不同剂量枸橼酸舒芬太尼对克鲁宗综合征颅面重建术患儿镇痛效果的影响

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中图分类号　R91　　**文献标志码**　A　　**文章编号**　1001-0408（2016）29-4139-04
DOI　10.6039/j.issn.1001-0408.2016.29.35

摘　要　目的：探讨不同剂量枸橼酸舒芬太尼对克鲁宗综合征患儿颅面重建术的血流动力学指标和应激性反应指标的影响。方法：选择2010年1月—2016年1月在我院接受治疗的60例克鲁宗综合征需行颅面重建术的患儿，按照随机数字表法分为A组、B组和C组，各20例。3组患儿行麻醉诱导后，泵注丙泊酚注射液4～8 mg/（kg·h）+枸橼酸舒芬太尼注射液[A组0.3 μg/（kg·h），泵注；B组0.6 μg/（kg·h），泵注；C组1.0 μg/kg，iv，0.5 h/次]维持麻醉深度，间隔40 min给予注射用苯磺顺阿曲库铵0.1 mg/kg，iv，于手术结束前5 min停止给药。观察3组患儿不同时刻的血流动力学指标[动脉压（MAP）和心率（HR）]、应激性反应指标[促肾上腺皮质激素（ACTH）和皮质醇]，以及不良反应发生情况。结果：C组患儿切皮后5 min、手术后1 h、手术结束即刻的MAP均明显高于麻醉前，B组患儿同时刻MAP明显低于C组患儿；A组患儿手术后1 h和C组患儿切皮后5 min、手术后1 h的HR明显高于其麻醉前，B组患儿手术后1 h的HR明显低于A组患儿，且切皮后5 min、手术后1 h的HR明显低于C组患儿；3组患儿切皮后5 min、手术后1 h、手术结束即刻的ACTH水平均明显高于麻醉前，B组患儿切皮后5 min、手术后1 h、手术结束即刻的ACTH水平均明显低于A组和C组患儿，A组患儿同时刻明显低于C组患儿；A组患儿手术后1 h和C组患儿切皮后5 min、手术后1 h、手术结束即刻的皮质醇水平明显高于麻醉前，B组患儿手术后1 h的皮质醇水平明显低于A组患儿，A组患儿切皮后5 min、手术结束即刻的皮质醇水平和B组患儿切皮后5 min、手术后1 h、手术结束即刻均明显低于C组患儿，以上比较差异均有统计学意义（$P<0.05$）。3组患儿麻醉期间均未见明显不良反应发生。结论：泵注枸橼酸舒芬太尼0.6 μg/（kg·h）维持小儿克鲁宗综合征颅面重建术的麻醉深度，患儿血流动力学稳定，可有效抑制术中应激性反应，且安全性高。

关键词　枸橼酸舒芬太尼；克鲁宗综合征；颅面重建术；血流动力学；应激性反应

Effects of Different Doses of Sufentanil Citrate on Analgesic Effects of Crouzon Syndrome Children with Craniofacial Reconstruction

