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· 论 著 ·

右美托咪定滴鼻复合七氟醚吸入诱导对先天性心脏病介入封堵术患儿脑糖氧代谢及认知功能的影响

张文静, 王蓉, 温旭, 杜倩, 刘洪, 庞小翼 (四川绵阳四〇四医院, 四川绵阳 621000)

[摘要]目的:探讨右美托咪定滴鼻复合七氟醚吸入诱导在先天性心脏病介入封堵术的应用价值。方法:选取 2020 年 4 月至 2021 年 4 月在我院接受介入封堵术治疗的先天性心脏病患儿 87 例,根据住院时间排序,奇数纳入观察组($n=44$),偶数纳入对照组($n=43$)。观察组术前 30 min 以盐酸右美托咪定注射液滴鼻,对照组给予等量生理盐水处理,后均以 8% 七氟醚面罩吸入诱导麻醉,5% 七氟醚维持麻醉。分别记录两组患儿滴鼻前(T0)、滴鼻后 10 min(T1)、滴鼻后 30 min(T2)、麻醉诱导前(T3)、麻醉诱导后(T4)、手术结束时(T5)、苏醒时(T6)的心率(HR)和平均动脉压(MAP),采集患儿桡动脉和颈内静脉球部血液,计算颈内动-静脉氧含量差值(Da-jvO₂)、脑氧摄取率(CERO₂)、血糖差值(A-VGlu)和乳酸差值(A-VLac)。于术前 24 h 及术后 1 周、3 个月、1 年采用韦氏儿童智力量表第 IV 版(WISC-IV)评价患儿认知功能。于术后 10、30、60 min 采用小儿麻醉苏醒期躁动评分量表(PAED)评价患儿麻醉苏醒期躁动情况。结果:与 T0~T2 比较,对照组 T3~T6 时 HR 降低($P<0.05$);T1~T6 时,观察组 HR、Da-jvO₂、CERO₂、A-VGlu 及 A-VLac 水平均低于对照组($P<0.05$)。观察组术后 1 周和 3 个月时 WISC-IV 评分高于对照组($P<0.05$),术后 10、30、60 min 时 PAED 评分均低于对照组($P<0.05$),苏醒期躁动发生率低于对照组($P<0.05$)。结论:先天性心脏病介入封堵术患儿采用右美托咪定滴鼻复合七氟醚吸入诱导麻醉有助于降低术中脑糖氧代谢,减少因脑缺血、缺氧所致的认知功能损害,提高苏醒质量,且对血流动力学影响较小。

[关键词]先天性心脏病;介入封堵术;右美托咪定;滴鼻;七氟醚;脑糖氧代谢;认知功能

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Effects of Dexmedetomidine Nasal Drops Combined with Sevoflurane Inhalation Induction on Cerebral Oxygen Metabolism and Cognitive Function in Children Undergoing Interventional Occlusion of Congenital Heart Disease

Zhang Wenjing, Wang Rong, Wen Xu, Du Qian, Liu Hong, Pang Xiaoyi (Mianyang 404 Hospital, Sichuan Mianyang 621000, China)

[Abstract] Objective: To probe into the application value of dexmedetomidine nasal drops combined with sevoflurane inhalation induction in children undergoing interventional occlusion of congenital heart disease. **Methods:** From Apr. 2020 to Apr. 2021, 87 children with congenital heart disease who received interventional occlusion in our hospital were selected. According to the admission sequence, the odd number was included in the observation group ($n=44$), and the even number was included in the control group ($n=43$). The observation group was treated with dexmedetomidine hydrochloride by nasal drip 30 min before surgery, while the control group received the same amount of normal saline. After that, all patients were induced anesthesia with 8% sevoflurane mask inhalation, and 5% sevoflurane maintained anesthesia. The heart rate (HR) and mean arterial pressure (MAP) of two groups were recorded before nasal drip (T0), after nasal drip of 10 min (T1), after nasal drip of 30 min (T2), before anesthesia induction (T3), after anesthesia induction (T4), at the end of surgery (T5) and at the time of awakening (T6). The blood of radial artery and internal jugular vein bulb were collected, and the difference of internal jugular artery and vein oxygen content (Da-jvO₂), cerebral oxygen extraction (CERO₂), difference of blood glucose (A-VGlu), difference of lactate (A-VLac) were calculated. The cognitive function of children was evaluated by Wechsler intelligence scale for children-IV (WISC-IV) before surgery of 24 h, after surgery of 1 week, 3 months and 1 year. At 10 min, 30 min, and 60 min after surgery, the agitation during anesthesia recovery period was evaluated by pediatric anesthesia emergence delirium (PAED). **Results:** Compared with T0 to T2, the HR of control group decreased significantly from T3 to T6 ($P<0.05$). From T1 to T6, the HR, Da-jvO₂, CERO₂, A-VGlu and A-VLac of the observation group were significantly lower than those of the control group ($P<0.05$). The WISC-IV score in the observation group was significantly higher than that in the control group after surgery of 1 week and 3 months ($P<0.05$). At 10 min, 30 min, and 60 min after surgery, the PAED score of the observation group was significantly lower than that of the control group ($P<0.05$), the incidence of restlessness in the observation group was significantly lower than that in the control group ($P<0.05$). **Conclusion:** Dexmedetomidine nasal drip combined with sevoflurane inhalation induction in children with interventional closure of congenital heart disease is helpful to reduce intraoperative cerebral oxygen metabolism, decrease cognitive

