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依托咪酯用于乳腺癌手术的麻醉效果及对患者应激水平和术后苏醒质量的影响 *

甘 宁 王爱忠[△] 李 静 武凯旋 钟文晖

(上海交通大学附属第六人民医院东院麻醉科 上海 201309)

摘要 目的:探讨依托咪酯用于乳腺癌手术的麻醉效果及对患者应激水平和术后苏醒质量的影响。**方法:**选择我院 2017 年 7 月~2018 年 7 月收治的 93 例乳腺癌患者,按随机数字表法分为对照组(43 例)和研究组(50 例),对照组予以丙泊酚静脉维持麻醉,研究组予以依托咪酯静脉维持麻醉,比较两组不同时点促肾上腺皮质激素(ACTH)、醛固酮、皮质醇水平、心率(HR)、舒张压(DBP)、收缩压(SBP)、Ramsay 镇静评分,术后苏醒质量和不良反应的发生情况。**结果:**气管插管时,研究组 ACTH 浓度较麻醉诱导前上升,醛固酮、皮质醇浓度相应下降,对照组 ACTH、醛固酮、皮质醇均较麻醉诱导前上升,组间差异有统计学意义($P<0.05$);术后 24 h,两组 ACTH、醛固酮、皮质醇较麻醉诱导前无统计学意义($P>0.05$);气管插管时,对照组 HR、DBP、SBP 均上升,研究组变化不明显,两组差异有统计学意义($P<0.05$);拔管后即刻,两组 Ramsay 评分较麻醉诱导前下降,组间比较差异无统计学意义($P>0.05$)。两组拔管时间、睁眼时间、定向力恢复时间比较差异无统计学意义($P>0.05$)。两组总不良反应发生率比较差异无统计学意义($P>0.05$)。**结论:**依托咪酯用于乳腺癌手术可获得良好的麻醉效果,能够抑制机体应激反应,维持血流动力学的稳定,术后苏醒质量满意,安全性高。

关键词:乳腺癌手术;依托咪酯;应激水平;苏醒质量

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Anesthetic Effect of Etomidate for the Breast Cancer Surgery and its Effect on the Stress Level and Postoperative Recovery Quality*

GAN Ning, WANG Ai-zhong[△], LI Jing, WU Kai-xuan, ZHONG Wen-hui

(Department of Anesthesiology, East Hospital of the Sixth People's Hospital, Shanghai Jiaotong University, Shanghai, 201309, China)

ABSTRACT Objective: To investigate the anesthetic effect of etomidate in breast cancer surgery and its effect on the stress level and postoperative recovery quality. **Methods:** 93 cases of breast cancer patients who were treated from July 2017 to July 2018 in our hospital were selected and divided into 43 cases of the control group and 50 cases of research group according to random number table method. These patients, the control group was given propofol intravenous maintenance anesthesia, while the research group was given etomidate intravenous maintenance anesthesia, the changes of serum adrenocorticotrophic hormone (ACTH), aldosterone, cortisol levels, heart rate (HR), diastolic blood pressure (DBP), systolic blood pressure (SBP), Ramsay sedation score before and after treatment, postoperative recovery quality and incidence of adverse reactions were compared between two groups. **Results:** The endotracheal intubation, ACTH concentration in the research group was higher than that before anesthesia induction, the concentrations of aldosterone and cortisol decreased, ACTH, aldosterone, and cortisol in the control group were higher than those before induction of anesthesia ($P<0.05$); at 24 h after surgery, the serum ACTH, aldosterone and cortisol levels in the two groups showed no significant difference ($P>0.05$). At the time of tracheal intubation, the HR, DBP and SBP of control group was increased, which showed no obvious difference compared with the research group ($P<0.05$). Immediately after extubation, the Ramsay scores of both groups were decreased before induction of anesthesia, and there was no significant difference between the two groups ($P>0.05$). There was no significant difference in the time of extubation, blinking time, incidence of total adverse reactions and recovery time between the two groups ($P>0.05$). **Conclusion:** Etomidate can be used for breast cancer surgery to obtain good anesthetic effect, it can inhibit the body's stress response, maintain the hemodynamic stability, satisfactory quality of life after surgery.