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ABSTRACT　OBJECTIVE: To investigate the effects of different doses of sufentanil citrate on hemodynamic indexes and stress response indexes of Crouzon syndrome children with craniofacial reconstruction. METHODS: 60 cases of Crouzon syndrome undergoing craniofacial reconstruction were selected from our hospital during Jan. 2010-Jan. 2016, and then randomly divided into group A, group B and group C, with 20 cases in each group. 3 groups were given pump injection of Propofol injection 4-8 mg/(kg·h) for anesthesia induction+Sufentanil citrate injection [group A 0.3 μg/(kg·h), pump injection; group B 0.6 μg/(kg·h), pump injection; group C 1.0 μg/kg, iv, 0.5 h/time] for anesthesia maintenance, Cisatracurium besilate for injection 0.1 mg/kg, iv, every 40 min, drug withdrawal 5 min before the end of surgery. The hemodynamic indexes (MAP, HR) and stress response indexes (ACTH, cortisol) were observed in 3 groups at different time points as well as the occurrence of ADR. RESULTS: MAP levels of group C at 5 min after skin incision, 1 h after operation and immediately at the end of surgery were significantly higher than before anesthesia, while those of group B were significantly higher than group C at same time points. HR of group A at 1 h after surgery and that of group B at 5 min after skin incision and 1 h after surgery were significantly higher than before anesthesias; HR of group B at 1 h after surgery was significantly lower than that of group A, and its HR at 5 min after skin incision and 1 h after surgery were significantly lower than those of group C. ACTH levels of 3 groups at 5 min after skin incision, 1 h after surgery and immediately after the end of surgery were significantly higher than before anesthesia. ACTH levels of group B at 5 min after skin incision, 1 h after surgery and immediately after the end of surgery were significantly lower than those of group A and C, and the group A was significantly lower than the group C at same time points. Cortisol levels of group A at 1 h after surgery, and those of group C at 5 min after skin incision, 1 h after surgery and immediately after the end of surgery were significantly higher than before anesthesia. Cortisol levels of group B at 1 h after surgery were significantly lower than those of group A; cortisol levels of group A at 5 min after skin incision and immediately after the end of surgery and those of group B at 5 min after skin incision, 1 h after surgery and immediately after the end of surgery were all significantly lower than those of group C. There were statistical significance all above ($P<0.05$). No obvious ADR was found in 3 groups. CONCLUSIONS: Pump injection of sufentanil citrate 0.6 μg/(kg·h) can maintain analgesic effect of Crouzon syndrome children with craniofacial reconstruction, can keep hemodynamics sta-

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ble and effectively inhibit stress response during surgery with good safety.
KEYWORDS Sufentanil citrate; Crouzon syndrome; Craniofacial reconstruction; Hemodynamic; Stress response

克鲁宗综合征(Crouzon syndrome)是一组由多发性颅部骨缝和面部骨缝早闭引起的颅部和面部复合畸形的症候群,为常染色体显性遗传疾病,常伴有颅内压增高症。先天性颅缝早闭症患儿中约4.8%为克鲁宗综合征,其在新生儿中的发病率约为0.33‰～0.04‰[1]。克鲁宗综合征引起的颅缝早闭可见于冠状缝、矢状缝等,表现为舟状头、三角头等头颅异常,严重影响患者生活质量。颅面重建术治疗克鲁宗综合征可取得明显效果,手术时间较长,手术过程中要求有效镇痛和血流动力学指标的平稳。芬太尼和舒芬太尼均为阿片类受体激动药,芬太尼在小儿麻醉中取得了一定效果,但舒芬太尼在维持患者血流动力学稳定性和镇痛效果等方面均优于芬太尼[2-3]。目前,舒芬太尼用于克鲁宗综合征患儿颅面重建术中对血流动力学指标的影响和镇痛效果的相关报道较为少见。鉴于此,本研究观察了不同剂量枸橼酸舒芬太尼对克鲁宗综合征患儿颅面重建术的血流动力学指标和应激性反应指标的影响,现报道如下。

1 资料与方法

1.1 纳入与排除标准

纳入标准:(1)符合克鲁宗综合征诊断标准[4]和手术指征;(2)年龄<16岁;(3)患儿监护人均知情同意并签署知情同意书。

排除标准:(1)合并先天性心脏病者;(2)严重肝、肾功能不全者;(3)合并其他重大疾病不能耐受麻醉和手术者。

1.2 研究对象

本研究方案经医院医学伦理委员会审核通过后,选择2010年1月—2016年1月在我院接受治疗的60例克鲁宗综合征需行颅面重建术的患儿,按照随机数字表法分为A组、B组和C组,各20例。其中,A组患儿男性11例,女性9例;年龄8个月～11岁,平均(3.6±2.3)岁;体质量(16.8±3.9)kg。B组患儿男性13例,女性7例;年龄7个月～12岁,平均(3.9±2.2)岁;体质量(17.3±4.2)kg。C组患儿男性10例,女性10例;年龄9个月～13岁,平均(3.8±2.5)岁;体质量(16.3±3.2)kg。3组患儿在性别比、年龄和体质量等一般资料方面比较,差异均无显著统计学意义($P>0.05$),具有可比性。