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作者简介:张文静(1988.04-),女,大学本科,主治医师,主要从事临床麻醉工作,E-mail:zl20141018@163.com。

通信作者:庞小翼(1983.07-),女,硕士,主任医师,主要从事临床麻醉工作,E-mail:pxy-2002@163.com。

impairment induced by cerebral ischemia and hypoxia, improve the quality of awakening, and has less hemodynamic impact.

[**Keywords**] congenital heart disease; interventional occlusion; dexmedetomidine; nasal drops; sevoflurane; cerebral oxygen metabolism; cognitive function

先天性心脏病是由胎儿期心血管发育异常引起的先天畸形, 占所有先天畸形的 28%。介入封堵术为治疗儿童先天性心脏病常用的有效手段之一^[1]。七氟醚因挥发后可产生带特殊香味气体, 且吸入后具有良好的镇静、镇痛作用及诱导迅速等特点, 常用于小儿手术麻醉^[2]。考虑患儿配合度较差, 无法配合七氟醚吸入麻醉, 同时术中应激反应明显, 需选用稳定且安全的麻醉方案。近来有学者^[3]提出, 右美托咪定不仅具有良好的镇静、镇痛效果, 还具有一定脑保护作用。动物实验^[4]发现, 右美托咪定可通过介导 Wnt/GSK-3 β / β -链蛋白信号通路, 抑制七氟醚诱导的认知功能障碍。相对于静脉或肌肉注射给药, 滴鼻给药无创且操作简便。有报道^[5]称, 与芬太尼和咪达唑仑相比, 右美托咪定滴鼻虽起效时间较长, 但其作用时间延长, 术后镇静效果更好。目前国内外对右美托咪定滴鼻复合七氟醚吸入诱导对脑糖氧代谢及近远期认知功能影响的相关报道尚少。本研究选取 2020 年 4 月至 2021 年 4 月于我院接受介入封堵术治疗的先天性心脏病患儿 87 例进行分析, 现报道如下。

1 资料与方法

1.1 一般资料

本研究经医院伦理委员会批准, 所有患儿及其法定监护人签署知情同意书。选取 2020 年 4 月至 2021 年 4 月于我院接受介入封堵术治疗的先天性心脏病患儿 87 例, 根据住院时间排序, 奇数纳入观察组 ($n=44$), 偶数纳入对照组 ($n=43$)。纳入标准: (1) 年龄 6~16 岁; (2) 明确诊断为先天性心脏病^[6], 心功能分级^[7]为 I~II 级; (3) 符合介入封堵术指征并同意接受治疗; (4) 美国麻醉医师协会 (ASA) 分级^[8]为 I~II 级; (4) 体质量在标准体质量 $\pm 20\%$ 范围内。排除标准: (1) 合并其他先天性疾病; (2) 过敏体质或对麻醉药物过敏; (3) 合并肺肝肾功能异常、感染性疾病或其他心脏畸形; (4) 术前已存在认知功能障碍; (5) 合并智力、意识等障碍无法完成评估。观察组 44 例, 男 20 例, 女 24 例, 年龄 6~14 (8.45 $\pm$ 2.23) 岁, 体质量 (24.43 $\pm$ 10.36) kg; 心功能分级: I 级 25 例, II 级 19 例; ASA 分级: I 级 28 例, II 级 16 例; 疾病种类: 室间隔缺损 15 例, 房间隔缺损 18 例, 房室间隔缺损 11 例。对照组 43 例, 男 18 例, 女 25 例, 年龄 6~16 (8.51 $\pm$ 2.24) 岁, 体质量 (25.26 $\pm$ 10.42) kg; 心功能分级: I 级 23 例, II 级 20 例; ASA 分级: I 级 24 例, II 级 19 例; 疾病种类: 室间隔缺损 15 例, 房间隔缺损 18 例, 房室间隔缺损 10 例。两组患儿年龄、性别、体质量、心功能分级、ASA 分级以及疾病种类比较, 差异均无统计学意义 ($P>0.05$), 具有可比性。

