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小剂量舒芬太尼在乳腺肿物切除术患者术后镇痛中的应用价值 *

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摘要 目的:探讨与分析小剂量舒芬太尼在乳腺肿物切除术患者术后镇痛中的应用价值。**方法:**2019 年 6 月到 2020 年 6 月选择在南京大学医学院附属南京鼓楼医院进行乳腺肿物切除术的患者 84 例作为研究对象，根据随机信封抽签原则把患者分为研究组与对照组各 42 例。所有患者均采用气管插管全身麻醉,研究组与对照组术后分别采用剂量为 0.010 mg/kg 与 0.020 mg/kg 舒芬太尼进行自控静脉镇痛。记录两组患者围术期相关指标以及并发症发生情况;在术后 12 h、24 h 与 36 h 评定患者的疼痛状况;术前 1 d 与术后 7 d 应用放射免疫分析法检测血清肿瘤坏死因子(Tumor necrosis factor,TNF)-α、白介素(Interleukin,IL)-6 等炎症因子含量。**结果:**所有患者均顺利完成手术与麻醉。研究组术后 7 d 的呼吸抑制、寒颤、躁动、恶心呕吐、肌肉僵硬等并发症发生率为 4.8%,显著低于对照组的 28.6%(P<0.05)。两组术后 7 d 的血清 TNF-α、IL-6 水平低于术前 1 d,研究组均显著低于对照组(P<0.05)。其余指标两组差异均无统计学意义(P>0.05)。**结论:**小剂量舒芬太尼在乳腺肿物切除术患者术后镇痛中的应用能抑制炎症因子的释放,且不会影响手术、麻醉与镇痛效果,能减少患者术后并发症的发生。

关键词:剂量;舒芬太尼;乳腺肿物切除术;镇痛;炎症因子;并发症

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Analysis of the Application Value of Low-dose Sufentanil in Postoperative Analgesia of Patients Undergoing Breast Lumpectomy*

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ABSTRACT Objective: To explore and analysis the application value of low-dose sufentanil in postoperative analgesia for patients undergoing breast tumor resection. **Methods:** From June 2019 to June 2020, 84 cases of patients who underwent breast tumor resection in Nanjing Gulou Hospital, Nanjing University School of Medicine were selected as the research objects. All the cases were divided into the study group and control group with 42 cases each groups accorded to the principle of random envelope drawing. All patients underwent general anesthesia with tracheal intubation. The study group and the control group were treated with 0.010 mg/kg and 0.020 mg/kg sufentanil for self-controlled intravenous analgesia after operation. Perioperative indicators and complications of the two groups of patients were recorded; The pain status of patients at 12 h, 24 h and 36 h after operation was assessed; Radioimmunoassay was used to detect serum TNF-α, IL-6 and other inflammatory factors 1d before operation and 7d after operation. **Results:** All patients successfully completed the operation and anesthesia. The incidence of complications such as respiratory depression, chills, restlessness, nausea and vomiting, and muscle stiffness in the study group 7 days after operation was 4.8%, which was significantly lower than the 28.6% in the control group (P<0.05). The levels of serum tumor necrosis factor (TNF)-α and interleukin (IL)-6 on the 7th day after operation in the two groups were lower than those on the 1 day before operation (P<0.05). The study group was significantly lower than the control group (P<0.05). There was no statistically significant difference in the other indexes between the two groups (P>0.05). **Conclusion:** The application of low-dose sufentanil in postoperative analgesia for patients with breast tumor resection can inhibit the release of inflammatory factors without affect the effects of surgery, anesthesia and analgesia, and it can reduce the incidence of postoperative complications in patients.

