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右美托咪定联合罗哌卡因腹横肌平面阻滞对老年腹腔镜胃癌根治术患者应激反应、炎症反应及术后谵妄的影响 *

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摘要 目的:探讨右美托咪定联合罗哌卡因腹横肌平面阻滞(TAPB)对老年腹腔镜胃癌根治术患者炎症反应、应激反应及术后谵妄的影响。**方法:**选择2017年7月~2019年10月期间我院接收的行腹腔镜胃癌根治术的老年患者118例,按随机信封抽签法将其分为A组(n=59,罗哌卡因TAPB麻醉)和B组(n=59,右美托咪定联合罗哌卡因TAPB麻醉),对比两组血流动力学指标、应激反应、炎症反应、术后疼痛、术后谵妄及不良反应发生率。**结果:**两组TAPB阻滞即刻(T1)~拔管时(T4)时间点心率(HR)、平均动脉压(MAP)均较麻醉前(T0)时间点升高($P<0.05$),B组T1~T4时间点HR、MAP低于A组($P<0.05$)。两组术后3d、术后5d皮质醇(Cor)、去甲肾上腺素(NE)、白介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)水平高于术前,但术后5d低于术后3d($P<0.05$),B组术后3d、术后5d的IL-6、TNF- α 、Cor、NE水平低于A组($P<0.05$)。B组的术后谵妄发生率较A组降低($P<0.05$),两组不良反应发生率对比无差异($P>0.05$)。B组术后6h、术后12h、术后24h、术后48h视觉模拟评分法(VAS)评分低于A组($P<0.05$)。**结论:**老年腹腔镜胃癌根治术患者采用右美托咪定联合罗哌卡因TAPB可维持血流动力学稳定,减轻应激反应、炎症反应,降低术后谵妄发生率,术后镇痛效果良好,且安全性较好。

关键词:右美托咪定;罗哌卡因;腹横肌平面阻滞;老年;腹腔镜胃癌根治术;应激反应;炎症反应;谵妄

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Effects of Dexmedetomidine Combined with Ropivacaine Transverse Abdominis Plane Block on Stress Response, Inflammatory Response and Postoperative Delirium in Elderly Patients Undergoing Laparoscopic Radical Gastrectomy for Gastric Cancer*

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ABSTRACT Objective: To investigate the effects of dexmedetomidine combined with ropivacaine transversus abdominis plane block (TAPB) on stress response, inflammatory response and postoperative delirium in elderly patients undergoing laparoscopic radical gastrectomy for gastric cancer. **Methods:** 118 elderly patients who underwent laparoscopic radical gastrectomy in our hospital from July 2017 to October 2019 were selected, and randomly divided into group A (n=59, anesthesia with ropivacaine TAPB) and group B (n=59, anesthesia with dexmedetomidine combined with ropivacaine TAPB) according to the random envelope drawing. Hemodynamic indexes, stress response, inflammatory response, postoperative pain, postoperative delirium and incidence of adverse reactions were compared between two groups. **Results:** Heart rate (HR) and mean arterial pressure (MAP) of TAPB block from immediate (T1) to extubation (T4) time points in both groups were increased than those before anesthesia ($P<0.05$). HR and MAP in group B at T1~T4 time points were lower than those in group A ($P<0.05$). The levels of cortisol (Cor), norepinephrine (NE), interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) in both groups at 3 d after operation and 5 d after operation were higher than that before operation, bu 5 days after operation were lower than 3 days after operation ($P<0.05$). The levels of IL-6, TNF- α , Cor and NE in group B at 3 d after operation and 5 d after operation were lower than those in group A ($P<0.05$). The incidence of postoperative delirium in group B was lower than that in group A ($P<0.05$). There was no significant difference in the incidence of adverse reactions between two groups ($P>0.05$). The visual analogue scale (VAS) scores in group B were lower than those in group A at 6 h, 12 h, 24 h and 48 h after operation ($P<0.05$). **Conclusion:** In elderly patients undergoing laparoscopic radical gastrectomy, dexmedetomidine combined with ropivacaine TAPB can maintain hemodynamic stability, reduce stress response and inflammatory response, reduce postoperative delirium incidence, and achieve good postoperative analgesia effect and good safety.