1.2 方法

两组患儿术前常规禁食禁水 8 h, 且术前均未用药; 入室后连接心电监护, 建立静脉通道; 观察组患儿在术前 30 min 给予盐酸右美托咪定注射液, 一侧鼻腔滴鼻, 1.5 μ g/kg, 对照组给予等量生理盐水滴鼻; 滴鼻后 30 min, 均以 8% 七氟醚, 面罩吸入, 氧流量 8 L/min; 待患儿睫毛反射消失后调整氧流量为 2 L/min, 七氟醚浓度则根据脑电双频指数 (BIS) 和呼气末二氧化碳分压调整, 保持 BIS 45~55, 呼吸末二氧化碳分压 <50 mm Hg; 术毕关闭七氟醚挥发罐, 氧流量调至 6 L/min。

1.3 观察项目

1.3.1 血流动力学 分别记录两组患儿滴鼻前 (T0)、滴鼻后 10 min (T1)、滴鼻后 30 min (T2)、麻醉诱导前 (T3)、麻醉诱导后 (T4)、手术结束时 (T5)、苏醒时 (T6) 的心率 (HR) 和平均动脉压 (MAP)。数据来自同一厂家的同一型号心电监护仪。

1.3.2 脑糖氧代谢 采用 Seldinger 法经颈静脉插入 14 号导管 8~12 cm, 头端位于颈静脉球部, 套肝素帽, 以 5 U/mL 肝素液封管; 分别于 T0、T1、T2、T3、T4、T5、T6 抽取颈内静脉和桡动脉血液, 血气分析仪 (深圳迈瑞, BC-20) 测定动脉血氧分压 (P_{aO_2})、动脉血氧饱和度 (SaO_2)、颈内静脉球部血氧饱和度 (S_{jvO_2}), 全自动生化分析仪 (深圳迈瑞, BS-220) 测定血红蛋白 (Hb) 水平, 后根据公式计算颈内动-静脉氧含量差值 ($Da-jvO_2$)、脑氧摄取率 ($CERO_2$)。动脉氧含量 (CaO_2) = $Hb \times 1.38 \times SaO_2\% + 0.00315 \times PaO_2$, 颈内静脉氧含量 (C_{jvO_2}) = $Hb \times 1.38 \times S_{jvO_2}\% + 0.00315 \times S_{jvO_2}$, $Da-jvO_2 = CaO_2 - C_{jvO_2}$, $CERO_2 = Da-jvO_2 / CaO_2$ 。脑糖代谢指标包括动静脉血糖差值 (A-VGlu) 和乳酸差值 (A-VLac)。

1.3.3 认知功能 于术前 24 h 及术后 1 周、3 个月、1 年采用韦氏儿童智力量表第 IV 版 (WISC-IV)^[9] 评价患儿认知功能。由言语理解、知觉推理、工作记忆以及加工速度 4 个量表组成, 共 10 个子项目; 将各量表分数录入评分网站 (<http://wisc.king-may.com.cn/login.jhtml>) 进行处理, 得出言语理解指数、知觉推理指数、工作记忆指数、加工速度指数, 后合成二阶因素指数, 最终得出总智商, 得分越高提示该方面水平越高。

1.3.4 苏醒期躁动情况 于术后 10、30、60 min 采用小儿麻醉苏醒期躁动评分量表 (PAED)^[10] 评价患儿麻醉苏醒期躁动情况, 总分 0~20 分, 得分越高提示躁动水平越高。