Key words: Dose; Sufentanil; Breast tumor resection; Analgesia; Inflammatory factors; Complications

Chinese Library Classification(CLC): R655.8; R737.9; R614 Document code: A

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前言

乳腺肿物是临床上女性常发恶性肿瘤之一,手术是治疗乳腺肿物的主要根治方法,能提高患者的生存率,但是对于麻醉的要求比较高[1,2]。特别是乳腺肿物患者的自身免疫功能较正常人低下,手术创伤、麻醉等因素可导致患者术后剧烈疼痛,可使

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得患者出现持久性的炎症反应,不利于患者的康复[3]。乳腺肿物切除术能显著降低患者的死亡率,改善患者的预后,但是在术中需要配合合理的麻醉[4,5]。舒芬太尼复合异丙酚静脉麻醉是临床常用的全麻方法,具有使用广泛、安全性高、起效迅速、控制良好等特点[6,7]。异丙酚的优点是长时间使用无明显蓄积效应,术后清醒质量较高[8]。特别是舒芬太尼的镇痛效果比较好,是目前较为理想的静脉麻醉靶控输注药物[9]。并且舒芬太尼可有效地抑制手术造成的应激反应,并维持患者心血管功能的稳定,有利于其术后早期活动,减少术后气管插管和肺部感染的危险[10,11]。但随舒芬太尼剂量的增加,可能引起延迟性呼吸抑制等并发症的发生[12]。本文具体探讨与分析了小剂量舒芬太尼在乳腺肿物切除术患者术后镇痛中的应用价值,以明确舒芬太尼的最佳应用剂量,为其临床应用提出指导意见。

1 资料与方法

1.1 研究对象

2019 年 6 月到 2020 年 6 月选择在南京大学医学院附属南京鼓楼医院进行乳腺肿物切除术的患者 84 例作为研究对象,纳入标准:美国麻醉医师协会 (The American Society of Anesthesiologists,ASA) Ⅰ-Ⅱ级;年龄 20-70 岁,适应手术治疗;患者或其家属签署知情同意书;南京大学医学院附属南京鼓楼医院伦理委员会批准了此次研究;术前均无感染发热疾病;无过敏体质,心肺肝肾功能良好。排除标准:吸毒史、酗酒史、精神病史患者;合并严重肝肾心脑血管疾病;妊娠与哺乳期妇女;临床资料缺乏者。

根据随机信封抽签原则把患者分为研究组与对照组各 42 例,两组患者的病理类型、手术方法、肿块直径、手术方法等表 1 资料对比差异无统计学意义(P>0.05)。

表 1 一般资料

Table 1 General information

General clinical data		Study group(n=42)	Control group(n=42)
Pathological type	Malignant	12	11
	Benign	30	31
Diameter of mass(cm)		3.13± 0.32	3.09± 0.44
Age (years)		54.22± 4.22	54.98± 5.11
Body mass index(kg/m^2)		22.08± 3.09	22.38± 3.10
Heart rate (sub/min)		83.58± 5.48	83.62± 4.44
Method of operation	modified type I	17	18
	modified type II	15	16
	standard radical operation	10	8

1.2 麻醉方法

所有患者都采用气管插管全身麻醉,术前建立外周静脉通道,研究组与对照组采用 0.5 μg/L 舒芬太尼 (国药准字 H20054171,宜昌人福药业有限责任公司)预先给药。待患者意识消失后,面罩吸氧,手动控制呼吸,氧流量降为 4 L/min 进行机械通气,术中维持平均动脉压波动幅度不超过基础值 20 %。术毕待患者意识清楚、肌力恢复满意、自主呼吸恢复后拔除气管导管,送麻醉恢复室。

两组术毕行静脉自控镇痛,镇痛泵设定方法,负荷量 6 mL,2.5 mL/h 泵入,自控追加剂量 1.6 mL。研究组与对照组的镇痛药物分别为舒芬太尼 0.010 mg/kg 与 0.020 mg/kg,两组使用的舒芬太尼都使用生理盐水稀释至 100 mL,锁定时间 16 min。

