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右美托咪定复合罗哌卡因对膝关节置换术后镇痛镇静效果、睡眠质量及应激反应的影响*

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摘要 目的:探讨右美托咪定复合罗哌卡因对膝关节置换术后的临床效果。**方法:**选取 2015 年 2 月~2018 年 12 月期间在武警陕西省总队医院择期行膝关节置换术患者 103 例,根据随机数字表将患者分成对照组($n=51$)和研究组($n=52$),对照组股神经阻滞时给予罗哌卡因,研究组在对照组基础上联合右美托咪定。比较两组患者镇痛镇静效果、睡眠质量、应激反应以及不良反应。**结果:**研究组术后 12 h、术后 24 h、术后 48 h 视觉模拟评分(VAS)低于对照组($P<0.05$),Ramsay 镇静评分则高于对照组($P<0.05$)。研究组术后 24 h、术后 48 h 阿森斯失眠量表(AIS)评分均低于术前,且呈先降低后升高趋势($P<0.05$)。研究组术后 24 h、术后 48 h AIS 评分低于对照组($P<0.05$)。两组患者手术开始即刻、术毕的去甲肾上腺素(NE)、肾上腺素(E)水平均上升,且呈先升高后降低趋势($P<0.05$);研究组手术开始即刻、术毕的 NE、E 水平低于对照组($P<0.05$)。两组不良反应发生率对比无统计学差异($P>0.05$)。**结论:**右美托咪定复合罗哌卡因方案应用于膝关节置换术,镇痛镇静效果确切,可减轻术中应激反应,有效改善睡眠质量,且不增加不良反应发生率,临床应用价值较高。

关键词:右美托咪定;罗哌卡因;膝关节置换术;镇痛;镇静;睡眠质量;应激反应

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Effects of Dexmedetomidine Combined with Ropivacaine on Analgesia, Sedation, Sleep Quality and Stress Response after Knee Arthroplasty*

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ABSTRACT Objective: To explore the clinical effects of dexmedetomidine combined with ropivacaine on knee arthroplasty. **Methods:** 103 patients with knee arthroplasty in Shaanxi Provincial Armed Police Corps Hospital from February 2015 to December 2018 were selected, and they were divided into control group ($n=51$) and study group ($n=52$) according to the random number table. Ropivacaine was given to the control group when femoral nerve was blocked. The study group was combined with dexmedetomidine on the basis of the control group. The analgesic and sedative effects, sleep quality, stress reaction and adverse reactions were compared between the two groups. **Results:** Visual analogue score (VAS) of the study group were lower than that of the control group at 12 h, 24 h and 48 h after operation ($P<0.05$), while Ramsay sedation score was higher than that of the control group ($P<0.05$). The Athens insomnia score (AIS) of the study group at 24 h after operation and 48 h after operation were lower than that of before operation, and it decreased first and then increased ($P<0.05$). AIS score of study group at 24 h and 48 h after operation were lower than that of control group ($P<0.05$). The levels of norepinephrine (NE) and epinephrine (E) increased immediately at immediately after the operation began and after operation in both groups, the trend of increase first and then decrease ($P<0.05$). The levels of NE and E in the study group at immediately after the operation began and after operation were lower than those in the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Dexmedetomidine combined with ropivacaine has a definite analgesic and sedative effect after knee arthroplasty. It can alleviate intraoperative stress reaction and improve sleep quality effectively without increasing the incidence of adverse reactions. Which has a high clinical value.

Key words: Dexmedetomidine; Ropivacaine; Knee arthroplasty; Analgesia; Sedation; Sleep quality; Stress response

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前言

膝关节是下肢重要的负重关节,其中膝关节退行性骨关节炎已成为临床的常见疾病。近年来,由于严重的膝关节退行性骨关节炎发病率上升,需要进行膝关节置换术的患者也逐渐增多。膝关节置换术可有效纠正患者膝关节畸形^[1],然而该术式作为一种损伤较大的手术,术后常伴有剧烈的疼痛,可引起机体严重的应激反应,影响患者预后^[2]。股神经阻滞一直是全膝关节置换术后镇痛的“金标准”,该镇痛方式可通过神经刺激仪,超声精确地定位阻滞区域而发挥镇痛效果^[3]。罗哌卡因是临床常用的局麻药,以往研究证实单次注射罗哌卡因的作用时间可长达8~14 h,镇痛效果确切^[4]。右美托咪定作为高选择性的 α_2 受体激动剂,具有镇静、镇痛、抗交感神经等作用^[5]。鉴于此,本研究通过对我院收治的行膝关节置换术患者给予右美托咪定复合罗哌卡因股神经阻滞,取得了较好的疗效,现作报道如下。

