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右美托咪定联合罗哌卡因连续股神经阻滞对全膝关节置换术后患者镇痛效果、炎性因子和神经递质的影响*

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摘要 目的:探讨右美托咪定联合罗哌卡因连续股神经阻滞对全膝关节置换术(TKA)后患者镇痛效果、炎性因子和神经递质的影响。**方法:**选取2017年2月~2019年12月期间我院收治的行TKA的患者98例,采用随机数字表法分为对照组和研究组,各49例。对照组给予罗哌卡因连续股神经阻滞,研究组在对照组的基础上联合右美托咪定,比较两组患者镇痛效果、炎性因子、神经递质和不良反应。**结果:**两组术后1h、6h、12h、24h、48h静息及运动状态的视觉疼痛模拟评分法(VAS)评分均呈先升高后降低趋势($P<0.05$);研究组术后1h、6h、12h、24h、48h静息及运动状态的VAS评分均低于对照组($P<0.05$)。两组术前、术后24h、术后48h白介素-1 β (IL-1 β)、白介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)呈先升高后下降趋势,但研究组术后24h、术后48hIL-1 β 、IL-6、TNF- α 低于对照组($P<0.05$)。两组术前、术后24h、术后48h P物质、 β -内啡肽及孤啡肽呈先升高后下降趋势,但研究组术后24h、术后48h P物质、 β -内啡肽及孤啡肽低于对照组($P<0.05$)。两组不良反应发生率对比未见统计学差异($P>0.05$)。**结论:**行TKA患者采用罗哌卡因联合右美托咪定连续股神经阻滞,术后镇痛效果确切,可减少炎性因子和神经递质水平,且不增加不良反应发生率,安全性佳。

关键词:右美托咪定;全膝关节置换术;连续股神经阻滞;镇痛效果;罗哌卡因;炎性因子;神经递质

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The Effect of Dexmedetomidine Combined with Ropivacaine for Continuous Femoral Nerve Block on Analgesia, Inflammatory Factors and Neurotransmitters in Patients after Total Knee Arthroplasty*

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ABSTRACT Objective: To investigate the effect of dexmedetomidine combined with ropivacaine for continuous femoral nerve block on analgesia, inflammatory factors and neurotransmitters in patients after total knee arthroplasty (TKA). **Methods:** From February 2017 to December 2019, 98 patients who underwent TKA in our hospital were selected, they were divided into control group and study group by random number table method, each group with 49 cases. The control group was given ropivacaine for continuous femoral nerve block, and the study group was combined with dexmedetomidine on the basis of the control group, the analgesic effect, inflammatory factors, neurotransmitters and adverse reactions of the two groups were compared. **Results:** The visual pain simulation score (VAS) of resting and exercise state of the two groups at 1h, 6h, 12h, 24h, 48h after operation showed a trend of first increase and then decrease ($P<0.05$), and the VAS score of resting and exercise state of the study group at 1h, 6h, 12h, 24h, 48h after operation were lower than those of the control group ($P<0.05$). The interleukin-1 β (IL-1 β), interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) of the two groups before operation, 24h, 48h after operation increased first and then decreased, but IL-1 β , IL-6 and TNF- α of the study group were lower than those of the control group at 24h and 48h after operation ($P<0.05$). Substance P, β -endorphin and orphanin FQ of the two groups before operation, 24h, 48h after operation increased first and then decreased, but substance P, β -endorphin and orphanin FQ of the study group were lower than those of the control group at 24h and 48h after operation ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Dexmedetomidine combined with ropivacaine for continuous femoral nerve block in TKA patients, the analgesic effect after operation is definite, which can reduce the level of inflammatory factors and neurotransmitters, without increasing the incidence of adverse reactions, and has a good safety.