1.3 观察指标

(1)记录两组患者术后住院时间、术后苏醒时间、术后拔管时间、术中出血量、手术时间等指标。(2)记录两组术后 7 d 出现的呼吸抑制、寒颤、躁动、恶心呕吐、肌肉僵硬等并发症发生情况。(3)在术后 12 h、24 h 与 36 h 采用疼痛视觉模拟评分法(Visual Analogue Scale/Score,VAS)评定患者的疼痛状况,分为 0-10 分评分,0 分无痛,7-10 分患者有渐强烈疼痛,分数越高,疼痛越严重。(4)所有患者在术前 1d 与术后 7d 采集患者外周静脉血 2-3 mL,分离血清后,应用放射免疫分析法检测血清肿瘤坏死因子(Tumor necrosis factor,TNF)-α、白介素(Interleukin,IL)-6 等炎症因子含量。

1.4 统计方法

统计软件为 EXCEL2007 与 SPSS23.00,计数数据采用率、%等表示(x^2 检验),计量资料以($\bar{x}\pm s$)表示(t 检验),检验水准为α=0.05。

2 结果

2.1 围手术期指标对比

所有患者均顺利完成手术与麻醉,两组患者围术期所有指标对比差异无统计学意义(P>0.05)。见表 2。

2.2 并发症情况对比

研究组术后 7 d 的呼吸抑制、寒颤、躁动、恶心呕吐、肌肉僵硬等并发症发生率显著低于对照组(P<0.05)。见表 3。

2.3 疼痛评分变化对比

两组术后 12 h、24 h 与 36 h 的疼痛 VAS 评分对比差异无统计学意义(P>0.05)。见表 4。

2.4 血清炎症因子变化对比

两组术后 7 d 的血清 IL-6、TNF-α 水平均显著低于术前 1 d (P<0.05),研究组也均显著低于对照组(P<0.05)。见表 5。

表 2 两组围手术期指标对比($\bar{x}\pm s$)

Table 2 The comparison of the perioperative period index between the study group and the control group($\bar{x}\pm s$)

Groups	n	Operation time (min)	Intraoperative bleeding(ml)	Timeubation time (min)	Recovery time (min)	Postoperative hospitalization(d)
Study group	42	138.25± 22.49	126.93± 6.40	17.66± 1.48	12.01± 2.61	10.42± 2.11
Control group	42	139.10± 24.17	130.93± 8.22	17.00± 2.17	11.76± 1.28	10.76± 1.72

表 3 两组术后并发症发生情况对比(n, %)

Table 3 The comparison of postoperative complications between the study group and the control group(n, %)

Groups	n	Respiratory depression	Shivering	Dysphoria	Nausea and vomitting	Muscle stiffness	Total
Study group	42	0	1	0	1	0	2(4.8%)*
Control group	42	2	3	2	3	2	12(28.6%)

Note: Compared with the control group, *$P<0.05$.

表 4 两组术后不同时间点的疼痛 VAS 评分对比(分, $\bar{x}\pm s$)

Table 4 The comparison of pain VAS scores between the between the study group and the control group at different postoperative time points (scores, $\bar{x}\pm s$)

Groups	n	12 h	24 h	36 h
Study group	42	2.01± 0.32	1.67± 0.33	0.98± 0.21
Control group	42	2.00± 0.41	1.68± 0.21	0.98± 0.31

表 5 两组手术前后血清炎症因子变化对比(ng/mL)

Table 5 The comparison of serum inflammatory factors between between the study group and the control group before and after operation(ng/mL)

Groups	n	IL-6		TNF-α	
		1 d preoperative	7 d postoperatively	1 d preoperative	7 d postoperatively
Study group	42	31.66± 2.39	9.14± 0.38*#	36.32± 4.94	9.71± 1.33*
Control group	42	31.68± 2.27	15.87± 1.74#	36.28± 3.33	19.03± 2.57#

Note: Compared with the control group, *$P<0.05$, Compared with 1 d preoperative, #$P<0.05$.

