

·论著·

东莨菪碱改善先天性室间隔缺损合并肺动脉高压患儿体外循环术后氧合指数的效果探讨

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【摘要】目的 检测东莨菪碱改善先天性室间隔缺损(VSD)合并肺动脉高压(PH)患儿体外循环(CPB)术后氧合指数(OI, $\text{PaO}_2/\text{FiO}_2$)的效果。**方法** 将49例VSD合并PH患儿随机分为两组,治疗组26例,均在麻醉前30分钟肌肉注射东莨菪碱(0.01 mg/kg)和术后静脉注射东莨菪碱(初始剂量 $0.03 \sim 0.05 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$);对照组23例,不用此类药物。两组其它治疗方案均相同。监测和对比两组患儿术后6 h内平均OI、平均气道峰压、机械通气时间,以及拔管后IO,以评价东莨菪碱的疗效。

结果 治疗组术后6 h内平均OI为 $(268.5 \pm 58.0) \text{ mmHg}$,对照组为 $(233.5 \pm 40.8) \text{ mmHg}$,经统计学分析差异有意义($t = 2.402, P = 0.011$);治疗组平均气道峰压 $(21.2 \pm 2.2) \text{ cmH}_2\text{O}$,对照组为 $(22.0 \pm 3.2) \text{ cmH}_2\text{O}$,经统计学分析差异无意义($t = 0.979, P = 0.164$);机械通气时间治疗组 $(13.7 \pm 7.9) \text{ h}$,短于对照组的 $(19.7 \pm 13.0) \text{ h}$,经统计学分析差异有意义($t = 1.935, P = 0.029$);治疗组拔管后氧合指数为 $(285.0 \pm 32.3) \text{ mmHg}$,对照组 $(243.7 \pm 40.1) \text{ mmHg}$,差异有统计学意义($t = 3.897, P = 0.001$)。2例患儿出现用药不良反应(腹胀)。**结论** 东莨菪碱的适量应用能明显提高VSD合并PH患儿CPB术后OI,缩短术后机械通气时间。

【关键词】 室间隔缺损;高血压,肺性;东莨菪碱;体外循环

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【Abstract】Objective To detect the improving effect of scopolamine on oxygenation index (OI, $\text{PaO}_2/\text{FiO}_2$) in children with congenital ventricular septal defect (VSD) and pulmonary hypertension (PH) after cardiopulmonary bypass. **Methods** A total of 49 VSD/PH children were randomly divided into treatment ($n = 26$) and control ($n = 23$) groups. In treatment group, at 30 min before anesthesia, there was an intramuscular injection of scopolamine $0.01 \text{ mg} \cdot \text{kg}^{-1}$ and followed by a continuous intravenous infusion of scopolamine at the end of operation (an initial dose $0.03 \sim 0.05 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$). In control group, scopolamine was not used. The remaining schedules were the same. The values of average OI within 6h post-operation, average peak airway pressure, mechanical ventilation time (MVT) and OI post-extubation were monitored, compared and used for evaluating the curative effect of scopolamine. **Results** Two cases were removed out of treatment group. Compared with monitoring values of control group, the average OI of treatment group significantly increased within 6h post-operation (268.5 ± 58.0 vs. $233.5 \pm 40.8 \text{ mmHg}, P < 0.05$). No significant difference existed in average peak airway pressure (21.2 ± 2.2 vs. $22.0 \pm 3.2 \text{ cmH}_2\text{O}, P > 0.05$). MVT (13.7 ± 7.9 vs. $19.7 \pm 13.0 \text{ h}, P < 0.05$) and OI post-extubation (285.0 ± 32.3 vs. $243.7 \pm 40.1 \text{ mmHg}, P < 0.05$) obviously improved in treatment group. Drug adverse reactions: there were 2 cases of abdominal distension. **Conclusion** An optimal amount of scopolamine may improve OI and shorten the duration of mechanical ventilation in VSD/PH children after CPB.