1 资料与方法

1.1 一般资料

选取武警陕西省总队医院于2015年2月~2018年12月间收治的103例择期行膝关节置换术患者,此次研究已通过我院伦理学委员会批准进行。纳入标准:(1)均择期行膝关节置换术者;(2)美国麻醉医师协会(American Society of Anesthesiologists, ASA)分级I~II级^[6];(3)无股神经阻滞禁忌证者;(4)患者家属知情本次研究且签署了同意书;(5)同意进行全身麻醉联合外周神经阻滞者;(6)均由同一组医师进行手术操作。排除标准:(1)合并精神疾患、认知障碍者;(2)严重的中枢神经系统疾病者;(3)凝血功能障碍者;(4)严重心血管病变,肝肾功能不全者;(5)长期服用止痛药者;(6)酒精或者药物成瘾史者。根据随机数字表法将患者分成对照组($n=51$)和研究组($n=52$),其中对照组男22例,女29例,年龄34~67岁,平均 (49.31 ± 4.28) 岁;体质指数(Body mass index, BMI)21.8~25.6 kg/m²,平均 (23.09 ± 0.72) kg/m²;ASA分级:I级31例,II级20例。研究组男25例,女27例,年龄33~69岁,平均 (50.07 ± 5.29) 岁;BMI22.3~26.9 kg/m²,平均 (23.16 ± 0.83) kg/m²;ASA分级:I级32例,II级20例。各组临床资料进行对比无差异($P>0.05$)。

1.2 方法

术前常规禁饮禁食,入室后开放静脉通道,给予咪达唑仑(江苏恩华药业股份有限公司,国药准字H20031071,规格:5 mL:5 mg)0.02 mg/kg镇静。随后给予单次股神经阻滞,具体如下:采用美国SonoSite公司生产的高频线阵探头10~20 Hz的超声仪,患者取仰卧位,由一名麻醉医师和一名助手在超声引导下,用神经刺激仪短针进行穿刺(电流1 mA)。将探头置于腹股沟韧带下方约2 cm与大腿长轴垂直处,当由外到内排列的股神经、股动脉、股静脉清晰可见时,从大腿外侧进针直至髂腰肌表面的股神经处。当患者股四头肌收缩与髌骨跳动时,电流减小至0.5 mA,回抽无血后即可注射麻醉药物。对照组给予40 mL 0.5%罗哌卡因[广东嘉博制药有限公司,国药准字H20173194,规格:20 mL:200 mg(按盐酸罗哌卡因计)],边推药边回抽,同时在超声下观察麻醉药物扩散。研究组则给予40 mL 0.5%罗哌卡因和150 μ g右美托咪定混合液[宜昌人福药业有限责任公司,国药准字H20183390,规格:2 mL:200 μ g(按右美

托咪定计)]。神经阻滞完成20 min后进行全身麻醉诱导。两组均给予相同方案的麻醉诱导:顺式阿曲库铵[浙江仙琚制药股份有限公司,国药准字H20090202,规格:5 mg(以顺阿曲库铵计)]1 mg/kg、舒芬太尼(宜昌人福药业有限责任公司,国药准字H20054256,规格:按 $C_{22}H_{30}N_2O_5S$ 计5 mL:250 μ g)0.3 μ g/kg、竞安(广东嘉博制药有限公司,国药准字H20133360,规格:50 mL:500 mg)2 mg/kg,置入合适尺寸SLIPA喉罩,若喉罩通气效果不佳,则给予气管插管。

1.3 观察指标

(1)于术前、术后12 h、24 h、48 h采用视觉模拟评分(Visual analogue score, VAS)^[7]、Ramsay镇静评分^[8]评价患者镇痛镇静效果。其中VAS评分0~10分,0分表示无痛,10分表示难以忍受之痛,分数越高,疼痛感越强烈。Ramsay镇静评分1~6分,其中深睡为6分、入睡为5分、浅睡眠为4分、嗜睡为3分、安静合作为2分、烦躁不安为1分。(2)于术前、术后24 h、术后48 h采用阿森斯失眠量表(Athens insomnia score, AIS)^[9]评价两组患者睡眠质量,该量表内容包括夜间入睡时间、苏醒次数、总睡眠时间、白天情绪、总睡眠质量、比期望的时间早醒、白天嗜睡情况、白天身体功能等8项,每个项目按0~3分评分,分数越高,表示睡眠质量越差。(3)于术前、手术开始即刻、术毕采集两组患者肘静脉血4 mL,2900 r/min离心13 min,离心半径8 cm,取上清液,置于-20℃冰箱中待测。采用高效液相色谱法检测去甲肾上腺素(Norepinephrine, NE)、肾上腺素(Adrenaline, E)水平,严格遵守试剂盒(南京建成生物工程有限公司)说明书进行操作。(4)记录术中不良反应情况。