Key words: Dexmedetomidine; Total knee arthroplasty; Continuous femoral nerve block; Analgesic effect; Ropivacaine; Inflammatory factor; Neurotransmitter

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前言

全膝关节置换术(TKA)是治疗终末期膝关节疾病的主要方法,可有效地根除晚期膝关节病痛,极大地提高病人的生活质量^[1]。随着我国人口老龄化进程加速,关节类疾病的发病率也随之升高,使得临床TKA的应用率也随之增加^[2]。但由于TKA的应用对象多为中老年群体,中老年群体由于身体各项机能减退,生理储备功能较差,常常无法耐受术中麻醉药物的刺激及术后剧烈的疼痛,增加了术后并发症发生风险,严重者甚至可引发死亡^[3,4]。因此,选取最佳镇痛方式,对提高TKA手术效果,改善患者预后具有积极的临床意义。连续股神经阻滞是目前TKA常用的镇痛方法之一,罗哌卡因则是连续股神经阻滞的常用麻醉药物,镇痛效果良好^[5,6]。但单独应用罗哌卡因行连续股神经阻滞的效果不甚理想。右美托咪定是一种高选择性的 α_2 -肾上腺素能受体激动剂,镇静、镇痛效果确切^[7]。本研究通过对我院收治的部分行TKA患者给予右美托咪定联合罗哌卡因连续股神经阻滞,获得了较好的效果。

1 资料与方法

1.1 一般资料

选取2017年2月~2019年12月期间我院收治的行TKA的患者98例,纳入标准:(1)均具备手术指征,择期行TKA者;(2)均为首次行TKA者;(3)美国麻醉医师协会(ASA)^[8]分级为I~II级者;(4)患者及其家属知情本研究且签署了同意书。排除标准:(1)合并心、肺、肾等脏器功能障碍者;(2)合并感染、免疫缺陷者;(3)伴有凝血功能障碍者;(4)存在长期服用阿片类药物史者;(5)患有精神疾病或认知功能障碍者;(6)不能配合临床观察者。采用随机数字表法将患者分为对照组和研究组各49例。其中研究组男30例,女19例,年龄42~65岁,平均(52.48±4.19)岁;体质指数22~26kg/m²,平均(23.15±0.83)kg/m²;ASA分级:I级26例,II级23例。对照组男27例,女22例,年龄44~68岁,平均(52.93±4.37)岁;体质指数21~26kg/m²,平均(23.46±0.93)kg/m²;ASA分级:I级27例,II级22例。两组一般资料比较无差异($P>0.05$),具有可比性。此次研究已获得我院医学伦理委员会批准。

1.2 方法

两组患者术前常规禁饮禁食,入室后开放静脉通路,常规进行血氧饱和度、心电图监测等。麻醉前输注复方乳酸钠林格氏液300~500mL,常规实施全身麻醉;麻醉由同一组医师完成。在快速静脉诱导后,行气管插管。采用0.2%的罗哌卡因(江苏恒瑞医药股份有限公司,国药准字H20060137,规格:10mL:100mg)维持术中麻醉状态。连续股神经阻滞:利用超声引导技术,由大腿外侧皮肤进针,沿超声束扫描平面向头侧与皮肤成30~45°角进针,在神经刺激器引导下患侧股神经穿刺。回抽无血后对照组注入罗哌卡因20mL,研究组则注入罗哌卡因+右美托咪定(宜昌人福药业有限责任公司,国药准字H20183390,规格:2mL:200μg)混合溶液20mL,撤出针芯,向

头侧置管约3~5cm,作皮下隧道,埋管5cm,术后于该导管中安装镇痛泵,持续镇痛2d。

1.3 观察指标

(1)记录两组患者术后1h、术后6h、术后12h、术后24h、术后48h的静息及运动状态的视觉疼痛模拟评分法(Visual analogue scale, VAS)^[9]评分。其中VAS评分0~10分,分数越高,疼痛感越强烈。(2)抽取两组术前、术后24h、术后48h的肘静脉血4mL,经3500r/min离心12min,离心半径13cm,分离上清液,置于冰箱中待测。参考上海桑戈生物科技有限公司试剂盒说明书,采用酶联免疫吸附试验检测炎症因子:白介素-1 β (IL-1 β)、白介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)及神经递质:P物质、 β -内啡肽及孤啡肽。(3)记录不良反应情况。

1.4 统计学方法

采用SPSS24.0处理数据,计量资料以($\bar{x}\pm s$)表示,实施t检验,计数资料以[n(%)]表示,实施 χ^2 检验,将 $\alpha=0.05$ 作为检验标准。

2 结果

2.1 两组静息及运动状态的VAS评分比较

两组术后1h、6h、12h、24h、48h静息及运动状态的VAS评分均呈先升高后降低趋势($P<0.05$);研究组术后1h、6h、12h、24h、48h静息及运动状态的VAS评分均低于对照组($P<0.05$);详见表1。