1.3 麻醉方法

3组患儿均给予盐酸戊乙奎醚注射液(成都力思特制药股份有限公司,批准文号:国药准字H20051948,规格:1 ml∶1 mg)0.01 mg/kg+枸橼酸芬太尼注射液(宜昌人福药业有限责任公司,批准文号:国药准字H20054171,规格:1 ml∶50 μg)3 μg/kg+咪达唑仑注射液(江苏恩华药业股份有限公司,批准文号:国药准字H20031037,规格:2 ml∶2 mg)0.05 mg/kg+丙泊酚注射液(江苏恩华药业股份有限公司,批准文号:国药准字H20123138,规格:20 ml∶0.2 g)1.0～1.5 mg/kg+注射用苯磺顺阿曲库铵(上海恒瑞医药股份有限公司,批准文号:国药准字H20060869,规格:10 mg)0.15 mg/kg,iv行麻醉诱导;行气管插管后均泵注丙泊酚注射液4～8 mg/(kg·h)+枸橼酸舒芬太尼注射液维持麻醉深度。其中,A组患儿泵注枸橼酸舒芬太尼0.3 μg/(kg·h),B组患儿泵注枸橼酸舒芬太尼0.6 μg/(kg·h),C组患儿于切皮前给予枸橼酸舒芬太尼1.0 μg/kg,iv,0.5 h/次;3组患儿均间隔40 min给予注射用苯磺顺阿曲库铵0.1 mg/kg,iv。3组患儿均行桡动脉穿刺、深静脉穿刺监测有创动脉压(MAP)和中心静脉压,并于颅面重建术手术结束前5 min停止给药。

1.4 观察指标

(1)观察3组患儿麻醉前、麻醉诱导后、切皮后5 min、手术后1 h、手术结束即刻的血流动力学指标,如MAP、心率(HR);(2)观察3组患儿麻醉前、麻醉诱导后、切皮后5 min、手术后1 h和手术结束即刻的促肾上腺皮质激素(ACTH)和皮质醇水平;(3)观察3组患儿麻醉期间的不良反应发生情况。

1.5 统计学方法

采用SPSS 13.0软件对数据进行统计分析。计量资料以$\bar{x}\pm s$表示,采用t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 3组患儿MAP比较

3组患儿麻醉前MAP比较,差异均无统计学意义($P>0.05$)。C组患儿切皮后5 min、手术后1 h、手术结束即刻的MAP均明显高于麻醉前,B组患儿同时刻MAP明显低于C组患儿,差异均有统计学意义($P<0.05$)。3组患儿不同时刻MAP比较见表1。

表1 3组患儿不同时刻MAP比较($\bar{x}\pm s$,mm Hg)

Tab 1 Comparison of MAP levels among 3 groups at different time points($\bar{x}\pm s$, mm Hg)

组别	n	麻醉前	麻醉诱导后	切皮后5 min	手术后1 h	手术结束即刻
A组	20	71.3±5.6	69.9±5.4	73.9±4.9	72.5±5.4	73.4±5.4
B组	20	70.9±6.2	68.3±5.9	71.5±5.2#	70.8±4.6#	71.6±5.1#
C组	20	71.4±5.3	70.1±6.1	77.4±4.6△	76.1±4.9△	75.9±4.3△

注:1 mm Hg=0.133 kPa;与C组比较,#$P<0.05$;与麻醉前比较,△$P<0.05$

Note: 1 mm Hg=0.133 kPa; vs. group C, #$P<0.05$; vs. before anesthesia, △$P<0.05$

2.2 3组患儿HR比较

3组患儿麻醉前HR比较,差异均无统计学意义($P>0.05$)。A组患儿手术后1 h和C组患儿切皮后5 min、手术后1 h的HR明显高于其麻醉前,差异均有统计学意义($P<0.05$)。B组患儿手术后1 h的HR明显低于A组患儿,且切皮后5 min、手术后1 h的HR明显低于C组患儿,差异均有统计学意义($P<0.05$)。3组患儿不同时刻HR比较见表2。