Key words: Breast cancer surgery; Etomidate; Stress level; Awakening quality

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作者简介:甘宁(1976-),男,硕士,主治医师,主要从事临床麻醉方向研究

[△] 通讯作者:王爱忠(1968-),男,博士,主任医师,电话:18930174975, E-mail:gggaamm@163.com

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前言

乳腺癌为女性常见恶性肿瘤,恶性程度高,患者预后多不良。目前,乳腺癌的治疗仍以手术为主,其中乳腺癌根治术的效果已得到临床研究证实^[1],其能够尽可能的清除病灶,减轻瘤负荷。但麻醉及手术创伤可引起一定程度的应激反应,导致神经系统过度兴奋,刺激多种细胞因子的异常分泌,影响机体循环系统及术后恢复^[2]。相关研究报道^[3]如何既确保麻醉安全及质量,又减轻对机体的干扰,是临床麻醉的一大热点。

依托咪酯为咪唑类静脉镇静药,可快速通过血脑屏障,具有起效快速、可控性强、恢复平稳等特点,能够起到简便、安全及足够深度的镇静作用,现已广泛应用于全身麻醉诱导^[4,5]。但有研究显示^[6]依托咪酯对肾上腺皮质可能有一定的抑制作用,近年来有研究认为^[7]依托咪酯此不良反应为一过性,术后可快速恢复。尽管目前临床有关依托咪酯在乳腺癌手术中的研究较多,但其可行性及安全性尚存争议,本研究分析了依托咪酯用于乳腺癌手术的麻醉效果及对应激水平和术后苏醒质量的影响,以期临床麻醉提供更多参考依据。

1 资料与方法

1.1 一般资料

选择我院 2017 年 7 月~2018 年 7 月收治的 93 例乳腺癌患者,纳入标准^[8]:经实验室检查、影像学特征、病理组织学活检明确诊断为乳腺癌,并接受乳腺癌根治术治疗;预计生存期在 6 个月以上,卡氏评分 >60 分;肿瘤学 TNM 分期 I/II 级,美国麻醉医师协会(ASA) I/II 级。排除标准:术前接受放化疗;乳腺癌复发,或者合并其他恶性肿瘤;心肝肾等器官功能不全,肾上腺皮质功能障碍;高血压、糖尿病、心脏病等病史;严重电解质紊乱、活动性结核;长时间接受镇静、镇痛药物;妊娠或者哺乳期。所有患者按随机数字表法分为 43 例对照组和 50 例研究组,对照组 27~66 岁,平均(47.04±8.21)岁;体重 43~79 kg,平均(63.52±3.85) kg;TNM 分期: I 期 24 例, II 期 19 例;ASA 分级: I 级 20 例, II 级 23 例。研究组 26~67 岁,平均(48.03±7.13)岁;体重 45~77 kg,平均(61.99±3.27) kg;TNM 分期: I 期 29 例, II 期 21 例;ASA 分级: I 级 26 例, II 级 24 例。两组一般资料比较无统计学差异($P>0.05$)。

1.2 麻醉方法

所有患者术前常规禁饮、禁食 6 h,入室后常规创建静脉通道,静脉点滴 8~10 mL/kg·h 林格液,接通静脉麻醉泵,监测心率(HR)、舒张压(DBP)、收缩压(SBP)、脉搏氧饱和度等生命体征。术前 20 min 静脉注射液 5~10 mg 地塞米松(规格:0.5 mL:2.5 mg, 厂家: 安阳平原药业集团有限责任公司, 批号: 20170123),肌肉注射 0.5 mg 阿托品(规格:1 mL:0.5 mg, 厂家: 广东南国药业有限公司, 批号: 20161021)。麻醉诱导:常规给氧去氮 5 min,对照组静脉注射 2.0~3.0 μ g/kg 芬太尼(规格:2 mL:0.1 mg/支, 厂家: 国药集团工业有限公司, 批号: 20160710), 1~1.5 mg/kg 丙泊酚(规格:10 mL:100 mg, 厂家: 广东嘉博制药有限公司, 批号: 20161209), 0.6 mg/kg 罗库溴铵(规格:2.5 mL:25 mg, 厂家: 华北制药股份有限公司, 批号: 20160803),待肌肉松弛后放置喉罩,控制呼吸。研究组予以静脉注射 0.3 mg/kg 依