1.4 统计学方法

应用 SPSS 20.0 软件, 正态分布计量资料以 $\bar{x} \pm s$ 表示, 采用 t 检验; 非正态分布计量资料以 $M(P_{25}, P_{75})$ 表示, 采用非参数 Wilcoxon U 检验; 计数资料以率表示, 采用 χ^2 检验, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组患儿血流动力学及脑糖氧代谢指标比较

与 T0 ~ T2 比较, 对照组 T3 ~ T6 时 HR 降低 ($P < 0.05$); T1 ~ T6 时, 观察组 HR、Da-jvO₂、CERO₂、A-VGlu 及 A-VLac 水平均小于对照组 ($P < 0.05$), 见表 1。

表 1 两组患儿血流动力学及脑糖氧代谢指标比较

项目	组别	T0	T1	T2	T3	T4	T5	T6
MAP/mm Hg	观察组	81.39 (77.38, 84.34)	80.67 (78.21, 83.26)	79.15 (77.70, 83.14)	79.43 (77.23, 82.26)	80.17 (76.39, 82.67)	82.38 (77.48, 82.49)	83.35 (78.38, 82.47)
	对照组	83.92 (77.23, 83.97)	82.37 (78.45, 84.42)	81.28 (78.36, 84.26)	80.23 (77.34, 81.98)	81.45 (76.51, 83.14)	83.28 (77.32, 81.76)	84.31 (78.56, 82.64)
	Z	2.484	1.726	1.625	0.651	1.883	0.938	0.625
	P	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
HR/(次/分)	观察组	112.58±12.43	110.69±10.25	109.35±10.42	108.54±10.67	106.73±9.21	107.58±8.95	107.62±9.93
	对照组	117.36±12.51	116.12±9.78	116.78±9.83	113.22±6.25	110.36±5.43	111.25±4.69	110.96±4.63
	t	1.788	2.527	3.419	2.489	2.233	2.387	2.003
	P	>0.05	<0.05	<0.01	<0.05	<0.05	<0.05	<0.05
Da-jvO ₂ /(mmol/L)	观察组	45.75±11.57	34.21±9.64	30.29±8.23	31.43±7.89	25.41±6.49	27.98±5.37	37.39±6.49
	对照组	47.21±12.24	39.84±9.75	34.16±8.14	35.21±7.85	29.26±6.52	30.63±5.34	33.29±6.58
	t	0.572	2.708	2.205	2.240	2.760	2.308	2.926
	P	>0.05	<0.01	<0.05	<0.05	<0.01	<0.05	<0.01
CERO ₂ /%	观察组	34.38±12.32	26.23±8.91	22.84±6.46	23.97±5.59	21.13±5.74	26.68±4.61	29.87±5.74
	对照组	34.87±12.43	30.16±8.86	27.45±6.32	28.39±5.43	25.75±5.62	29.45±4.75	32.48±5.83
	t	0.185	2.063	3.364	3.740	3.792	2.760	2.104
	P	>0.05	<0.05	<0.01	<0.01	<0.01	<0.01	<0.05
A-VGlu/(mmol/L)	观察组	0.35±0.04	0.25±0.03	0.23±0.04	0.22±0.03	0.23±0.02	0.23±0.03	0.24±0.03
	对照组	0.36±0.05	0.27±0.04	0.26±0.03	0.24±0.04	0.25±0.03	0.25±0.02	0.26±0.02
	t	1.031	2.642	3.951	3.964	3.667	3.650	3.650
	P	>0.05	<0.05	<0.01	<0.01	<0.01	<0.01	<0.01
A-VLac/(mmol/L)	观察组	1.32±0.21	1.21±0.13	1.16±0.15	0.95±0.11	0.86±0.09	0.84±0.06	0.82±0.05
	对照组	1.34±0.18	1.27±0.15	1.23±0.14	1.14±0.13	0.91±0.07	0.89±0.05	0.87±0.04
	t	0.476	1.995	2.249	7.365	2.888	4.218	5.143
	P	>0.05	<0.05	<0.05	<0.01	<0.01	<0.01	<0.01

2.2 两组患儿苏醒期躁动情况比较

观察组术后 10、30、60 min 时 PAED 评分均小于对照组 ($P < 0.05$), 苏醒期躁动发生率低于对照组 ($P < 0.05$), 见表 2。