表2 3组患儿不同时刻HR比较($\bar{x}\pm s$,次/min)

Tab 2 Comparison of HR among 3 groups at different time points($\bar{x}\pm s$, time/min)

组别	n	麻醉前	麻醉诱导后	切皮后5 min	手术后1 h	手术结束即刻
A组	20	112.1±19.6	125.6±21.4	129.6±24.5	136.5±18.9△	121.2±15.9
B组	20	115.4±20.7	124.1±20.5	118.5±16.8#	116.4±17.4*#	114.2±15.6
C组	20	109.7±21.5	119.8±19.9	137.5±21.0△	139.5±16.3△	124.5±17.3

注:与A组比较,*$P<0.05$;与C组比较,#$P<0.05$;与麻醉前比较,△$P<0.05$

Note: vs. group A, *$P<0.05$; vs. group C, #$P<0.05$; vs. before anesthesia, △$P<0.05$

2.3 3组患儿ACTH水平比较

3组患儿麻醉前ACTH水平比较,差异均无统计学意义($P>0.05$)。3组患儿切皮后5 min、手术后1 h、手术结束即刻的ACTH水平均明显高于麻醉前,差异均有统计学意义($P<0.05$)。B组患儿切皮后5 min、手术后1 h、手术结束即刻的ACTH水平均明显低于A组和C组患儿,A组患儿同时刻明显低于C组患儿,差异均有统计学意义($P<0.05$)。3组患儿不同时刻ACTH水平比较见表3。

表3　3组患儿不同时刻ACTH水平比较（$\bar{x}\pm s$，pg/ml）

Tab 3　Comparison of ACTH levels among 3 groups at different time points（$\bar{x}\pm s$，pg/ml）

组别	n	麻醉前	麻醉诱导后	切皮后5 min	手术后1 h	手术结束即刻
A组	20	15.1±2.3	17.6±2.9	26.8±3.9$^{\#\Delta}$	32.5±4.2$^{\#\Delta}$	45.7±5.9$^{\#\Delta}$
B组	20	14.6±2.5	18.5±3.1	21.5±3.6$^{*\#\Delta}$	24.5±4.1$^{*\#\Delta}$	32.5±6.4$^{*\#\Delta}$
C组	20	14.9±2.6	18.4±3.2	31.4±4.2$^{\Delta}$	39.6±5.4$^{\Delta}$	68.7±5.4$^{\Delta}$

注：与A组比较，$^{*}P<0.05$；与C组比较，$^{\#}P<0.05$；与麻醉前比较，$^{\Delta}P<0.05$

Note：vs. group A，$^{*}P<0.05$；vs. group C，$^{\#}P<0.05$；vs. before anesthesia，$^{\Delta}P<0.05$

2.4　3组患儿皮质醇水平比较

3组患儿麻醉前皮质醇水平比较，差异均无统计学意义（$P>0.05$）。A组患儿手术后1 h和C组患儿切皮后5 min、手术后1 h、手术结束即刻的皮质醇水平明显高于麻醉前，差异均有统计学意义（$P<0.05$）。B组患儿手术后1 h的皮质醇水平明显低于A组患儿，A组患儿切皮后5 min、手术结束即刻的皮质醇水平和B组患儿切皮后5 min、手术后1 h、手术结束即刻均明显低于C组患儿，差异均有统计学意义（$P<0.05$）。3组患儿不同时刻皮质醇水平比较见表4。

表4　3组患儿不同时刻皮质醇水平比较（$\bar{x}\pm s$，ng/ml）

Tab 4　Comparison of cortisol levels among 3 groups at different time points（$\bar{x}\pm s$，ng/ml）