2.2 两组炎症因子水平比较

两组术前IL-1 β 、IL-6、TNF- α 比较差异无统计学意义($P>0.05$);两组术后24h、术后48hIL-1 β 、IL-6、TNF- α 呈先升高后下降趋势,但研究组术后24h、术后48hIL-1 β 、IL-6、TNF- α 低于对照组($P<0.05$);详见表2。

2.3 两组神经递质水平比较

两组术前P物质、 β -内啡肽及孤啡肽比较差异无统计学意义($P>0.05$);两组术后24h、术后48hP物质、 β -内啡肽及孤啡肽呈先升高后下降趋势,但研究组术后24h、术后48hP物质、 β -内啡肽及孤啡肽低于对照组($P<0.05$);详见表3。

2.4 两组不良反应发生率比较

两组不良反应发生率对比无差异($P>0.05$);详见表4。

3 讨论

TKA在临床上常用于晚期膝关节疾病患者的治疗,该手术的主要治疗目标在于缓解患者疼痛、恢复患者膝关节功能,同时对畸形的膝关节进行矫正处理^[10,11]。而TKA术后的康复过程始终遭受以下几个因素的干扰:手术时期、手术给患者带来的损伤及疼痛感、是否在TKA术后进行适宜的运动锻炼^[12,13]。上述因素对TKA的手术结果及患者预后均有至关重要的意义,其中以如何减少术后疼痛最为迫切。现临床有关TKA的术后镇痛方案较多,而连续股神经阻滞因其安全、有效的优势被广泛应用。现临床连续股神经阻滞的药物多为单一用药,以罗哌卡因较为常见,但不少临床研究证实^[14,15],低浓度的局麻药又

表 1 两组静息及运动状态的 VAS 评分比较($\bar{x} \pm s$, 分)Table 1 Comparison of VAS scores of resting and exercise state between the two groups($\bar{x} \pm s$, scores)

Groups	Time points	VAS of resting	VAS of exercise
Control group(n=49)	1h after operation	2.35±0.26	2.52±0.27
	6h after operation	3.02±0.23 ^a	3.19±0.25 ^a
	12h after operation	3.73±0.39 ^{ab}	3.86±0.29 ^{ab}
	24h after operation	4.36±0.21 ^{abc}	4.47±0.21 ^{abc}
	48h after operation	2.78±0.25 ^{abcd}	2.93±0.23 ^{abcd}
Study group(n=49)	1h after operation	2.11±0.18 ^c	2.18±0.24 ^c
	6h after operation	2.69±0.16 ^{ac}	2.78±0.35 ^{ac}
	12h after operation	3.14±0.27 ^{abc}	3.28±0.29 ^{abc}
	24h after operation	3.79±0.26 ^{abcc}	3.93±0.27 ^{abcc}
	48h after operation	2.42±0.24 ^{abcde}	2.35±0.24 ^{abcde}

Note: compared with 1h after operation, ^a $P<0.05$; compared with 6h after operation, ^b $P<0.05$; compared with 12h after operation, ^c $P<0.05$; compared with 24h after operation, ^d $P<0.05$; compared with control group, ^e $P<0.05$.

表 2 两组炎症因子水平比较($\bar{x} \pm s$)Table 2 Comparison of inflammatory factors between the two groups($\bar{x} \pm s$)

Groups	Time points	IL-1 β (ng/mL)	IL-6(pg/mL)	TNF- α (pg/mL)
Control group(n=49)	Before operation	209.19±17.36	146.31±21.28	218.71±23.52
	24h after operation	368.59±26.25 ^a	241.84±25.73 ^a	496.38±25.49 ^a
	48h after operation	297.62±25.91 ^{ab}	195.41±21.49 ^{ab}	372.83±31.69 ^{ab}
Study group(n=49)	Before operation	208.21±23.87	145.25±18.55	216.73±22.71
	24h after operation	295.46±20.52 ^{ac}	194.93±23.16 ^{ac}	454.54±20.68 ^{ac}
	48h after operation	253.37±22.47 ^{abc}	167.01±24.82 ^{abc}	294.59±28.74 ^{abc}

Note: compared with before operation, ^a $P<0.05$; compared with 24h after operation, ^b $P<0.05$; compared with control group, ^c $P<0.05$.

