺功能、D-二聚体水平的变化及盐酸氨溴索的干预效果研究。**方法:** 2016年1月至2019年12月期间我院收治的重症肺炎婴幼儿122例作为肺炎组,另选取同期来我院行健康体检的婴幼儿100例作为对照组,肺炎组患儿采用随机数字表法分为A组(n=61,常规治疗)和B组(n=61,常规治疗基础上联合盐酸氨溴索治疗),对比对照组、肺炎组潮气呼吸肺功能、D-二聚体水平,对比A组、B组两组的疗效、潮气呼吸肺功能、D-二聚体、症状缓解时间及不良反应。**结果:** 肺炎组呼吸频率(RR)、D-二聚体水平高于对照组,潮气量(VT)、达峰时间(TPTEF)、吸气时间(TI)、呼气时间(TE)短于对照组($P<0.05$)。B组治疗1周后的总有效率高于对照组($P<0.05$)。两组治疗1周后RR、D-二聚体水平均下降,且B组低于A组($P<0.05$),两组治疗1周后VT、TPTEF、TI、TE均升高,且B组高于A组($P<0.05$)。B组退热时间、咳嗽缓解时间、气促缓解时间、啰音消失时间均短于A组($P<0.05$)。A组、B组两组患儿不良反应总发生率对比未见差异($P>0.05$)。**结论:** D-二聚体以及潮气呼吸肺功能检测可作为婴幼儿重症肺炎治疗效果、病情程度评价的重要指标,经盐酸氨溴索干预后患儿D-二聚体及潮气呼吸肺功能均可得到显著改善,临床症状可有效缓解,疗效肯定,且不增加不良反应发生。

关键词: 婴幼儿;重症肺炎;潮气呼吸肺功能;D-二聚体;盐酸氨溴索;干预效果

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Changes of Tidal Breathing Pulmonary Function and D-dimer Level in Infants with Severe Pneumonia and Study of the Intervention Effect of Ambroxol Hydrochloride*

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ABSTRACT Objective: To investigate the changes of tidal breathing pulmonary function and D-dimer level in infants with severe pneumonia and the study of intervention effect of ambroxol hydrochloride. **Methods:** 122 infants with severe pneumonia admitted to our hospital from January 2016 to December 2019 were selected as the pneumonia group, and 100 infants who came to our hospital for health examination at the same period were selected as the control group. The pneumonia group was randomly divided into group A (n=61, conventional treatment) and group B (n=61, combined with ambroxol hydrochloride on the basis of conventional treatment) by random number table method, and the tidal breathing, pulmonary function and D-dimer level of control group and pneumonia group was compared. The curative effect, tidal breathing pulmonary function, D-dimer, symptom remission time and adverse reactions of group A and group B were compared. **Results:** The respiratory rate (RR) and D-dimer levels in the pneumonia group were higher than those in the control group, while the tidal volume (VT), time to peak (TPTEF), inspiratory time (TI) and expiratory time (TE) in the pneumonia group were lower than those in the control group ($P<0.05$). The total effective rate in group B was higher than that in control group at 1 week after treatment ($P<0.05$). 1 week after treatment, RR and D-dimer in both groups were decreased, and group B was lower than the control group ($P<0.05$). 1 week after treatment, VT, TPTEF, TI, TE in both groups were increased, and group B was higher than group A ($P<0.05$). The antipyretic time, cough relief time, shortness of breath remission time and rales disappearance time in group B were shorter than those in group A ($P<0.05$). There was no difference in the total incidence of adverse reactions between group A and group B ($P>0.05$). **Conclusion:** The detection of D-dimer and tidal breathing pulmonary function can be used as an important index to evaluate the severity and treatment effect of severe pneumonia in infants. After ambroxol hydrochloride intervention, tidal breathing pulmonary function and D-dimer can be significantly improved, clinical symptoms can be effectively alleviated, the curative effect is affirmative, and there is no increase in adverse reactions.