组别	n	麻醉前	麻醉诱导后	切皮后5 min	手术后1 h	手术结束即刻
A组	20	139.5±8.9	141.1±8.5	144.5±8.1$^{\#}$	159.2±9.6$^{\Delta}$	145.6±8.7$^{\#}$
B组	20	142.5±8.1	143.1±8.4	144.5±8.2$^{\#}$	148.7±9.4$^{*\#}$	142.2±8.2$^{\#}$
C组	20	143.2±9.2	144.2±9.1	156.4±7.9$^{\Delta}$	165.4±10.2$^{\Delta}$	157.8±8.9$^{\Delta}$

注：与A组比较，$^{*}P<0.05$；与C组比较，$^{\#}P<0.05$；与麻醉前比较，$^{\Delta}P<0.05$

Note：vs. group A，$^{*}P<0.05$；vs. group C，$^{\#}P<0.05$；vs. before anesthesia，$^{\Delta}P<0.05$

2.5　不良反应

3组患儿麻醉期间均未见明显不良反应发生。

3　讨论

克鲁宗综合征患儿行颅面重建术要求镇痛有效和血流动力学平稳，患儿的器官发育尚未完全成熟，该手术持续时间较长，出血量较大，围术期风险较大，对麻醉要求较高。麻醉诱导、气管插管和术中操作等均可造成剧烈刺激，导致机体发生一系列变化，如血流动力学指标、血浆ACTH和皮质醇水平等[5-7]。因此，克鲁宗综合征患儿颅面重建术的麻醉方案的选择具有重要的临床意义。

芬太尼为临床常用镇痛药物，舒芬太尼为芬太尼的衍生物，其亲脂性为芬太尼的2倍，镇痛作用强于芬太尼[8-9]。舒芬太尼扩散至机体组织，更易透过血脑屏障达到有效血药浓度，其起效时间短于芬太尼[10-12]。芬太尼因结合α-酸性糖蛋白较为疏松，在血浆中含量较少，故更易分布于机体组织，分布容积较大；舒芬太尼分布容积较小，清除半衰期较短，清除率较高，作用持续时间和苏醒时间均较短，且反复用药在机体的蓄积较少，对术后苏醒具有临床意义[12-13]。舒芬太尼作为最为强效的阿片类镇痛药物，其镇痛强度为芬太尼的5～13倍，应用于临床维持血流动力学平稳和抑制术中创伤所致的应激性反应具有明显优势[14]。本研究结果显示，A组和B组患儿通过泵注枸橼酸舒芬太尼维持术中麻醉深度，相较于C组患儿的血流动力学指标更平稳，且ACTH和皮质醇水平均低于不同时刻的C组患儿，可见泵注枸橼酸舒芬太尼应用于小儿克鲁宗综合征颅面重建术的镇痛效果较佳，与其他研究较为一致。王小燕等[15]给予心脏手术患儿舒芬太尼的研究显示，术中患儿的MAP、HR等指标波动均明显低于芬太尼组患儿，可见舒芬太尼用于患儿的手术麻醉有助于维持其血流动力学平稳。

枸橼酸舒芬太尼应用安全范围较大，但关于其在小儿克鲁宗综合征颅面重建术中的剂量和效果的讨论较为少见。本研究结果显示，B组患儿经麻醉诱导后泵注枸橼酸舒芬太尼0.6 μg/（kg·h）的血流动力学指标较A组患儿给予的0.3 μg/（kg·h）更平稳。动物研究给予犬不同剂量的舒芬太尼，iv，结果显示舒芬太尼4 μg/kg的剂量可使犬的HR降低22%，心输出量降低30%；增加舒芬太尼剂量至500 μg/kg时，其血流动力学相关指标并未发生显著变化[16-17]。本研究结果亦显示，泵注枸橼酸舒芬太尼0.6 μg/（kg·h）对患儿血流动力学并未造成明显波动，仅在手术后1 h时患儿的HR值明显低于A组患儿。本研究进一步比较3组患儿应激性反应的相关指标，结果显示B组患儿的ACTH和皮质醇水平波动均较A组和C组患儿平稳，可见泵注枸橼酸舒芬太尼0.6 μg/（kg·h）可有效抑制术中应激性反应。3组患儿麻醉期间均未见明显不良反应发生，可见其安全性高。