托咪酯(规格:10 mL:20 mg, 厂家: 江苏恒瑞医药股份有限公司, 批号: 20170219),除丙泊酚其余麻醉诱导和研究组相同。对照组持续输注 6~8 mg/kg·h 丙泊酚进行麻醉维持;研究组持续输注 10~15 μ g/kg·min 依托咪酯进行维持麻醉。两组均予以全凭静脉麻醉,术中维持脑电双频指数为 40~55,心率低于 50 次/min,予以 0.5 mg 阿托品;发生血压降低可加快滴注速度扩充血容量,平均动脉压较基础值下降 25%或收缩压 <90 mmHg,适当静脉注射 5~10 mg 麻黄碱(规格:1 mL:30 mg, 厂家: 鲁南贝特制药有限公司, 批号: 20170402),保持血压波动为基础值 $\leq$ 25%。术毕前 20 min 静脉注射 5 mg 地佐辛(规格:1 mL:5 mg, 厂家: 深圳万乐药业有限公司, 批号: 20161021),避免术后疼痛。缝皮前停止给予丙泊酚、依托咪酯和瑞芬太尼。术后待患者恢复自主呼吸、呼之睁眼后拔除气管。记录患者术毕至拔管时间(术毕至拔除喉罩时间)、睁眼时间(术毕至呼之可睁眼时间)、定向力恢复时间(术毕至患者可正确回答所处环境、名字),和不良反应发生情况。

1.3 观察指标

记录患者麻醉诱导前、气管插管时 HR、DBP、SBP。分别在麻醉诱导前、气管插管时和术后 24 h 在外周静脉处采集 3 mL 血液,放置于抗凝管,常规分离血清,采用电化学发光法检测血浆促肾上腺皮质激素(ACTH)、醛固酮、皮质醇浓度。于麻醉诱导前、拔管后即刻评价患者 Ramsay 评分^[9]:呼唤不醒记为 6 分,呼唤反应迟钝记为 5 分,睡眠状态可唤醒记为 4 分,嗜睡、可听从指令记为 3 分,安静可合作记 2 分,烦躁记为 1 分。

1.4 统计学分析

数据处理选用 SPSS18.0 软件包,计量资料用($\bar{x} \pm s$)表示,组间比较选用 t 检验,不同时间点计量资料采用单因素方差分析,计数资料用[(例)%]表示,组间比较用 χ^2 检验,以 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 两组不同时间点 ACTH、醛固酮、皮质醇浓度比较

麻醉诱导前,两组 ACTH、醛固酮、皮质醇浓度比较差异无统计学意义($P>0.05$);气管插管时,研究组 ACTH 浓度较麻醉诱导前上升,醛固酮、皮质醇浓度相应下降,对照组 ACTH、醛固酮、皮质醇均较麻醉诱导前上升,组间差异有统计学意义($P<0.05$);术后 24 h,两组 ACTH、醛固酮、皮质醇较麻醉诱导前差异无统计学意义($P>0.05$),见表 1。

2.2 两组不同时间点 HR、DBP、SBP 比较

麻醉诱导前,两组 HR、MAP 比较差异无统计学意义($P>0.05$);气管插管时,对照组 HR、DBP、SBP 均上升,研究组变化不明显,两组差异有统计学意义($P<0.05$),见表 2。

2.3 两组不同时间点 Ramsay 镇静评分比较

麻醉诱导前,两组 Ramsay 镇静评分比较差异无统计学意义($P>0.05$);拔管后即刻,两组 Ramsay 评分较麻醉诱导前下降,组间比较差异无统计学意义($P>0.05$),见表 3。

2.4 两组术后苏醒质量比较

两组拔管时间、睁眼时间、定向力恢复时间比较差异无统计学意义($P>0.05$),见表 4。

表 1 两组不同时间点 ACTH、醛固酮、皮质醇浓度比较($\bar{x} \pm s$)

