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右美托咪定联合瑞芬太尼对全身麻醉下髋关节置换术患者脑氧代谢、血流动力学和认知功能的影响*

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摘要 目的: 瑞芬太尼、右美托咪定对全身麻醉下髋关节置换术患者的脑氧代谢、血流动力学和认知功能的影响。**方法:** 选取 2016 年 6 月~2019 年 10 月期间我院收治的 100 例行髋关节置换术的患者。采用随机数字表法分为对照组和研究组, 各 50 例。对照组患者麻醉中予以瑞芬太尼, 研究组则在对照组的基础上复合右美托咪定, 比较两组患者血流动力学、脑氧代谢和认知功能情况, 记录两组患者围术期间不良反应发生率。**结果:** 两组手术开始后 30 min(T1)~手术结束时(T2)时间点平均动脉压(MAP)、心率(HR)均呈下降趋势, 但研究组高于对照组($P<0.05$)。两组 T1~T2 时间点动脉血氧含量(CaO_2)、颈内静脉血氧含量(CjvO_2)均呈下降趋势, 且研究组低于对照组($P<0.05$); 两组 T1~T2 时间点颈静脉球部血氧饱和度(SjvO_2)呈上升趋势, 且研究组高于对照组($P<0.05$)。两组术前~术后 7 d 简明精神状态量表(MMSE)评分均呈下降后上升趋势($P<0.05$); 研究组术后 3 d、术后 7 d MMSE 评分高于对照组($P<0.05$)。研究组术后 3 d、术后 7 d 的认知功能障碍(POCD)发生率低于对照组($P<0.05$)。两组不良反应发生率比较无差异($P>0.05$)。**结论:** 全身麻醉下髋关节置换术患者麻醉方案选用右美托咪定联合瑞芬太尼, 可减轻血流动力学波动, 维持脑氧供需平衡, 可减少 POCD 发生风险, 且安全性较好。

关键词: 髋关节置换术; 右美托咪定; 脑氧代谢; 全身麻醉; 瑞芬太尼; 血流动力学; 认知功能

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Effects of Dexmedetomidine and Remifentanyl on Cerebral Oxygen Metabolism, Hemodynamics and Cognitive Function in Patients Undergoing Hip Replacement Under General Anesthesia*

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ABSTRACT Objective: To investigate the effects of remifentanyl and dexmedetomidine on cerebral oxygen metabolism, hemodynamics and cognitive function in patients undergoing hip replacement under general anesthesia. **Methods:** 100 patients with hip replacement were selected from June 2016 to October 2019. The patients were divided into control group and study group, each with 50 cases. Remifentanyl was given to the patients in the control group during anesthesia, while dexmedetomidine was given to the patients in the study group on the basis of the control group. The hemodynamics, cerebral oxygen metabolism and cognitive function of the two groups were compared, and the incidence of adverse reactions during perioperative period was recorded. **Results:** The mean arterial pressure (map) and heart rate (HR) of the two groups decreased from 30 minutes (T1) to the end of operation (T2), but the study group was higher than the control group ($P<0.05$). The arterial blood oxygen content (CaO_2) and the internal jugular vein blood oxygen content (CjvO_2) in the two groups showed a downward trend, and the study group was lower than the control group ($P<0.05$). The jugular bulb blood oxygen saturation (SjvO_2) in the two groups showed an upward trend, and the study group was higher than the control group ($P<0.05$). The Concise mental state scale (MMSE) scores of the study group were higher than those of the control group ($P<0.05$). The incidence of Cognitive impairment (POCD) in the study group was lower than that in the control group ($P<0.05$). There was no difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Dexmedetomidine combined with remifentanyl can reduce the hemodynamic fluctuation, maintain the balance of cerebral oxygen supply and demand, reduce the risk of POCD, and have a good safety.

Key words: Hip replacement; Dexmedetomidine; Cerebral oxygen metabolism; General anesthesia; Remifentanyl; Hemodynamics; Cognitive function

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前言

髋关节置换术是治疗终末期严重髋关节病最有效的方法之一,可有效缓解髋关节功能障碍^[1]。由于髋关节置换术的手术过程中患者意识清晰,患者处于一定程度的恐惧、焦虑状态,加之行此类手术患者多为老年群体,常合并多种基础疾病,术中各种刺激可引起血流波动,影响脑血液供应及脑氧代谢,引起一系列心脑血管的并发症和危险发生,进而影响患者预后^[2-4]。故术中给予合理的麻醉方案是手术顺利进行的前提条件。瑞芬太尼是一种麻醉性镇痛药,常用于全身麻醉中,起效快,镇痛效果确切,但单独用药效果不佳^[5]。右美托咪定镇痛、镇静效果确切,并具有一定的稳定血流动力学效果^[6,7]。本院通过对部分行髋关节置换术的患者全身麻醉中给予瑞芬太尼、右美托咪定,取得了较好的效果,现整理报道如下。