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前言

胃癌属于消化道内的多发肿瘤,腹腔镜胃癌根治术是胃癌患者有效且安全的治疗方式^[1]。腹腔镜胃癌根治术属于微创术式,但需要对可能转移的淋巴结、原发肿瘤及被浸润的组织进行切除,术中具有无法避免的创伤,术后应激反应剧烈,增加了手术痛苦^[2-4]。尤其针对老年胃癌患者,因围术期的各种刺激还可增加术后谵妄的发生风险,降低治疗效果^[5]。合理的麻醉方案对于减轻胃癌围术期各种刺激,降低术后并发症发生率有积极的改善作用。腹横肌平面阻滞(TAPB)是于超声显像下腹内斜肌、腹横肌之间肌膜层注射局麻药,可获得较好的镇痛效果^[6,7],但有关TAPB中使用的具体局麻药尚无统一标准。罗哌卡因是TAPB的常用局麻药物,镇痛效果良好^[8]。右美托咪定作为一种镇静镇痛性较强的药物,可产生抗交感神经的效果^[9]。本研究拟探讨罗哌卡因联合右美托咪定TAPB对老年腹腔镜胃癌根治

术患者的麻醉效果,旨在为该术式麻醉药物的选择提供参考。

1 资料与方法

1.1 一般资料

选择2017年7月~2019年10月期间我院接收的行腹腔镜胃癌根治术的118例老年患者,纳入标准:患者及其家属知情本研究且签署同意书;美国麻醉医师协会(ASA)^[10]分级为I-II级者;年龄60岁以上;均符合手术指征,成功完成手术者。排除标准:对本次研究用药过敏者;穿刺部位感染者;合并心、肺、肾等脏器功能障碍者;语言或意识障碍无法配合者;合并感染、免疫缺陷者;存在长期服用阿片类药物史者;伴有凝血功能障碍者;术前认知功能障碍者。本研究经我院伦理学委员会批准进行。按随机信封抽签法将患者分为A组(n=59)和B组(n=59),两组一般资料比较无差异($P>0.05$),详细见表1。

表1 两组一般资料组间比较

Table 1 Comparison between two groups of general data

Groups	Male/female	Age(years old)	Body mass index (kg/m ²)	ASA classification	
				Grade I	Grade II
Group A(n=59)	38/21	71.92±4.38	22.39±1.82	37	22
Group B(n=59)	36/23	71.73±5.21	22.47±1.73	35	24
χ^2/t	0.145	0.214	0.245	0.143	
P	0.703	0.831	0.807	0.706	

1.2 方法

两组患者术前禁饮禁食8 h,入室后监测心率(HR)、平均动脉压(MAP)等。开放静脉通路,两组均于麻醉开始前行TAPB,穿刺点周围皮肤消毒铺巾,选择飞利浦EPIQ 5超声仪,探头频率6~13MHz,垂直腋前线放置于肋缘与髂嵴之间,识别腹内斜肌、腹外斜肌、腹横肌与腹膜等结构,使用无菌线头保护套,采用80 mm长22G的穿刺针,经平面内技术从内测向外侧进针,当针尖达到腹内斜肌与腹横肌之间的筋膜层时,回抽无血无气后,A组注入0.25%的罗哌卡因[广东嘉博制药有限公司,国药准字H20173193,规格:20 mL:150 mg(按盐酸罗哌卡因计)]62.5 mg,B组则注入0.25%的罗哌卡因62.5 mg联合右美托咪定[江苏华泰晨光药业有限公司,国药准字H20193379,2 mL:0.2 mg(按右美托咪定计)]1 μg/kg。TAPB均由同一组经验丰富的麻醉医师完成。

1.3 观察指标

(1)记录两组患者麻醉前(T0)、TAPB阻滞即刻(T1)、气管插管即刻(T2)、切皮时(T3)、拔管时(T4)的MAP、HR变化情况。(2)抽取两组术前、术后3 d、术后5 d的空腹肘静脉血5 mL,经4°C、3700 r/min离心18 min(离心半径12 cm),分离上清液,

置于冰箱中保存备用,采用酶联免疫吸附试验测定血清皮质醇(Cor)、去甲肾上腺素(NE)、白介素-6(IL-6)、肿瘤坏死因子-α(TNF-α)浓度。(3)记录两组患者术后6 h、术后12 h、术后24 h、术后48 h的视觉模拟评分法(VAS)^[11]。其中VAS评分0~10分,分数越高,痛感越强。(4)术后3 d采用意识模糊评估量表(CAM)^[12]评估患者谵妄情况,注意力不集中、急性起病、思维混乱、意识水平改变,同时具备2项以上即可确诊为术后谵妄。(5)记录两组围术期间苏醒期躁动、恶心呕吐、呼吸抑制的发生情况。

1.4 统计学方法

采用SPSS 25.0软件进行数据分析,采用Levene法检验方差齐性,采用Kolmogorov-Smirnov检验计量资料正态性,均符合正态分布具备方差齐性以均数±标准差表示。两组间比较采用独立样本t检验。不同观测时间点比较采用重复测量方差分析。计数资料以百分率表示采用 χ^2 检验。检验水准 $\alpha=0.05$ 。