表 3 两组神经递质水平比较($\bar{x} \pm s$)Table 3 Comparison of neurotransmitters levels between the two groups($\bar{x} \pm s$)

Groups	Time points	Substance P(ng/L)	β -endorphin(ng/L)	Orphanin FQ(ng/L)
Control group(n=49)	Before operation	26.34±2.39	11.27±1.25	5.86±0.65
	24h after operation	38.21±2.26 ^a	23.83±1.94 ^a	13.97±1.29 ^a
	48h after operation	33.41±2.92 ^{ab}	18.63±1.83 ^{ab}	9.62±0.93 ^{ab}
Study group(n=49)	Before operation	26.53±2.88	11.49±1.61	5.75±0.64
	24h after operation	33.79±2.27 ^{ac}	18.14±2.58 ^{ac}	9.67±0.92 ^{ac}
	48h after operation	29.46±2.12 ^{abc}	14.17±1.41 ^{abc}	7.28±0.77 ^{abc}

Note: compared with before operation, ^a $P<0.05$; compared with 24h after operation, ^b $P<0.05$; compared with control group, ^c $P<0.05$.

表 4 两组不良反应发生率比较【例(%)】

Table 4 Comparison of adverse reactions between the two groups[n(%)]

Groups	Respiratory depression	Hypotension	Tachycardia	Nausea and vomiting	Total incidence rate
Control group(n=49)	2(4.08)	1(2.04)	1(2.04)	1(2.04)	5(10.20)
Study group(n=49)	3(6.12)	2(4.08)	1(2.04)	2(4.08)	8(16.33)
χ^2					0.803
P					0.372

会导致阻滞不完全,术后疼痛缓解不明显,增加并发症发生风险。而高浓度的局麻药会在感觉神经阻滞的同时阻断运动神经,延缓康复进程。同时右美托咪定为美托咪定的药理活性右旋异构体,近年来其作为神经阻滞辅助用药的研究报道也逐渐增加^[16,17]。

本次研究结果显示,两种麻醉方案均有一定的镇痛作用,且右美托咪定联合罗哌卡因连续股神经阻滞者的镇痛效果明显更佳。究其原因,罗哌卡因对神经细胞膜钠离子通道有较强的选择性,可抑制神经细胞钠离子通道,进而阻滞冲动传导,从而发挥较好的镇痛作用^[18,19]。而右美托咪定的镇静镇痛作用机制主要体现为:通过作用于脑干蓝斑区的 α_2 受体,引发并维持自然非动眼睡眠,达到镇静的目的^[20-22]。同时激动突触前的 α_2 受体,抑制疼痛信号传导,达到镇痛的目的^[23]。两种麻醉药物从不同的作用机制出发,产生协同作用,发挥更好的镇痛效应。P 物质分布于神经系统,参与了疼痛发生、发展的过程;孤啡肽为内源性阿片肽受体,其含量与疼痛时长成正比; β -内啡肽为内源性阿片肽,手术、疼痛等应激情况下会使其水平升高^[24-26]。TKA 是一种有创操作,麻醉药物、手术创伤均会带来不同程度的应激反应,而剧烈的应激反应可引起炎症细胞因子如 IL-1 β 、IL-6、TNF- α 的大量分泌,IL-6 是一种多功能细胞因子,手术应激状态下,交感-肾上腺髓质系统兴奋引起 IL-1 β 、TNF- α 大量释放,且上述炎症因子均参与了疼痛的发生与发展^[27]。本研究中两组患者神经递质和炎症因子水平均有所改善,且研究组的改善效果更佳。这可能是因为右美托咪定作用于外周神经的局部麻醉药物可增强其感觉和运动神经阻滞作用,可有效增强阻滞效果,减轻机体应激反应^[28]。此外,右美托咪定还可抑制突触前膜 p 物质、 β -内啡肽及孤啡肽的释放,终止疼痛的信号传导,进一步加强镇痛效果^[29]。另两组不良反应发生率对比未见明显差异,可能是因为右美托咪定本身无呼吸抑制,同时还可减少罗哌卡因的使用剂量,中和麻醉药所带来的不良反应^[30]。

综上所述,行 TKA 患者采用罗哌卡因联合右美托咪定连续股神经阻滞,可减少炎症因子和神经递质水平,且不增加不良反应发生率,安全性佳,发挥良好的镇痛效果。

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