表 2 两组患儿苏醒期躁动情况比较

组别	例数	PAED 评分/分			躁动/ 例(%)
		术后 10 min	术后 30 min	术后 60 min	
观察组	44	15.38±3.42	8.12±2.37	3.85±1.45	3(6.82)
对照组	43	18.09±3.46	11.94±2.43	5.71±1.41	10(23.26)
t 或 χ^2		3.674	7.423	6.064	4.623
P		<0.01	<0.01	<0.01	<0.05

2.3 两组患儿认知功能比较

术前 24 h 和术后 1 年, 两组患儿 WISC-IV 评分比较差异无统计学意义 ($P > 0.05$); 观察组术后 1 周和 3 个月时 WISC-IV 评分高于对照组 ($P < 0.05$), 见表 3。

表 3 两组患儿 WISC-IV 评分比较

组别	例数	术前 24 h	术后 1 周	术后 3 个月	术后 1 年
观察组	44	48.38±12.49	56.29±6.57	63.98±4.29	68.34±6.11
对照组	43	49.92±12.46	53.12±6.49	58.73±4.35	65.98±5.92
t		0.576	2.264	5.668	1.829
P		>0.05	<0.05	<0.01	>0.05

3 讨论

先天性心脏病患儿术后可因手术等因素造成脑部缺血、缺氧, 进而引起术后认知功能障碍^[11]。亦有报道^[12]称, 先天性心脏病患儿可能术前即已存在神经系统功能异常。一直以来, 围术期脑保护成为麻醉医师关注重点。

七氟醚为新型吸入性麻醉药物, 诱导和苏醒较现有的强效麻醉药迅速, 且因其对循环呼吸系统影响小、易控制, 是小儿麻醉常用的药物^[13]。有研究^[14]显示, 与丙泊酚相比, 七氟醚用于持续时间 <1 h 的儿科手术全身麻醉维持显著减少了术中氯胺酮用量, 缩短术后恢复时间。但有报道^[15]称, 七氟醚的暴露可诱导长期认知缺陷和皮质及海马神经元变性。与本研究结果相符, 另外本研究还发现七氟醚吸入诱导尚可降低患儿术中脑糖氧代谢, 发挥神经保护作用, 与 Cheng A 等^[16]报道相符。

右美托咪定为 α_2 肾上腺素受体激动剂, 具有强效的镇静作用, 常作为麻醉辅助剂。近来有研究^[17]发现, 2.5% 七氟醚对海马 CA1 区和 CA2/3 区的损伤大于 1% 七氟醚, 1% 七氟醚虽无法进行完全麻醉, 但通过复合右美托咪定不仅可达到相当于 2.5% 七氟醚的麻醉水平,

还有可能减轻七氟醚诱导的神经变性。相较于年长儿童或成人,低龄儿童配合度较差。滴鼻途径给药不仅大大降低了操作难度,提高患儿配合度,同时减少了对儿童的刺激。本研究以单纯七氟醚吸入麻醉为对照,观察组在对照组基础上术前 30 min 使用右美托咪定滴鼻,结果显示,对照组患儿在 T3~T6 时 HR 较 T0~T2 时显著降低,观察组患儿在 T0~T6 的 HR 和 MAP 水平均无显著变化,提示右美托咪定滴鼻对七氟醚吸入麻醉血流动力学影响具有稳定作用,可减轻患儿应激反应^[18-19]。

围术期脑氧供需平衡与先天性心脏病患儿皮层脑功能有关^[20]。本研究结果显示,T1~T6 时,观察组 Da-jvO₂、CERO₂、A-VGlu 及 A-VLac 水平均显著小于对照组,提示右美托咪定滴鼻复合七氟醚吸入诱导有助于降低术中脑糖氧代谢,具有较好的脑保护作用^[21]。已有研究^[22]证实,先天性心脏病患儿术后可出现不同程度脑认知功能障碍,这与术中脑氧供需失衡有关。本研究发现,观察组术后 1 周和术后 3 个月时认知功能水平显著高于对照组,但术后 1 年两组患儿认知功能比较差异无统计学意义,提示术前右美托咪定滴鼻可减少围术期因脑缺血、缺氧所致的认知功能损害,且其作用主要表现在对近期认知功能的影响。躁动是苏醒期主要并发症。本研究发现,术前使用右美托咪定滴鼻,而后加以七氟醚吸入麻醉可减少麻醉苏醒期躁动发生,提高苏醒质量,分析原因可能与其镇静作用有关^[23]。