Table 1 Comparison of the ACTH, aldosterone, and Cortisol concentrations at different time points between the two groups($\bar{x} \pm s$)

Groups	n	Time	ACTH(ng/L)	Aldosterone(pmol/L)	Cortisol(nmol/L)
Control group	43	Before anesthesia induction	6.11± 0.62	329.07± 45.76	319.09± 33.85
		Endotracheal intubation	7.65± 0.93 ^a	357.03± 50.32 ^a	350.28± 47.39 ^a
		24 h after surgery	6.20± 0.72	335.39± 42.11	323.66± 40.85
Research group	50	Before anesthesia induction	6.02± 0.66	338.29± 40.21	315.84± 36.49
		Endotracheal intubation	6.80± 0.85 ^{ab}	295.40± 40.28 ^{ab}	279.85± 30.27 ^{ab}
		24 h after surgery	6.23± 0.60	328.77± 47.59	310.31± 39.28

Note: Compared with control group ^a $P<0.05$; Compared with the same group before anesthesia induction ^a $P<0.05$.

表 2 两组不同时间点 HR、DBP、SBP 比较($\bar{x} \pm s$)

Table 2 Comparison of the HR, DBP, SBP at different time points between the two groups($\bar{x} \pm s$)

Groups	n	Time	HR(times/min)	DBP(mmHg)	SBP(mmHg)
Control group	43	Before anesthesia induction	79.31± 10.33	79.54± 9.85	120.09± 16.94
		Endotracheal intubation	86.16± 14.49 ^a	85.44± 13.27 ^a	129.65± 15.84 ^a
Research group	50	Before anesthesia induction	80.40± 12.05	80.21± 8.96	121.33± 15.21
		Endotracheal intubation	82.32± 10.85 [#]	81.09± 10.04 [#]	122.90± 13.90 [#]

Note: Compared with control group ^a $P<0.05$; Compared with the same group before anesthesia induction ^a $P<0.05$.

表 3 两组不同时间点 Ramsay 镇静评分比较($\bar{x} \pm s$)

Table 3 Comparison of the Ramsay calm score at different time points between the two groups($\bar{x} \pm s$)

Groups	n	Time	Ramsay score(points)
Control group	43	Before anesthesia induction	3.54± 0.48
		Immediately after extubation	2.46± 0.40 ^a
Research group	50	Before anesthesia induction	3.47± 0.53
		Immediately after extubation	2.35± 0.33 ^a

Note: Compared with the same group before anesthesia induction ^a $P<0.05$.

表 4 两组术后苏醒质量比较($\bar{x} \pm s$)

Table 4 Comparison of postoperative recovery quality between the two groups($\bar{x} \pm s$)

Groups	n	Tube extubation time(min)	Eye opening time(min)	Directional force recovery time(min)
Control group	43	7.82± 1.30	10.53± 1.88	17.70± 2.51
Research group	50	8.26± 1.09	11.22± 1.67	18.58± 2.09

2.5 两组不良反应发生情况比较

反应发生率比较差异无统计学意义($P>0.05$),见表 5。

两组均有拔管后躁动、恶心呕吐、注射痛发生,组间总不良

表 5 两组不良反应发生情况比较[例(%)]

Table 5 Comparison of the incidence of adverse reaction between the two groups[n(%)]

Groups	n	Inciting after extubation	Nausea and vomiting	Injection pain	Total adverse reaction rate
Control group	43	2(4.65)	2(4.65)	1(2.32)	5(11.63)
Research group	50	2(4.00)	4(8.00)	3(6.00)	9(18.00)

3 讨论

近年来,乳腺癌发病率呈上升趋势,已成为女性最常见恶性肿瘤之一^[10,11]。手术是治疗乳腺癌的重要手段,其疗效已得到临床研究证实,但乳腺癌手术对麻醉可控性的要求极高,既需

保持一定的麻醉深度,又不影响患者术后苏醒,相应增加麻醉要求。全凭静脉麻醉具有诱导快速、可控性高、苏醒时间短等特点,其麻醉效果已得到临床认可^[12]。丙泊酚为短效镇静药,其起效平稳、快速、代谢快、无蓄积作用,但其作为脂肪乳剂,静脉推注时可能引起血管产生刺激作用,引起剧烈疼痛^[13,14]。研究显示