3 讨论

随着人口基数的增长以及老龄化日益显现,乳腺肿物的发病人数越来越多。手术为乳腺肿物的主要切除方法,能降低患者的死亡率,但是任何手术都有一定的应激作用,对患者也有一定的创伤,为此对于麻醉的要求比较高[12,13]。静脉麻醉与术后自控镇痛为乳腺肿物切除术的主要麻醉方法,能消除患者的焦虑和恐惧,促进患者的术后康复[14]。舒芬太尼属于强效的阿片类镇痛药,具有作用时间短、血流动力学稳定性好、半衰期较长等特点[15,16]。其对于μ 受体的亲和力要强于芬太尼,为此具有更好的镇痛效果,且镇痛时间也比较长[17,18]。

研究显示舒芬太尼的作用时间、不良反应与剂量具有相关性,因此需要在临床上合理选择恰当的药物剂量,尽量减少不良反应的影响[19]。有研究表明舒芬太尼对循环系统也有一定干扰,也可影响单肺通气时的肺内分流[20]。本研究显示:两组患者围术期所有指标对比差异无统计学意义($P>0.05$);研究组术后 7 d 的呼吸抑制、寒颤、躁动、恶心呕吐、肌肉僵硬等并发症发生率为 4.8 %,低于对照组的 28.6 %($P<0.05$),表明小剂量舒芬太尼在乳腺肿物切除术患者术后镇痛中的应用不会影响手术与麻醉效果,且能减少术后并发症的发生。李君晴[21]等研究显示:小剂量舒芬太尼可减少剖宫产术中欣母沛引起的的不良反应,可使手术不同时间点患者的心脑血管循环维持平稳状态,且有一定的镇静效果,可安全有效用于临床,与本研究结果相似。

当前肿物切除术后患者的镇痛当前得到了广泛的重视,术后疼痛比较轻的患者可实现早期翻身活动, 甚至下床运动,从而促进患者机体功能的恢复。舒芬太尼属于 " 超短效 " 的阿片类药,在进入人体后能够迅速达到血 - 脑平衡[22-24]。不过当舒芬太尼使用剂量较高时,部分肿瘤切除术后患者可出现痛觉丧失与某些精神病症状。并且舒芬太尼对心血管有负性肌力、负性传导作用,可诱导患者出现低氧反应与呼吸抑制[25]。本研究显示: 两组术后 12 h、24 h 与 36 h 的疼痛 VAS 评分对比差异无统计学意义($P>0.05$),表明:小剂量舒芬太尼的应用不会对患者的术后镇痛效果造成不良影响,分析其原因主要在于小剂量舒芬太尼就能阻断手术区域大多数交感神经冲动传导,减弱了疼痛刺激的传入量,有效减少感觉神经的敏感性,继而达到更好的镇痛效果,另外相关研究提出,舒芬太尼引起的肌肉僵硬呈剂量依赖性,为此在临床上尽量进行小剂量应用[26,27]。

随着医学技术的发展, 乳腺肿物根治术的微创性越来越好,但是在手术中也可诱发机体应激反应,促进炎症因子的释放。IL-6、TNF-α 对炎症反应具有促进作用,可直接影响肿瘤的生长状况与免疫功能[28,29]。舒芬太尼是一种超短效的阿片类药物,具有持续输注时间长、起效快、清除快等特点[30,31]。本研究显

示两组术后 7d 的血清 IL-6、TNF-α 水平低于术前 1 d(P<0.05)，研究组也显著低于对照组(P<0.05)，表明小剂量舒芬太尼的应用后，患者血清炎症反应水平较低，有助于患者更快恢复。相关研究[32-34]显示：舒芬太尼能够抑制应激反应导致的心肌氧供氧耗失衡，增加了心内膜与心外膜的血流分布，可减轻心脏前后负荷状况，从而抑制炎症因子的释放，支持了本研究上述舒芬太尼对炎症反应影响相关结论并对其作出解释。本研究也存在一定的不足，没有对患者进行中长期随访，且纳入样本数量较少，将在后续研究中深入分析。

总之，小剂量舒芬太尼在乳腺肿物切除术患者术后镇痛中的应用能抑制炎症因子的释放，且不会影响手术、麻醉与镇痛效果，能减少患者术后并发症的发生。

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