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Key words: Infant; sSevere pneumonia; Tidal breathing pulmonary function; D-dimer; Ambroxol hydrochloride; Intervention effect

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前言

肺炎是临床常见的呼吸道系统性疾病,由于婴幼儿本身具有气道狭窄、免疫力低下等特点,导致其发病率较高^[1,2]。当肺炎患儿出现出现低血压、休克等循环衰竭表现,或者急性呼吸衰竭或严重低氧血症需要通气支持和其他器官功能障碍即可确诊为重症肺炎^[3,4]。重症肺炎婴幼儿具有病情严重且进展迅速、易损伤其他脏器等诸多特点,患病死亡风险较高^[5,6]。盐酸氨溴索是一种黏液溶解剂,既往将其用于治疗肺炎的疗效较好,可有效保护患儿呼吸系统^[7],但有关其用于重症肺炎婴幼儿的疗效报道尚不十分多见。潮气呼吸肺功能指标常作为肺炎诊断、治疗、预后评价的重要参数,且重症肺炎婴幼儿D-二聚体水平通常呈高表达状态,故D-二聚体有望对早期疾病诊断提供辅助^[8,9]。本研究通过探讨重症肺炎婴幼儿D-二聚体水平、潮气呼吸肺功能的变化及盐酸氨溴索的干预效果,以期对重症肺炎婴幼儿的治疗提供参考,报道如下。

1 资料与方法

1.1 一般资料

将我院于2016年1月至2019年12月间收治的122例重症肺炎婴幼儿作为肺炎组,其中男65例,女57例,平均年龄(12.71 ± 2.96)月;平均病程(4.22 ± 1.16)d;平均体质量指数(14.62 ± 1.26)kg/m²。纳入标准:(1)诊断标准参考《实用儿科学》^[10],经胸部影像学确诊;(2)年龄 ≤ 24 个月者;(3)患儿家属知情本研究且签署同意书;(4)配合完成研究者。排除标准:(1)严重心脑血管及消化、循环系统疾病者;(2)对本组研究用药存在禁忌者;(3)伴有其他原发性肺部疾病者;(4)合并免疫力低下者;(5)合并其他重症疾病者。肺炎组患儿采用随机数字表法分为A组(n=61)和B组(n=61),其中A组男33例,女28例,平均年龄(12.74 ± 3.09)月;平均病程(4.25 ± 1.24)d;平均体质量指数(14.65 ± 1.42)kg/m²。B组男32例,女29例,平均年龄(12.67 ± 3.34)月;平均病程(4.19 ± 1.06)d;平均体质量指数(14.58 ± 1.37)kg/m²。A组、B组患儿性别比例、年龄、病程、体质量指数对比未见统计学差异($P>0.05$),具有可比性。另选取同期来我院行健康体检的婴幼儿100例作为对照组,对照组男56例,女44例,平均年龄(12.69 ± 2.37)月;平均体质量指数(14.62 ± 1.17)kg/m²。对照组、肺炎组患儿性别比例、年龄、体

量指数对比未见统计学差异($P>0.05$)。本研究经医院伦理委员会批准。

1.2 方法

1.2.1 治疗方法 A组给予常规治疗,包括解痉、平喘、化痰、吸痰、雾化、吸氧、纠正心衰、中毒性脑病、呼衰、中毒性肠麻痹等对症及保证能量供应、水电解质平衡支持治疗等综合治疗。B组在常规治疗的基础上联合盐酸氨溴索(上海勃林格殷格翰药业有限公司,国药准字J20140032,规格:2 mL:15 mg)治疗,将其以7.5 mg/kg缓慢静脉注射,2次/d。两组均连续治疗1周。

1.2.2 潮气呼吸肺功能检测 对照组于体检当天,肺炎组患儿于治疗前、治疗1周后采用MasterScreen型肺功能仪(伟亚安医疗器械上海有限公司)测定潮气呼吸肺功能指标:呼吸频率(RR)、潮气量(VT)、达峰时间(TPTEF)、吸气时间(TI)、呼气时间(TE)。

1.2.3 D-二聚体检测 对照组于体检当天,肺炎组患儿于治疗前、治疗1周后抽取3 mL肘静脉血,经离心处理,速率为3300 r/min,离心10min,离心半径12 cm,采用免疫比浊法检测D-二聚体水平,严格按照试剂盒(希森美康医用电子有限公司)说明书操作。

1.3 评价指标^[11]

(1)记录肺炎组患儿治疗1周后的总有效率。总有效率=有效率+显效率。显效:1周时间后患儿胸部影像学恢复正常,临床症状、体征全部消失。有效:1周时间后患儿胸部影像学基本恢复正常,临床症状、体征有所缓解。无效:患儿胸部影像学未见恢复,临床症状、体征无缓解甚至加重。(2)比较两组患儿的退热时间、咳嗽缓解时间、气促缓解时间、啰音消失时间。(3)对比重症肺炎患儿不良反应情况。

1.4 统计学方法

以SPSS25.0分析数据。以($\bar{x} \pm s$)表示计量资料,实施t检验。以比或率表示计数资料,实施卡方检验。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 肺炎组、对照组的潮气呼吸肺功能、D-二聚体水平比较