【Key words】 Heart Septal Defects, Ventricular; Hypertension, Pulmonary; Scopolamine; Extracorporeal Circulation

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先天性室间隔缺损(VSD)合并肺动脉高压(PH)患儿在体外循环(CPB)下行心内直视手术后,易发生低氧血症、肺部感染等情况^[1]。其原因为VSD合并PH患儿发育相对落后,术前有反复呼吸道感染病史、肺部血管病变、CPB和手术导致的急性肺损伤,术后血流动力学不稳定需要长时间镇静和机械通气损伤等^[2-5]。虽然近些年来有报道通过静脉泵入西地那非,吸入一氧化氮和伊洛前列素溶液(万他维),对稳定患儿CPB术后血流动力学有良好的治疗效果,明显降低了术后肺动脉高压危象^[6,7]。但对PH患儿CPB术后的肺水肿、肺部感染、低氧血症等情况的改善作用不明显^[8],鉴于在肺部重症疾病的救治中,东莨菪碱对于重症肺炎、急性肺损伤、肺水肿有显著的辅助治疗效果^[9-11],并且可以改善肺循环,增强术后镇静效果,降低消化道反应^[12]。2011年10月至2016年3月,本院在围术期应用东莨菪碱对VSD合并PH患儿CPB术后进行辅助治疗,现将其对术后氧合指数的改善情况报道如下。

材料与方法

一、一般资料

49例VSD合并PH患儿,男性28例,女性21例,年龄2.7~18.3岁,平均(10.1 ± 4.4)岁,按美国纽约心脏病学会(NYHA)制定的心功能分级标准^[13]:心功能I级44例,心功能II级5例;超声心动图报告:VSD直径6~18 mm,平均(10.5 ± 2.3) mm,干下型3例,膜周型46例,左心室增大49例,右心室增大32例,双向分流2例;术前静息下动脉氧分压(PaO₂)为70~94 mmHg,平均(87.6 ± 4.9) mmHg,平均肺动脉压(MPAP)30~70 mmHg,平均(40.4 ± 9.1) mmHg,肺血管阻力(PVR)326~1052 dyn·s·cm⁻⁵,平均(547.9 ± 164.7) dyn·s·cm⁻⁵,PP/PS:0.34~0.91,平均(0.51 ± 0.12),术前胸部DR片均显示肺部纹理增粗,心胸比例0.55~0.71,肺动脉段突出,无肺部感染及肺不张。

将患儿随机分为对照组和治疗组,对照组23例,治疗组26例,两组患儿年龄、体重、心功能、VSD直径、静息PaO₂、MPAP、PVR、PP/PS等指标比较差异无统计学意义(表1)。剔除标准:围术期发生肾功能衰竭、肺栓塞等严重并发症或死亡,明显影响统计结果的病例予以剔除。本研究术中1例因主动脉夹层导致中枢神经植物状态,1例术后11 h 因肺

动脉高压危象死亡,均发生在治疗组,因此该两例患儿从研究样本中剔除。

表1 两组患儿的临床资料

Table 1 Clinical data of two groups of children

项目	对照组 (n=23)	治疗组 (n=24)	t/χ^2 值	P值
年龄(岁)	10.3 ± 4.6	9.9 ± 4.4	0.292	0.39
男/女(例)	13/10	13/11	0.026	0.93
体重(kg)	30.5 ± 13.8	30.3 ± 14.0	0.039	0.48
室缺类型(干下/膜部)	2/21	1/23	0.604	0.48
室缺直径(mm)	10.3 ± 2.8	10.8 ± 1.8	0.657	0.26
NYHA 分级(I/II)	20/3	22/2	0.274	0.50
术前静息氧分压 (mmHg)	88.0 ± 5.0	87.3 ± 4.9	0.430	0.33
术前平均肺动脉压 (mmHg)	40.6 ± 9.7	40.2 ± 8.6	0.134	0.45
术前平均肺血管阻力 (dyn·s·cm ⁻⁵)	529.3 ± 161.7	565.8 ± 169.0	0.756	0.23
PP/PS	0.48 ± 0.13	0.55 ± 0.11	1.925	0.06