1.4 统计学方法

使用SPSS25.0软件进行统计学分析,计量资料以 $(\bar{x} \pm s)$ 表示,实施t检验,计数资料以比或率表示,实施卡方检验, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 镇静镇痛效果比较

两组患者术前VAS评分、Ramsay镇静评分比较无差异($P>0.05$);与术前相比,对照组术后12 h、24 h、48 h VAS评分升高,Ramsay镇静评分降低($P<0.05$);研究组术后12 h、24 h、48 h VAS评分均较术前升高($P<0.05$);研究组术后48 h Ramsay镇静评分均降低($P<0.05$);与术后12 h相比,两组术后48 h VAS评分、Ramsay镇静评分均降低($P<0.05$);研究组术后12 h、术后24 h、术后48 h的VAS评分低于对照组($P<0.05$),Ramsay镇静评分则高于对照组($P<0.05$);详见表1。

2.2 睡眠质量比较

两组患者术前AIS评分比较无差异($P>0.05$);对照组术后24 h、术后48 h AIS评分与术前比较差异无统计学意义($P>0.05$);研究组术后24 h、术后48 h AIS评分均低于术前,且呈先降低后升高趋势($P<0.05$);研究组术后24 h、术后48 h AIS评分低于对照组($P<0.05$);详见表2。

2.3 两组患者应激反应指标比较

两组患者术前NE、E水平比较差异无统计学意义($P>0.05$);两组患者手术开始即刻、术毕NE、E水平均上升,且呈先升高后降低趋势($P<0.05$);研究组手术开始即刻、术毕NE、E水平低于对照组($P<0.05$);详见表3。

表 1 两组镇静镇痛效果比较($\bar{x} \pm s$, 分)

Table 1 Comparison of sedative and analgesic effects between two groups($\bar{x} \pm s$, scores)

Groups	VAS score				Ramsay sedation score			
	Before operation	12 h after operation	24 h after operation	48 h after operation	Before operation	12 h after operation	24 h after operation	48 h after operation
Control group (n=51)	2.06 $\pm$ 0.34	4.95 $\pm$ 0.86 ^c	4.66 $\pm$ 0.74 ^c	3.78 $\pm$ 0.78 ^{abc}	2.79 $\pm$ 0.28	2.01 $\pm$ 0.53 ^c	1.82 $\pm$ 0.62 ^c	1.34 $\pm$ 0.22 ^{abc}
Study group (n=52)	2.09 $\pm$ 0.42	3.06 $\pm$ 0.61 ^c	2.93 $\pm$ 0.52 ^c	2.46 $\pm$ 0.39 ^{abc}	2.81 $\pm$ 0.32	3.05 $\pm$ 0.69	2.81 $\pm$ 0.68	2.19 $\pm$ 0.53 ^{abc}
t	0.398	19.386	22.468	17.645	0.337	9.390	8.496	9.864
P	0.691	0.000	0.000	0.000	0.737	0.000	0.000	0.000

Note: Compared with 12h after operation, ^aP<0.05; compared with 24 h after operation, ^bP<0.05; compared with before operation, ^cP<0.05.

表 2 睡眠质量比较($\bar{x} \pm s$, 分)

Table 2 Comparison of sleep quality between two groups($\bar{x} \pm s$, scores)

Groups	Before operation	24 h after operation	48 h after operation
Control group (n=51)	11.82 $\pm$ 1.78	11.34 $\pm$ 1.54	11.18 $\pm$ 1.55
Study group (n=52)	11.74 $\pm$ 1.65	8.38 $\pm$ 1.23 ^a	9.45 $\pm$ 1.26 ^{ab}
t	0.237	10.789	6.221
P	0.813	0.000	0.000

Note: Compared with before operation, ^aP<0.05; compared with 24 h after operation, ^bP<0.05.