肺炎组RR、D-二聚体水平高于对照组,VT、TPTEF、TI、TE短于对照组($P<0.05$),详见表1。

表1 对照组、肺炎组的潮气呼吸肺功能、D-二聚体水平比较($\bar{x} \pm s$)

Table 1 Comparison of tidal breathing pulmonary function and D-dimer level between control group and pneumonia group($\bar{x} \pm s$)

Groups	RR(beats/min)	VT(mL/kg)	TPTEF(s)	TI(s)	TE(s)	D-dimer(mg/L)
Control group (n=100)	29.18 $\pm$ 3.77	7.72 $\pm$ 1.53	0.38 $\pm$ 0.09	0.89 $\pm$ 0.12	1.19 $\pm$ 0.23	1.37 $\pm$ 0.29
Pneumonia group (n=122)	63.24 $\pm$ 7.68	4.56 $\pm$ 1.41	0.25 $\pm$ 0.06	0.57 $\pm$ 0.15	0.68 $\pm$ 0.17	2.26 $\pm$ 0.35
t	40.516	12.937	11.428	9.472	18.725	14.563
P	0.000	0.000	0.000	0.000	0.000	0.000

2.2 重症肺炎患儿治疗后的疗效分析

B 组治疗 1 周后的总有效率高于对照组($P<0.05$),详见表 2。

2.3 重症肺炎患儿治疗前后的潮气呼吸肺功能、D-二聚体水平分析

A 组、B 组两组治疗前 RR、D-二聚体、VT、TPTEF、TI、TE

组间比较差异无统计学意义($P>0.05$),两组治疗 1 周后 RR、D-二聚体水平均下降,且 B 组低于 A 组($P<0.05$),两组治疗 1 周后 VT、TPTEF、TI、TE 均升高,且 B 组高于 A 组($P<0.05$),详见表 3。

表 2 重症肺炎患儿治疗后的疗效分析 [例(%)]

Table 2 Curative effect analysis of infants with severe pneumonia after treatment [n(%)]

Groups	Remarkable effect	Effective	Invalid	Total effective rate
Group A(n=61)	15(24.59)	29(47.54)	17(27.87)	44(72.13)
Group B(n=61)	21(34.43)	35(57.38)	5(8.20)	56(91.80)
χ^2				6.367
P				0.012

表 3 重症肺炎患儿治疗前后的潮气呼吸肺功能、D-二聚体水平分析($\bar{x} \pm s$)

Table 3 Analysis of tidal breathing pulmonary function and D-dimer level in infants with severe pneumonia before and after treatment($\bar{x} \pm s$)

Groups	Time	RR(beats/min)	VT(ml/kg)	TPTEF(s)	TI(s)	TE(s)	D-dimer(mg/L)
Group A(n=61)	Before treatment	63.91± 4.53	4.58± 0.31	0.26± 0.07	0.58± 0.09	0.67± 0.06	2.24± 0.17
	1 week after treatment	43.28± 4.48 ^a	6.05± 0.34 ^a	0.31± 0.06 ^a	0.71± 0.06 ^a	0.91± 0.13 ^a	1.75± 0.18 ^a
Group B(n=61)	Before treatment	62.57± 5.07	4.54± 0.32	0.24± 0.06	0.57± 0.06	0.69± 0.08	2.28± 0.16
	1 week after treatment	30.17± 4.14 ^{ab}	6.98± 0.36 ^{ab}	0.37± 0.04 ^{ab}	0.82± 0.09 ^{ab}	1.08± 0.15 ^{ab}	1.41± 0.11 ^{ab}

Note: compared with before treatment, ^a $P<0.05$; compared with group A, ^b $P<0.05$.

2.4 重症肺炎患儿治疗后各症状体征缓解时间分析

B 组退热时间、咳嗽缓解时间、气促缓解时间、啰音消失时间均短于 A 组($P<0.05$),详见表 4。

2.5 重症肺炎患儿治疗期间对的安全性评价

A 组、B 组两组患儿不良反应总发生率对比未见差异($P>0.05$),详见表 5。

表 4 重症肺炎患儿治疗后各症状体征缓解时间分析($\bar{x} \pm s, d$)

Table 4 Analysis of remission time of symptoms and signs in infants with severe pneumonia after treatment($\bar{x} \pm s, d$)

Groups	Antipyretic time	Cough relief time	Shortness of breath remission time	Rales disappearance time
Group A(n=61)	4.06± 0.73	5.98± 0.76	3.39± 0.35	3.87± 0.39
Group B(n=61)	3.19± 0.64	3.31± 0.61	2.74± 0.29	2.23± 0.28
t	9.682	11.428	10.836	11.427
P	0.000	0.000	0.000	0.000