综上所述,先天性心脏病介入封堵手术患儿采用右美托咪定滴鼻复合七氟醚吸入诱导麻醉有助于降低术中脑糖氧代谢,减少因脑缺血、缺氧所致的认知功能损害,提高苏醒质量,且对血流动力学影响较小,具有临床应用价值。本研究尚存在不足之处,未对右美托咪定滴鼻复合七氟醚影响先天性心脏病介入封堵术患儿脑糖氧代谢及远近期认知功能进行机制分析,拟在今后进一步探讨。

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· 论著 ·

人免疫球蛋白联合甲泼尼龙治疗儿童重症肺炎的疗效评价

胡高声, 王夏林 (厦门市儿童医院, 福建厦门 361006)

[摘要]目的:探讨人免疫球蛋白在需甲泼尼龙(注射用甲泼尼龙琥珀酸钠)治疗的儿童重症肺炎的应用价值。方法:回顾性分析 2021 年 1 月至 2022 年 6 月在我院住院的重症肺炎患儿资料,选取其中使用了甲泼尼龙但未使用人免疫球蛋白辅助治疗的 44 例患儿为对照组,同时使用了甲泼尼龙和人免疫球蛋白辅助治疗的 47 例患儿为观察组,比较两组患儿的临床症状改善时间、治疗前后影像学、检验结果、疗效及不良反应发生情况。结果:观察组总有效率为 91.49%,高于对照组的 70.45%;临床症状改善时间短于对照组;治疗 2 周后肺部阴影吸收 $\geq 80\%$ 的患儿比例高于对照组;C 反应蛋白(CRP)、白细胞(WBC)计数、降钙素原(PCT)等检验指标降低幅度大于对照组(P 均 <0.05)。两组患儿均无药物不良反应发生。结论:在甲泼尼龙辅助治疗的儿童重症肺炎同时应用人免疫球蛋白安全可行,可有效提高临床疗效。但考虑静脉用人免疫球蛋白属于血液制品,价格昂贵并存在用药风险,建议用药前与患者家属充分沟通,严格遵照用药指征选用。

[关键词]儿童;重症肺炎;甲泼尼龙;人免疫球蛋白;辅助治疗;临床疗效

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Efficacy Evaluation of Human Immunoglobulin Combined with Methylprednisolone in the Treatment of Severe Pneumonia in Children

Hu Gaosheng, Wang Xialin (Xiamen Children's Hospital, Fujian Xiamen 361006, China)

[Abstract] Objective: To probe into the application value of human immunoglobulin in the treatment of severe pneumonia in children requiring methylprednisolone (methylprednisolone sodium succinate for injection). Methods: Clinical data of children with severe pneumonia hospitalized in our hospital from Jan. 2021 to Jun. 2022 were retrospectively analyzed. Forty-four children who received methylprednisolone but no human immunoglobulin as adjuvant therapy were selected as the control group, and 47 children who received methylprednisolone and human immunoglobulin as adjuvant therapy were selected as the observation group. The improvement time of clinical symptom, imaging before and after treatment, test results, efficacy and adverse drug reactions of two groups were analyzed. Results: The total effective rate of the observation group (91.49%) was higher than that of the control group (70.45%). The improvement time of clinical symptoms in the observation group was shorter than that of the control group. The proportion of children with lung shadow absorption $\geq 80\%$ was higher than that of control group after 2 weeks of treatment. The reduction of C-reactive protein (CRP), white blood cell (WBC) count and procalcitonin (PCT) in the observation group was greater than that in control group ($P < 0.05$). No adverse drug reactions occurred in two groups. Conclusion: The application of human immunoglobulin in children with severe pneumonia with methylprednisolone as adjuvant treatment is safe and feasible, which can effectively improve the clinical efficacy. Considering that intravenous human immunoglobulin is the blood product with high cost and medication risk, it is recommended that the clinicians should use human immunoglobulin strictly according to the indications after full communication with family members of patients. **[Keywords]** children; severe pneumonia; methylprednisolone; human immunoglobulin; adjuvant therapy; clinical efficacy

作者简介:胡高声(1969.12-),男,大学本科,副主任药师,主要从事医院药学工作,E-mail:hugaosheng88@126.com。

通信作者:王夏林(1979.07-),女,大学本科,副主任药师,主要从事医院药学工作,E-mail:619244428@qq.com。