2 结果

2.1 血流动力学指标对比

两组HR、MAP T0时间点对比无差异($P>0.05$),两组

T1~T4 时间点 HR、MAP 均较 T0 时间点升高 ($P<0.05$),B 组 T1~T4 时间点 HR、MAP 低于 A 组($P<0.05$),详见表 2。

表 2 两组血流动力学指标对比($\bar{x}\pm s$)
Table 2 Comparison of hemodynamic indexes between the two groups($\bar{x}\pm s$)

Groups	Time points	HR(beats/min)	MAP(mmHg)
Group A(n=59)	T0	74.71±6.52	85.19±6.39
	T1	86.38±5.49 ^a	99.01±7.26 ^a
	T2	85.83±6.69 ^a	98.46±6.92 ^a
	T3	84.73±5.71 ^a	97.53±5.88 ^a
	T4	83.54±7.68 ^a	96.79±7.27 ^a
Group B(n=59)	T0	74.59±6.74	85.46±6.12
	T1	79.27±7.25 ^{ab}	93.86±7.65 ^{ab}
	T2	81.83±6.94 ^{ab}	92.97±6.29 ^{ab}
	T3	80.63±5.83 ^{ab}	91.62±7.93 ^{ab}
	T4	78.49±6.61 ^{ab}	90.75±6.64 ^{ab}

Note: compared with T0 time points ,^a $P<0.05$; compared with group A,^b $P<0.05$.

2.2 两组应激反应指标比较

两组术前 Cor、NE 水平对比差异无统计学意义($P>0.05$),水平低于 A 组($P<0.05$),详见表 3。
两组术后 3 d、术后 5 d Cor、NE 水平高于术前,但术后 5 d Cor、

表 3 两组应激反应指标比较($\bar{x}\pm s$,ng/mL)
Table 3 Comparison of stress response indexes between the two groups($\bar{x}\pm s$,ng/mL)

Groups	Time	Cor	NE
Group A(n=59)	Before operation	279.19±37.36	246.31±21.28
	3d after operation	418.59±26.25 ^a	381.84±25.73 ^a
	5d after operation	357.62±25.91 ^{ab}	335.41±21.49 ^{ab}
Group B(n=59)	Before operation	278.21±26.87	245.25±28.55
	3d after operation	353.46±20.52 ^{ac}	334.93±23.16 ^{ac}
	5d after operation	313.37±22.47 ^{abc}	287.01±24.82 ^{abc}

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

2.3 两组炎症反应指标对比

两组术前 IL-6、TNF- α 水平对比差异无统计学意义($P>0.05$),两组术后 3 d、术后 5 d IL-6、TNF- α 水平高于术前,但术后 5 d IL-6、TNF- α 水平低于术后 3d($P<0.05$),B 组术后 3 d、术后 5 d IL-6、TNF- α 水平低于 A 组($P<0.05$),详见表 4。

2.4 两组术后不同时间点 VAS 评分对比

两组术后 12 h、术后 24 h、术后 48 h VAS 评分高于术后 6 h,术后 24 h 高于术后 12 h,但术后 48 h VAS 评分低于术后 24 h ($P<0.05$),B 组术后 6 h、术后 12 h、术后 24 h、术后 48 h VAS 评分低于 A 组($P<0.05$),详见表 5。

表 4 两组炎症反应指标对比($\bar{x}\pm s$,pg/mL)
Table 4 Comparison of inflammatory response indexes between the two groups($\bar{x}\pm s$,pg/mL)

Groups	Time	IL-6	TNF- α
Group A(n=59)	Before operation	32.78±4.25	15.93±2.23
	3d after operation	72.11±6.18 ^a	49.18±4.24 ^a
	5d after operation	59.69±5.16 ^{ab}	36.78±3.35 ^{ab}
Group B(n=59)	Before operation	33.14±5.27	15.28±2.39
	3d after operation	58.79±4.26 ^{ac}	36.93±3.27 ^{ac}
	5d after operation	46.42±5.24 ^{abc}	24.35±3.24 ^{abc}

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

表 5 两组术后不同时间点 VAS 评分对比($\bar{x}\pm s$, 分)Table 5 Comparison of VAS scores between the two groups at different time points($\bar{x}\pm s$, score)

Groups	6h after operation	12h after operation	24h after operation	48h after operation
Group A(n=59)	2.35±0.26	2.72±0.24 ^a	3.23±0.39 ^{ab}	2.86±0.29 ^{ac}
Group B(n=59)	1.52±0.23	2.19±0.25 ^a	2.76±0.21 ^{ab}	2.48±0.21 ^{ac}
t	18.366	11.747	8.150	8.152
P	0.000	0.000	0.000	0.000

Note: compared with 6h after operation, ^aP<0.05; compared with 12h after operation, ^bP<0.05; compared with 24h after operation, ^cP<0.05.