表 3 两组患者应激反应指标比较($\bar{x} \pm s$)

Table 3 Comparison of stress response indices between two groups($\bar{x} \pm s$)

Groups	NE(ng/mL)			E(ng/mL)		
	Before operation	Immediately after the operation began	After operation	Before operation	Immediately after the operation began	After operation
Control group (n=51)	254.53 $\pm$ 51.32	425.36 $\pm$ 43.26 ^a	386.52 $\pm$ 46.42 ^{ab}	63.16 $\pm$ 9.15	96.53 $\pm$ 10.54 ^a	88.45 $\pm$ 8.37 ^{ab}
Study group (n=52)	253.56 $\pm$ 48.01	362.64 $\pm$ 42.87 ^a	301.83 $\pm$ 34.31 ^{ab}	62.93 $\pm$ 1.36	84.13 $\pm$ 8.27 ^a	75.47 $\pm$ 7.34 ^{ab}
t	0.099	7.390	10.544	0.179	6.650	8.372
P	0.921	0.000	0.000	0.858	0.000	0.000

Note: Compared with before operation, ^aP<0.05; compared with immediate operation, ^bP<0.05.

2.4 两组患者不良反应比较

手术期间,对照组出现 7 例不良反应,包括 2 例呼吸抑制、2 例低血压、3 例心动过缓,不良反应发生率为 13.73%(7/51);研究组出现 8 例不良反应,包括 3 例呼吸抑制、2 例低血压、3 例心动过缓,不良反应发生率为 15.38%(8/52);两组不良反应发生率对比无差异($\chi^2=0.057$, $P=0.811$)。

3 讨论

膝关节置换术主要采用人工膝关节假体取代已严重损坏且无法行使正常功能的膝关节表面,进而达到消除疼痛、矫正畸形、恢复稳定性的治疗目的^[10-12]。由于膝关节置换术属于创伤较大的手术,可引发强烈的应激反应及疼痛,而术后疼痛程度以及麻醉药物的使用量又会加重睡眠障碍的程度,从多方面影响患者膝关节功能的恢复^[13-15]。因此,良好的术后镇痛对于患者预后积极意义。膝关节置换术后的常见镇痛方法有硬膜外患者自控镇痛、静脉患者自控镇痛以及连续外周神经阻滞,其中尤以连续外周神经阻滞技术中的股神经阻滞最为常见^[16,17]。股神经阻滞仅作用于局部,对全身影响轻微,在保证镇痛的同时还有助于机体功能恢复^[18]。罗哌卡因是一种低毒、高效、长效的酰胺类局麻药,具有感觉、运动神经分离阻滞的作用^[19]。右美托

咪定是临床常用麻醉辅助和镇痛药物,近年来不少动物实验证实右美托咪定可以延长局麻药作用时间且不增加副作用^[20,21]。

本次研究结果表明,研究组术后不同时间点 VAS 评分低于对照组,Ramsay 镇静评分则高于对照组,可见右美托咪定复合罗哌卡因可发挥良好的镇痛镇静效果,分析其原因,罗哌卡因的药理特性表现为较低的心脏神经系统毒性,代谢速度快,有较高的蛋白亲和力,因而可发挥较长时间的阻滞效果^[22]。右美托咪定通过与脊髓内 $\alpha 2$ 受体相结合,产生镇痛效果,通过作用于大脑蓝斑核而发挥镇静作用^[23]。右美托咪定可能通过以下机制发挥延长局麻药阻滞作用:通过作用于外周血管或神经发挥促进阻滞效果;通过收缩血管以延长局部麻醉药物吸收时间进而增强阻滞作用^[24]。

本研究中经右美托咪定复合罗哌卡因干预的患者的睡眠质量明显优于单用罗哌卡因者,这可能是因为右美托咪定联合罗哌卡因可以缩短术后制动时间,减轻术后疼痛、减轻机体刺激、延长镇痛时间有关^[25]。行膝关节置换术时,术中操作及麻醉等均可使机体产生强烈的应激反应,主要表现为肾素-血管紧张素-醛固酮系统的异常活跃以及交感-垂体-肾上腺素的分泌增多,最终引起儿茶酚胺增加,NE、E 的浓度升高^[26]。本次研究结果中研究组手术开始即刻、术毕 NE、E 水平低于对照组,

可见两种麻醉方案均可引起不同程度的应激反应,但右美托咪定复合罗哌卡因者明显更轻。这主要是因为右美托咪定可抑制儿茶酚胺的释放,减轻机体过度的应激反应,有利于维持机体循环稳定^[27,28]。另两组不良反应发生率对比无统计学差异,说明右美托咪定复合罗哌卡因安全性较好,这与张瑜等人^[29]研究基本一致。以往研究证实罗哌卡因具有潜在的收缩血管作用,可减少局麻药的收缩入血,这可能是该麻醉方案不良反应较小的原因之一^[30]。

综上所述,右美托咪定复合罗哌卡因应用于膝关节置换术,可减轻术中应激反应,有效改善睡眠质量,镇痛镇静效果确切,安全性较好。

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