注:PP/PS:肺循环平均动脉压比体循环平均动脉压,1 mmHg=0.133 kPa

二、麻醉、体外循环及手术方法

麻醉前30 min用药:对照组吗啡0.2 mg/kg肌肉注射,治疗组吗啡0.2 mg/kg+东莨菪碱0.01 mg/kg肌肉注射。麻醉诱导:静脉咪达唑仑0.05 mg/kg,舒芬太尼0.1 ug/kg,顺苯磺酸阿曲库铵0.2 mg/kg。切皮前适量追加并微量泵持续静脉泵入。CPB应用Sorin膜式氧合器及管道,预充人血白蛋白0.3~0.5 g/kg。体外循环中心温度30℃~32℃,体外循环转流时间55~116 min,主动脉阻断时间28~86 min。手术方式:均经胸骨正中切口,直视下VSD涤纶补片修补术,3例干下型经肺动脉根部修补VSD,2例双向分流患儿采用活瓣式补片修补。停CPB后经肺动脉测MPAP。

三、术后处理及东莨菪碱应用方法

所有患儿术后入监护室,给予咪达唑仑+舒芬太尼持续静脉泵入,充分镇静、镇痛,呼吸机辅助/控制呼吸,或间歇指令通气模式,呼吸频率18~24次/min,潮气量10 mL/kg,PEEP 3~8 cmH₂O,维持PaCO₂<40 mmHg,PH>7.45,吸痰前临时追加镇静及镇痛药物,并给予纯氧吸入。吸痰过程中注意观察心率、体循环血压、肺动脉血压、氧饱和度等检测指标变化情况^[14]。另外,给予抗感染(二代头孢类抗生素)、乌司他丁、多巴胺、前列地尔、西地那非等药物治疗^[15]。治疗组静脉泵入东莨菪碱^[10,11],初始剂量0.03~0.05 mg·kg⁻¹·h⁻¹,床旁DR未见明显肺部感染、水肿,肺部无明显湿性啰音并氧

合指数(OI, $\text{PaO}_2/\text{FiO}_2$)大于 200 mmHg, 将剂量调整为 $0.01 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$, 调整呼吸机模式和参数, 循环稳定, 可撤机拔除气管插管, 并逐步停用。

四、监测指标

分别于术后 1 h、3 h、6 h、9 h 复查动脉血气分析, 之后每 8 h 复查血气分析 1 次, 拔除气管插管前、后 0.5 h 复查血气分析, 检测血气分析时记录气道峰压、氧浓度, 拔管时记录机械通气时间。计算术后 6 h 内平均氧合指数($\text{MOI}_{6\text{h}}$), 平均气道峰压(MAPP, 记录气道峰压值 - PEEP 值)、机械通气时间(MVT), 以及拔管后 OI。

五、统计学处理

应用 SPSS 16.0 软件进行统计学分析。计量资料数据以均数 \pm 标准差($\bar{x} \pm s$)表示, 并进行正态分布检验和方差齐性分析, 符合正态分布、方差齐时采用 t 检验, 否则采用秩和检验; 计数资料以百分比表示, 采用 χ^2 检验, 以 $P < 0.05$ 视为差异有统计学意义。

结 果

治疗组 24 例和对照组 23 例患儿相比较, 治疗组术后 6 h 内平均 OI 为 (268.5 ± 58.0) mmHg, 对照组为 (233.5 ± 40.8) mmHg, 经统计学分析差异有意义($t = 2.402, P = 0.011$); 治疗组平均气道峰压 (21.2 ± 2.2) cmH₂O, 对照组为 (22.0 ± 3.2) cmH₂O, 经统计学分析差异无意义($t = 0.979, P = 0.164$); 机械通气时间治疗组 (13.7 ± 7.9) h, 短于对照组的 (19.7 ± 13.0) h, 经统计学分析差异有意义($t = 1.935, P = 0.029$); 治疗组拔管后氧合指数为 (285.0 ± 32.3) mmHg, 对照组 (243.7 ± 40.1) mmHg, 经统计学分析差异有意义($t = 3.897, P = 0.001$)。用药不良反应: 2 例患儿有腹胀, 停药后给予开塞露纳肛, 腹胀消失。

表 2 两组患儿的结果资料统计($\bar{x} \pm s$)

Table 2 Parametric statistics of two groups of children ($\bar{x} \pm s$)