2.5 两组术后谵妄和不良反应发生情况对比

A 组术后谵妄的发生率为 15.25%(9/59),B 组术后谵妄的发生率为 1.69%(1/59),B 组的术后谵妄发生率低于 A 组($\chi^2=6.993, P=0.008$)。B 组发生恶心呕吐 1 例、苏醒期躁动 1 例、呼吸抑制 1 例,不良反应发生率为 5.08%(3/59),A 组发生苏醒期躁动 2 例、恶心呕吐 1 例、呼吸抑制 2 例,不良反应发生率为 8.47%(5/59),两组不良反应发生率对比无差异($\chi^2=0.536, P=0.464$)。

3 讨论

随着现代生活方式、饮食结构的改变,胃癌患者的发病率不断增加,接受腹腔镜胃癌根治术的患者数量也在不断增长^[13]。老年腹腔镜胃癌根治术患者常伴免疫力低下,且存在多种慢性基础性疾病,麻醉时血流动力学波动和应激反应更大,术后谵妄的发生风险增加^[14,15]。患者在接受手术治疗过程中,要求麻醉药物不仅需要做到无法感知疼痛的效果,还应有效抑制术中刺激所造成的血流波动以及身体应激性反应,过度的应激反应可对机体心脑血管产生不利,使围手术期患者的预后不佳^[16,17]。因此老年腹腔镜胃癌根治术患者选择何种麻醉方案更优尚待探讨。TAPB 是通过注入局麻药以阻止前腹壁的神经,进而发挥良好的腹壁镇痛效果^[18,19],而 TAPB 所需的局麻药容量较大,既往常用的罗哌卡因的麻醉效果有待提升^[20],马燕等^[21]学者的研究将右美托咪定联合罗哌卡因 TAPB 应用于老年患者结直肠癌根治术中,可有效提高患者的恢复质量。故本研究尝试将右美托咪定联合罗哌卡因 TAPB 应用于老年腹腔镜胃癌根治术患者中,分析结果如下。

本研究发现,右美托咪定联合罗哌卡因 TAPB 术后镇痛效果确切,可有效减轻老年腹腔镜胃癌根治术患者的血流波动。罗哌卡因具有起效迅速、无体内蓄积的优点,而右美托咪定对交感神经系统调节作用较好,可以通过刺激脑干蓝斑核 α_2 受体充分发挥其镇静、镇痛作用,提高患者舒适感,减轻机体血流波动^[22,23]。本研究中右美托咪定联合罗哌卡因 TAPB 可降低患者术后炎症反应,TNF- α 、IL-6 是机体在急性创伤或感染时全身炎症反应启动和触发因子,以往的研究结果显示^[24],右美托咪定可有效抑制促炎因子的释放,降低血清炎症因子的水平。应激反应是指机体在遭受伤害性刺激后,导致机体垂体、下丘脑、肾上腺皮质以及交感-肾上腺素髓质轴的兴奋,引起 Cor、NE 等分泌增加^[25]。强烈的应激反应会引起患者血流动力学的变化,不利于手术的顺利进行,同时也是引起患者术后谵妄的主要危险因素之一^[26]。本研究中右美托咪定联合罗哌卡因

TAPB 患者的应激反应程度更轻,术后谵妄发生率更低,分析原因可能是因为右美托咪定通过激活交感神经末梢突触前和中枢神经突出后的 α_2 受体,有效阻止麻醉刺激引起的交感神经冲动发放,从而降低儿茶酚胺释放,起到对应激反应的抑制作用^[27]。机体应激反应的减轻,血流波动的减少,对患者心脑血管的损害更轻,进而消除患者恐惧、紧张等情绪,提高患者夜间睡眠质量,使得术后谵妄的发生率明显降低^[28]。国内外不少研究报道显示^[29,30],右美托咪定可通过减轻应激反应对脑组织、心肌细胞起到有效保护作用。对比两组不良反应发生率可知,联合麻醉药物阻滞方案不会增加不良反应发生率,利于老年患者耐受。此外,本研究的研究对象为老年患者,存在肝肾功能衰退的情况,药物代谢速度慢,存在局麻药中毒风险,故而有关局麻药及右美托咪定的最佳剂量有待进一步优化。

综上所述,老年腹腔镜胃癌根治术患者采用右美托咪定联合罗哌卡因 TAPB 麻醉,可维持血流动力学稳定,减轻应激反应、炎症反应,降低术后谵妄发生率,术后镇痛效果良好,且安全性较好。

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