[15,16]丙泊酚对呼吸循环系统有双重抑制作用,严重时可引起血流动力学剧烈波动,血压明显下降,难以有效维持平稳的生命体征,可能增加围手术期风险。

依托咪酯为新型催眠类静脉麻醉药,对血管无明显刺激,极少导致肌颤。有关研究显示^[17,18]容易维持心血管系统稳定为依托咪酯的突出优势之一,静脉注射 0.3 mg/kg 依托咪酯可适当减少末梢阻力,降低动脉压,增加心脏指数和心排血量,减慢心率,从而获得稳定的血流动力学。依托咪酯可轻度扩张冠脉血管,减少冠脉阻力,增加其血流,降低心肌耗氧量,对心肌收缩力的影响较小,尤其适用于冠心病、高血压等心肌血供受损者^[19]。另有研究报道^[20]依托咪酯进行全麻诱导和静脉麻醉维持时患者心指数和每搏容量较为稳定。

围手术期在麻醉、手术等外界刺激下可诱导机体功能代谢产生相应的变化,以交感神经-肾上腺髓质系统反应最为明显,导致儿茶酚胺大量释放,引起血压上升、心率加快,并促进皮质醇和 ACTH 分泌^[21]。既往研究已证实^[22]肾上腺皮质激素分泌和应激反应程度、持续时间有良好相关性,以皮质醇反应更为明显。依托咪酯能够抑制皮质醇的转化,减少醛固酮和皮质醇的分泌,诱导 17-羟孕酮、11-脱氧皮质醇等分泌,促进 ACTH 释放,一定程度的抑制肾上腺皮质功能^[23,24]。因此,依托咪酯在临床麻醉维持中的作用尚存争议。近年来,有研究显示诱导剂量的依托咪酯几乎不影响肾上腺皮质功能。Das D 等^[25]研究发现依托咪酯用于临床麻醉维持的效果确切,尽管皮质醇水平有所降低,但仍处于正常范围,且术后 24 h 恢复至术前浓度,未见与此直接相关的围手术期不良反应,表明其可安全用于全凭静脉麻醉。有关研究结果认为^[26,27],围手术期依托咪酯对患者肾上腺皮质功能的抑制作用可减轻应激状态下皮质醇大量分泌对机体所致的不良影响,可视为一种保护机制。

本研究结果显示气管插管时依托咪酯组 ACTH 较麻醉诱导前有所上升,醛固酮、皮质醇浓度相应下降,但 ACTH、醛固酮和 ACTH 浓度均处于正常范围,未导致明显的肾上腺皮质功能抑制,且抑制时间较为可逆、短暂,术后 24 h 以上血浆指标浓度均恢复至诱导前水平,说明依托咪酯能够减轻围手术期的应激反应。同时,本研究结果显示依托咪酯组气管插管时 HR、DBP 及 SBP 变化相对较小,说明其更有利于维持血流动力学的稳定。另外,本研究结果显示,依托咪酯组拔管时间、睁眼时间、定向力恢复时间和丙泊酚组相似,说明依托咪酯未延长患者拔管时间,苏醒质量满意。

依托咪酯仍存在些许不良反应,既往研究显示^[28,29]依托咪酯术后恶心呕吐发生率相对较高,且存在一定的注射痛。本研究结果显示,依托咪酯组术后发生恶心、呕吐和注射痛的患者较少,可能与小剂量静脉持续泵注给药有关。另外,两组均有少数患者发生拔管后躁动,可能与丙泊酚和依托咪酯均为速效、短效麻醉药,半衰期较短,无明显药物蓄积,手术结束时已停止药物输注,因此拔管时血浆浓度显著降低,加上拔管、吸痰等刺激增强机体交感神经系统活性,从而引起血流动力学波动,增加烦躁几率^[30]。

综上所述,依托咪酯用于乳腺癌手术可获得良好的麻醉效果,能够抑制机体应激反应,维持血流动力学的稳定,术后苏醒质量满意,安全性高。

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