1 资料与方法

1.1 一般资料

选取 2016 年 6 月~2019 年 10 月期间我院收治的 100 例行髋关节置换术的患者。纳入标准:(1)具备手术指征,择期行髋关节置换术;(2)对本研究知情且签署同意书;(3)美国麻醉医师协会(American Society of Anesthesiologists, ASA)分级 I-II 级。排除标准:(1)患有严重的心肝肺肾等脏器功能障碍者;(2)房室传导阻滞、心动过缓病史或正在服用 β 受体阻滞剂;(3)伴震颤麻痹、认知功能障碍、癫痫等精神科疾病者;(4)合并凝血功能障碍者;(5)长期滥用药物史者。采用随机数字表法将其分为对照组和研究组。其中对照组女 23 例,男 27 例,年龄 52~82 岁,平均(68.29 $\pm$ 5.06)岁;疾病类型:髋部骨折 10 例,髋关节骨关节炎 13 例,股骨头缺血性坏死 15 例,髋关节的其他疾病 12 例;病变部位:右髋 28 例,左髋 22 例;ASA 分级: I 级 27 例, II 级 23 例。研究组女 22 例,男 28 例,年龄 53~79 岁,平均(69.46 $\pm$ 5.58)岁;疾病类型:髋部骨折 11 例,髋关节骨关节炎 14 例,股骨头缺血性坏死 14 例,髋关节的其他疾病 11 例;病变部位:右髋 26 例,左髋 24 例;ASA 分级: I 级 28 例, II 级 22 例。两组一般资料对比无差异($P>0.05$),临床资料具有可比性。本次研究已通过我院伦理学委员会批准。

1.2 方法

两组术前常规禁饮、禁食,术前 0.5 h 肌注射阿托品(华润双鹤药业股份有限公司,国药准字 H11021897,规格:2 mL:硫酸阿托品 0.5 mg,盐酸异丙嗪 25 mg)0.5 mg,入室后常规监测

生命体征,包括平均动脉压(Mean arterial pressure, MAP)、心率(Heart rate, HR)等,打开静脉通路。研究组于麻醉诱导前 10 min 分别泵入右美托咪定(国药准字 H20090248,江苏恒瑞医药股份有限公司,规格:2 mL:200 μ g(按右美托咪定计))0.5 μ g/kg,对照组给予等量的 0.9%氯化钠注射液持续泵入。麻醉诱导:依次静脉注射瑞芬太尼(国药准字 H20143315,江苏恩华药业股份有限公司,规格:2 mg(以瑞芬太尼 $C_{20}H_{28}N_2O_5$ 计))2~4 μ g/kg,丙泊酚(国药准字 H20030114,四川国瑞药业有限责任公司,规格:50 mL:0.5 g)1~2 mg/kg,顺苯磺酸阿曲库铵(国药准字 H20090202,浙江仙琚制药股份有限公司,规格:5 mg(以顺阿曲库铵计))0.2 mg/kg,麻醉诱导成功后气管插管,调整呼吸机参数。麻醉维持:间断静脉推注顺苯磺酸阿曲库铵 0.1 mg/kg,丙泊酚 3~4 ng/mL 靶控输注维持,瑞芬太尼 0.5~2 ng/mL,研究组则同时给予 0.4 μ g/(kg $\cdot$ h)的右美托咪定持续静脉泵入,术中维持 BIS 在 40~60,维持患者术中生命征平稳。

1.3 观察指标

(1)记录两组患者术前(T0)、手术开始后 30 min(T1)、手术结束时(T2)的 HR、MAP 情况。(2)采集患者 T0、T1、T2 时点颈内静脉球部和颈内动脉血,采用丹麦雷度公司生产的 ABL800 血气分析仪进行血气分析,检测脑氧代谢指标:颈内动脉血氧含量(oxygen content, CaO₂)、颈静脉球部血氧饱和度(oxygen saturation, S_{jv}O₂)、颈内静脉血氧含量(Blood oxygen content of internal jugular vein, C_{jv}O₂)。(3)记录两组患者围术期间不良反应发生情况。(4)于术前、术后 3 d、术后 7 d 采用简明精神状态量表(Mini-mental state examination, MMSE)^[8]评价患者认知功能,MMSE 共 30 个评条,总分 30 分,分数越高,认知功能越好。其中 MMSE 评分 <27 分即为认知功能障碍(post-operative cognitive dysfunction, POCD)。