项目	对照组 (n=23)	治疗组 (n=24)	t 值	P 值
$\text{MOI}_{6\text{h}}(\text{mmHg})$	233.5 ± 40.8	268.5 ± 58.0	2.402	0.011
MAPP(cmH ₂ O)	22.0 ± 3.2	21.2 ± 2.2	0.979	0.164
MVT(h)	19.7 ± 13.0	13.7 ± 7.9	1.935	0.029
拔管后 OI(mmHg)	243.7 ± 40.1	285.0 ± 32.3	3.897	0.001

讨 论

患儿在全身麻醉、CPB、手术创伤之后, 灌注肺、全身炎症反应综合征(SIRS)导致肺水肿、肺不张、急性肺损伤、肺部感染, 甚至急性呼吸窘迫综合征(ARDS)等情况, 导致心脏术后低氧血症增高, MVT 延长^[19,20]。另外, 重度 PH 患儿肺血管病变严重, 术后影响循环稳定, 膈肌麻痹呈矛盾运动, 导致功能残气量降低和肺泡萎陷, 都可能进一步延长 MVT, 增加肺部感染机率^[6,21]。上述情况导致患儿术后 OI 下降、ICU 停留时间延长。

东莨菪碱为一种阻断 M 型胆碱能受体药物, 外周作用较强, 维持时间短, 对呼吸中枢有兴奋作用, 中枢神经以抑制作用为主, 能抑制腺体分泌, 解除毛细血管痉挛, 改善微循环, 扩张支气管, 解除平滑肌痉挛; 与其它镇静药物应用有协同作用。东莨菪碱因为以上作用不但在肺部感染、ARDS、慢性阻塞性肺气肿以及呼吸功能衰竭等辅助治疗中效果显著^[22-24], 而且在个别心脏外科中心将其作为术前降低 PH 的辅助用药。在国内也有少数 CPB 术后应用东莨菪碱的报道^[13], 通过静脉泵入东莨菪碱, 对纠正先心病术后低氧血症效果明显; 国外关于此类的报道较为罕见。

本研究受试者为 VSD 合并 PH 患儿, 术前肺部反复感染, 术后肺部情况及 OI 普遍较差, MVT 明显延长, 这与赖军华^[24]、颜洪顺^[25]和高毅^[7]等的研究结论是一致的。东莨菪碱的大脑皮质抑制作用有利于患儿术后充分的镇静, 避免术后躁动, 降低了肺动脉高压危象几率; 同时其对肺部支气管和肺泡的解痉、减少渗出和分泌作用, 改善了肺通气功能^[24]; 对肺部微循环的改善, 促进了肺血流重新分配, 优化气血比, 提高了肺部血气交换作用^[13,26]; 另外, 抗 M-胆碱作用其呼吸中枢兴奋作用也有利于患儿的脱机拔管。本研究中治疗组患儿的 $\text{MOI}_{6\text{h}}$ 、MVT、拔管后 OI 明显优于对照组。东莨菪碱的以上作用非常符合 VSD 合并 PH 患儿术后的病理生理特点, 适合作为该类患儿的围术期用药。另外, 东莨菪碱可通过抑制 IL-17 等炎性介质的释放, 减轻 SIRS, 降低气道炎症反应^[25,26]; 东莨菪碱还可减低体外循环时心肌内一氧化氮的表达, 降低心肌缺血再灌注损伤, 具有保护心肌的作用^[27,28,29]。

另外, 东莨菪碱还可通过抑制 IL-17 等炎性介质的释放, 减轻 SIRS, 降低气道炎症反应^[27,28]; 东莨

菪碱还可减低体外循环时心肌内一氧化氮的表达,降低心肌缺血再灌注损伤,具有保护心肌的作用^[29,30,31]。

东莨菪碱的适量应用能明显减轻室间隔缺损合并肺动脉高压患儿体外循环术后肺水肿、肺泡渗出和支气管腺体分泌,改善肺换气功能,并解除气管和支气管痉挛,改善肺通气功能,提高氧合指数;缩短机械通气时间。建议对 VSD 合并 PH 的患儿作为围术期一线用药。本研究的不足之处:未对肺动脉高压患儿按分级或分期进行亚组的分析报道,可能会对结果产生影响。

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