综上所述，泵注枸橼酸舒芬太尼0.6 μg/（kg·h）维持小儿克鲁宗综合征颅面重建术的麻醉深度，患儿血流动力学稳定，可有效抑制术中应激性反应，且安全性高。本研究存在的不足之处在于样本量小，还需要临床大样本的研究证实。

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匹多莫德联合孟鲁司特钠治疗儿童支气管哮喘的临床观察

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中图分类号　R725.6　　**文献标志码**　A　　**文章编号**　1001-0408（2016）29-4142-03
DOI　10.6039/j.issn.1001-0408.2016.29.36

摘　要　目的：观察匹多莫德联合孟鲁司特钠治疗儿童支气管哮喘的临床疗效及安全性。方法：选取支气管哮喘患儿120例，按随机数字表法分为对照组和观察组，各60例。两组患儿均给予雾化吸入糖皮质激素和积极抗感染等常规治疗。对照组患儿在常规治疗的基础上睡前口服孟鲁司特钠咀嚼片5 mg，qd；观察组患者在对照组基础上口服匹多莫德胶囊0.4 g，qd。两组患儿均持续治疗3个月。观察两组患儿临床疗效及治疗前后血清白细胞介素4（IL-4）、干扰素γ（IFN-γ）、免疫球蛋白E（IgE）水平、T淋巴细胞亚群及肺功能指标，并比较两组患儿不良反应发生情况。结果：观察组患儿临床有效率为88.3%，显著高于对照组的61.7%。两组患儿治疗前IL-4、IFN-γ、IgE水平、T淋巴细胞亚群、肺功能指标比较，差异无统计学意义（$P>0.05$），两组患者治疗后IL-4、IFN-γ、IgE水平、$CD4^+$、$CD4^+/CD8^+$、肺功能指标均显著改善，且观察组明显优于对照组，差异均有统计学意义（$P<0.05$）。两组患儿不良反应发生率比较，差异无统计学意义（$P>0.05$）。结论：匹多莫德联合孟鲁司特钠治疗儿童支气管哮喘疗效显著，能明显减轻患儿气道炎症，增强免疫能力，提高肺功能，且安全性较好。

关键词　匹多莫德；孟鲁司特钠；儿童；支气管哮喘

Clinical Observation of Pidotimod Combined with Montelukast Sodium in the Treatment of Children with Bronchial Asthma

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ABSTRACT　OBJECTIVE: To observe clinical efficacy and safety of pidotimod combined with montelukast sodium in the treatment of children with bronchial asthma. METHODS: 120 children with bronchial asthma were randomly divided into control group and observation group, with 60 cases in each group. Both group were given routine treatment as aerosol inhalation of glucocorticoid and anti-infective treatment. Control group was additionally given Montelukast sodium chewable tablet 5 mg orally, qd, at bedtime; observation group was additionally given Pidotimod capsule 0.4 g, qd, on the basis of control group. Both group received treatment for consecutive 3 months. Clinical efficacies of 2 groups were observed as well as IL-4, IFN-γ, IgE, T lymphocyte subset and lung function indexes of 2 groups before and after treatment. The occurrence of ADR were compared between 2 groups. RESULTS: The effective rate of observation group was 88.3%, which was significantly higher than that of control group (61.7%). There was no statistical significance in IL-4, IFN-γ, IgE, T lymphocyte subset and lung function indexes between 2 groups before treatment ($P>0.05$). After treatment, IL-4, IFN-γ, IgE, $CD4^+$, $CD4^+/CD8^+$ and lung function of 2 groups were improved significantly, and the observation group was significantly better than the control group, with statistical significance ($P<0.05$). There was no statistical significance in the incidence of ADR between 2 groups ($P>0.05$). CONCLUSIONS: Pidotimod combined with montelukast sodium is effective for children with bronchial asthma, and can significantly relieve airway inflammation, enhance immunity and improve lung function with good safety.

KEYWORDS　Pidotimod; Montelukast sodium; Children; Bronahial asthma

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（收稿日期：2016-03-30　修回日期：2016-08-22）
（编辑：陶婷婷）