1.4 统计学方法

采用 SPSS24.0 统计学软件进行数据处理,计数资料以%的形式表示,经 χ^2 检验处理,计量资料以($\bar{x} \pm s$)的形式表示,两组数据对比经 t 检验处理,以 $P<0.05$ 时差异有统计学意义。

2 结果

2.1 血流动力学比较

两组 T0 时间点 HR、MAP 比较差异无统计学意义($P>0.05$);两组 T1、T2 时间点 HR、MAP 均呈下降趋势,但研究组高于对照组($P<0.05$);详见表 1。

表 1 两组血流动力学指标比较($\bar{x} \pm s$)

Table 1 Comparison of hemodynamic indexes between the two groups($\bar{x} \pm s$)

Groups	Time	HR(beat/min)	MAP(mmHg)
Control group(n=50)	T0	82.38 $\pm$ 6.23	93.46 $\pm$ 6.23
	T1	69.11 $\pm$ 7.87 ^a	80.27 $\pm$ 8.17 ^a
	T2	63.79 $\pm$ 6.27 ^{ab}	73.79 $\pm$ 7.63 ^{ab}
Study group(n=50)	T0	82.60 $\pm$ 7.34	92.53 $\pm$ 8.54
	T1	75.90 $\pm$ 7.02 ^{ac}	86.95 $\pm$ 7.86 ^{ac}
	T2	69.39 $\pm$ 8.30 ^{abc}	80.62 $\pm$ 6.97 ^{abc}

Note: compared with T0 time point, ^a $P<0.05$; compared with T1 time point, ^b $P<0.05$; compared with control group, ^c $P<0.05$.

2.2 两组脑氧代谢指标比较

两组 T0 时间点 CaO_2 、 SjvO_2 、 CjvO_2 比较差异无统计学意义 ($P>0.05$); 两组 T1、T2 时间点 CaO_2 、 CjvO_2 呈下降趋势, 且研

究组低于对照组 ($P<0.05$); 两组 T1、T2 时间点 SjvO_2 呈升高趋势, 且研究组高于对照组 ($P<0.05$); 详见表 2。

表 2 两组脑氧代谢指标比较 ($\bar{x} \pm s$)Table 2 Comparison of brain oxygen metabolism indexes between the two groups ($\bar{x} \pm s$)

Groups	Time	CaO_2 (ml/L)	SjvO_2 (%)	CjvO_2 (ml/L)
Control group (n=50)	T0	153.77 $\pm$ 7.94	56.27 $\pm$ 4.40	98.31 $\pm$ 6.28
	T1	142.46 $\pm$ 9.55 ^a	59.78 $\pm$ 3.78 ^a	94.18 $\pm$ 7.41 ^a
	T2	139.88 $\pm$ 8.78 ^{ab}	63.26 $\pm$ 2.31 ^{ab}	87.45 $\pm$ 6.26 ^{ab}
Study group (n=50)	T0	153.24 $\pm$ 8.49	56.49 $\pm$ 2.32	98.15 $\pm$ 5.26
	T1	137.66 $\pm$ 6.74 ^{ac}	63.83 $\pm$ 3.25 ^{ac}	89.84 $\pm$ 5.22 ^{ac}
	T2	131.52 $\pm$ 9.46 ^{abc}	67.64 $\pm$ 3.54 ^{abc}	82.39 $\pm$ 6.23 ^{abc}

Note: compared with T0 time point, ^a $P<0.05$; compared with T1 time point, ^b $P<0.05$; compared with control group, ^c $P<0.05$.

2.3 两组 MMSE 评分比较

两组术前 MMSE 评分比较无差异 ($P>0.05$); 两组术后 3 d、

术后 7 d MMSE 评分均呈下降后升高趋势 ($P<0.05$); 研究组术后 3 d、术后 7 d MMSE 评分高于对照组 ($P<0.05$); 详见表 3。

表 3 两组 MMSE 评分比较 ($\bar{x} \pm s$, 分)Table 3 MMSE score comparison between the two groups ($\bar{x} \pm s$, score)

Groups	Before operation	3 d after operation	7 d after operation
Control group (n=50)	29.12 $\pm$ 0.26	24.53 $\pm$ 1.27 ^a	26.75 $\pm$ 1.34 ^{ab}
Study group (n=50)	29.06 $\pm$ 0.35	27.08 $\pm$ 0.21 ^a	28.68 $\pm$ 0.59 ^{ab}
t	0.973	14.008	11.416
P	0.333	0.000	0.000

Note: compared with before operation, ^a $P<0.05$; compared with 3 d after operation, ^b $P<0.05$.