表 5 重症肺炎患儿治疗期间对的安全性评价 [例(%)]

Table 5 Safety evaluation of infants with severe pneumonia during treatment [n(%)]

Groups	Palpitation	Diarrhea	Gastrointestinal abnormalities	Total incidence rate
Group A(n=61)	0(0.00)	2(3.28)	1(1.64)	3(4.92)
Group B(n=61)	1(1.64)	2(3.28)	2(3.28)	5(8.20)
χ^2				0.535
P				0.464

3 讨论

婴幼儿抵抗力差,各项脏器系统发育不完善,普通的肺炎极易发展成为重症肺炎。重症肺炎典型特点为肺功能损害,受

炎性反应、微血管内皮损伤等因素影响,重症肺炎婴幼儿易引发肺微循环障碍,严重时形成血栓,危及患儿生命^[12-14]。近年来随着医学进展,重症肺炎婴幼儿的死亡率有所下降,但其仍是5岁以下儿童死亡的主要原因之一^[15],即使经治疗后痊愈的婴幼儿,仍可能会遗留肺结构改变或肺功能的持续损害,导致患者发烧、咳嗽、气促、肺部湿啰音等临床症状反复发作,降低其生活质量^[16]。肺功能测定可评估呼吸系统疾病患者病情、疗效和预后,但由于婴幼儿肺功能测试的特殊性及难度性,临床应用受限^[17]。潮气呼吸肺功能检查无需患儿配合,简便易行,近年来逐渐用于婴幼儿呼吸类疾病的辅助判断指标之一^[18]。D-二聚体属于纤溶过程标记物,主要由纤溶酶溶解而成,其水平升高反映体内存在高凝状态及继发性纤溶亢进^[19,20]。通过对D-二聚体的检测可提示活动性纤溶亢进的存在,对血栓性、高凝性的疾病具有早期的预测意义。

本研究中肺炎组RR、D-二聚体水平高于对照组,VT、TPTEF、TI、TE短于对照组,推测原因可能因为重症肺炎患儿体内肺内通气/血液比例失调,引起气体弥散功能障碍,引起该碳酸血症和低氧血症,机体代偿性的增加RR以维持每分钟通气量,而VT则随之降低;此外,RR的增加导致每分钟通气量也随之增加,导致TI、TE均缩短^[21-23]。TPTEF可评价气道阻塞严重程度,其值与气道阻塞严重程度呈反比,婴幼儿呼吸系统特殊,易出现气道阻塞现象,导致TPTEF缩短^[24,25]。婴幼儿重症肺炎D-二聚体水平升高的主要原因在于重症肺炎机体炎症因子大量分泌,导致内皮素-1及血小板活化因子升高,引起血管内皮损伤及内皮下胶原暴露,从而激活血小板引起高能状态^[26,27]。本研究通过尝试在常规治疗的基础上联合盐酸氨溴索治疗,并以常规治疗为对照,结果显示,B组治疗1周后的症状恢复效果、D-二聚体以及潮气呼吸肺功能指标改善均优于对照组,疗效得到进一步的提升。盐酸氨溴索是一种稀化粘液祛痰药,可通过增强纤毛运动、降低痰液黏度来促进痰液排出,并促使肺表面活性物质分泌及支气管纤毛运动,有利于改善通气功能和呼吸困难,缓解呼吸障碍^[28]。此外,由于婴幼儿的呼吸系统处于发育阶段,机体长期处于炎性状态下难以维持小气道通畅,常规的治疗药物无法深入到肺组织内,对深部的气道组织作用非常有限,而盐酸氨溴索可突破这一限制,其可提高肺组织内抗生素浓度发挥协同增强抗感染效果,并可降低机体炎症反应,改善患儿免疫功能,进而改善疾病预后^[29,30]。另A组、B组两组患儿不良反应总发生率对比无差异,表明盐酸氨溴索应用于重症肺炎婴幼儿中安全可靠,疗效确切。本研究受限于样本量及观察时间,未能观察盐酸氨溴索干预治疗的远期疗效,后续将增加样本量及随访时间,以提高研究结果的准确性及科学性。

综上所述,D-二聚体以及潮气呼吸肺功能检测可作为评估重症肺炎婴幼儿病情程度、治疗效果的重要指标,经盐酸氨溴索干预后患儿D-二聚体及潮气呼吸肺功能均可得到显著改善,临床症状可有效缓解,疗效肯定,且不增加不良反应发生。

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