2.4 两组 POCD 发生率比较

两组术前 POCD 发生率比较差异无统计学意义 ($P>0.05$);

研究组术后 3 d、术后 7 d 的 POCD 发生率低于对照组 ($P<0.05$); 详见表 4。

表 4 两组 POCD 发生率比较 例 (%)

Table 4 Comparison of POCD incidence between the two groups n (%)

Groups	Before operation	3 d after operation	7 d after operation
Control group (n=50)	0 (0.00)	19 (38.00)	8 (16.00)
Study group (n=50)	0 (0.00)	9 (18.00)	1 (2.00)
χ^2	0.000	4.960	5.983
P	1.000	0.026	0.014

2.5 两组不良反应发生率比较

研究组术中出现 1 例低血压、2 例躁动、1 例呼吸抑制、2 例窦性心动过缓, 不良反应发生率为 12.00% (6/50); 对照组出现 1 例恶心呕吐、1 例躁动、1 例窦性心动过缓, 不良反应发生率为 6.00% (3/50); 两组不良反应发生率比较差异无统计学意义 ($\chi^2=1.099$, $P=0.295$)。

3 讨论

髋关节置换术由于病变处分布着许多重要大血管, 加之涉及重塑髋臼、股骨等重要操作, 故易造成周边神经、血管及组织的不同程度创伤, 引起机体的血流动力学不稳定^[9-11]。为提高患

者手术舒适度, 需给予一定的镇静、镇痛麻醉以保障手术的顺利进行。然而行髋关节置换术的患者多为老年人, 基础性疾病多, 这些因素均可引起局部脑组织损伤, 破坏机体脑氧代谢, 提高 POCD 发生风险^[12-14]。据统计, 髋关节置换术患者术后发生 POCD 的概率可达 25%~50%, 常常会导致患者康复延迟、生活质量下降、病死率增加, 甚至可能发展成为永久性的认知障碍, 这给临床麻醉管理带来极大的安全挑战^[15]。瑞芬太尼是一种超短效的阿片受体激动剂, 起效迅速, 镇痛作用强, 适用于老年麻醉管理, 但停药后作用消失太快, 单用药效果欠佳^[16,17]。右美托咪定是一种新型的辅助麻醉用药, 具有较好的稳定血流动力学作用, 对中枢神经影响较轻, 同时其在防治术后 POCD 中的作

用也逐渐被认识^[18-20]。

本次研究结果显示,两种麻醉方案均会对髋关节置换术患者的血流动力学产生一定影响,但右美托咪定联合瑞芬太尼者的血流波动程度明显更轻。究其原因,瑞芬太尼可在一定程度上抑制机体的应激反应,减轻手术对机体循环功能的影响;同时瑞芬太尼还可促进冠状血管扩张,改善 MAP^[21,22]。而右美托咪定可通过作用于患者蓝斑核 α_2 肾上腺素受体,影响机体去甲肾上腺素分泌,发挥催眠、镇静效果;通过作用于外周及中枢,发挥抗交感活性作用;通过作用于脊髓后角,抑制伤害性刺激传入,终止了疼痛信号的传递^[23,24]。上述两组药物从不同的作用机制出发,产生协同作用,共同促进机体循环趋于稳定。CaO₂、SjvO₂、CjvO₂ 均是目前常用的脑氧代谢监测指标。其中 SjvO₂<55%时表面大脑处于低灌注状态。本研究中两组术中 SjvO₂ 均处于正常范围内,可见两种麻醉方式均无氧供不足情况发生。CaO₂、CjvO₂ 可反映脑对氧的摄取,降低表明大脑氧代谢率下降,脑血流相对于充足^[25,26]。本研究中两组 T1~T2 时间点 CaO₂、CjvO₂ 呈下降趋势,且研究组低于对照组,表明右美托咪定联合瑞芬太尼可使患者脑细胞的代谢降低,利于维持脑氧代谢平衡,发挥脑保护效果。这主要是因为右美托咪定可作用于软脑膜动脉、小动脉等部位的平滑肌上的 α 受体,使其产生血管收缩,减少相应供血区域的脑血流量,维持脑细胞的供需平衡^[27,28]。本次研究结果中,麻醉方案选用瑞芬太尼、右美托咪定的患者术后认知功能受到的影响更轻,POCD 发生率更低,这可能是因为右美托咪定可避免破坏及剥夺睡眠,使机体处于觉醒-睡眠的周期状态,术后可迅速恢复^[29]。已有研究表明,右美托咪定、瑞芬太尼可使患者达到近事遗忘的效果,可有效缓解术中出现的负性情绪和应激反应^[30]。另两组不良反应发生率比较无差异,可见右美托咪定联合瑞芬太尼安全性较好,可靠程度佳。

综上所述,髋关节置换术患者麻醉方案选取右美托咪定联合瑞芬太尼,可减轻血流动力学波动,维持脑氧供需平衡,可减少 POCD 发生风险,且安全性较好。

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