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地塞米松预防乳腺癌患者术后恶心呕吐的有效性和安全性的临床研究*

余琼 刘咏辉 张洁 朱伟强 梁伟民[△]

(复旦大学附属华山医院麻醉科 上海 200040)

摘要 目的:分析地塞米松对接受乳腺癌根治术的患者术后恶心呕吐、血糖、皮质醇、出血和感染的影响,明确其临床使用的有效性和安全性。**方法:**将 160 例择期全麻下行单侧乳腺癌改良根治术的女性患者随机分为实验组(地塞米松组, n=80)和对照组(生理盐水组, n=80)。检测两组患者术后第 1 天和第 3 天血糖和血清皮质醇水平,记录术后 1~3 天恶心呕吐次数和抗呕吐药物的使用量,比较两组术后 1 周内出血和感染的发生情况。**结果:**实验组患者术后第 1 天的恶心发生率显著低于对照组,术后 1~2 天的呕吐发生率均显著低于对照组,术后第 1 天血清皮质醇较对照组显著降低($P<0.05$)。两组患者术后血糖水平比较无统计学差异($P>0.05$)。术后 1 周内,两组患者出血和感染的发生情况比较均无显著性差异($P>0.05$)。**结论:**地塞米松可有效地预防乳腺癌改良根治术患者术后恶心呕吐,短暂抑制术后内源性皮质醇水平,不增加患者术后高血糖、出血和感染的风险。

关键词:地塞米松;术后恶心呕吐;血糖;皮质醇;出血;感染

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Clinical Research on the Efficacy and Safety of Prophylactic Dexamethasone on Postoperative Nausea and Vomiting in Patients Undergoing Mastectomy*

YU Qiong, LIU Yong-hui, ZHANG Jie, ZHU Wei-qiang, LIANG Wei-min[△]

(Department of Anesthesiology, Huashan Hospital, Fudan University, Shanghai, 200040, China)

ABSTRACT Objective: To investigate the anti-emetic prophylactic effects of dexamethasone on the glucose, serum cortisol, postoperative blood loss and infection, and ensure the efficacy and safety of dexamethasone on postoperative nausea and vomiting (PONV) in patients undergoing mastectomy. **Methods:** 160 women undergoing selective unilateral modified radical mastectomy with general anesthesia were randomly divided into two groups: the experimental group (dexamethasone group, n=80) and control group (saline group, n=80). Blood glucose, serum cortisol, episodes of PONV and rescue antiemetics consumption were recorded during the first 3 days after surgery. Blood loss and infection was analyzed during the first week postoperation. **Results:** On the first day after surgery, the episode of nausea in the experimental group was significantly lower than that of the control group ($P<0.05$). The incidence of vomiting was also much lower in the experimental group than in the control group on the first two days after operation ($P<0.05$). The serum cortisol level of experimental group was significantly lower than that of the control group on the first day postoperation. There was no significant difference in the postoperative blood glucose, bleeding and infection between two groups. **Conclusion:** Dexamethasone could effectively prevent the PONV, transiently suppress the endogenous cortisol level, but did not increase the risk of postoperative hyperglycemia, blood loss and infection in patients undergoing mastectomy.

Key words: Dexamethasone; Postoperative nausea and vomiting; Blood glucose; Cortisol; Blood loss; Infection

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前言

术后恶心呕吐(postoperative nausea and vomiting, PONV)是常见的麻醉并发症之一,发生率为 20~80%,与患者情况、麻醉方式、手术类型及术后等诸多因素相关^[1]。持续严重的 PONV 可导致患者的不安不适、水电解质紊乱、术后恢复延迟、甚至医疗费用的增加。地塞米松已被广泛地单独或联合用于防治化疗和手术后的恶心呕吐。近年来,有学者对地塞米松的安全性提

出质疑,指出抗呕吐剂量的地塞米松能升高术后血糖、抑制内源性皮质醇水平^[2],增加术后感染的风险^[3]。本研究旨在探讨围术期单次剂量地塞米松防治 PONV 的有效性和安全性,并观察其对乳腺癌改良根治术患者术后恶心呕吐、血糖、皮质醇、出血和感染的影响。

1 资料与方法

1.1 病例选择

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作者简介:余琼(1978-),女,博士,主治医师,主要研究方向:围术期恶心呕吐的预防和治疗,

电话:021-52887693, E-mail: yu.qiong816@gmail.com

△ 通讯作者:梁伟民,电话:021-52887691, E-mail: chiefliang@sina.cn

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本研究选择本院乳腺外科 2012 年 8 月~2013 年 7 月行单侧乳腺癌改良根治术的女性患者 160 例,年龄 45~65 岁,ASA I~II 级。研究内容已通过复旦大学伦理委员会审查,并获得所有研究对象的知情同意。排除标准:1) ASAIII~IV 级;2)心肺功能异常;3)肝肾功能异常;4)垂体或肾上腺疾病;5)糖尿病;6)晕动病;7)既往 PONV 史;8)术前 24 小时内服用抗恶心呕吐药物(吩噻嗪类、东莨菪碱、皮质激素和三环类抗抑郁药);9)地塞米松过敏。将患者随机双盲分为 2 组:实验组(地塞米松组,n=80)和对照组(生理盐水组,n=80)。

1.2 麻醉方法

所有患者常规术前禁食禁饮,不予术前用药。入手术室后,给予常规心电图(三导联)、无创血压、脉搏氧饱和度、呼气末 CO₂ 和气道内吸入麻醉药气体检测。手术全程给予乳酸林格式液持续滴注。麻醉方式为全凭静脉麻醉。经静脉依次给予 2% 丙泊酚(TCI 模式、效应室浓度为 4 μg/ml)、芬太尼(2.5 μg/kg)和琥珀胆碱(1.5 mg/kg)后,置入 3 号或 4 号喉罩(Smiths Medical International Ltd,英国)。全麻诱导后即刻,实验组静脉给予地塞米松 8 mg,对照组给予生理盐水。麻醉维持期给予 2% 丙泊酚(TCI 模式、3.5~4 μg/ml),间断给予芬太尼(1~2 μg/kg)和顺式阿曲库铵(0.04~0.06 mg/kg)。术后,常规给予阿托品(0.02 mg/kg)和新斯的明(0.05 mg/kg)拮抗肌松残留。待患者清醒、恢复自主呼吸、TOF 比值大于 90% 后,拔除喉罩。所有患者术后在麻醉后恢复室(post anesthesia care unit, PACU)观察 0.5 小时后返回病房。所用实验用药由同一位麻醉护士准备,所有手术均由同一

组手术团队完成。

术后,若患者出现持续恶心大于 10 分钟或 30 分钟内呕吐 2 次以上,给予胃复安 10 mg 静注。若患者疼痛数字评分(NRS)大于 5 分,给予吗啡 10 mg 肌注。

1.3 指标收集和测定

(1)记录两组患者年龄、体重、是否吸烟、麻醉时间、手术时间、术中芬太尼、术中林格氏液和术后吗啡的用量;(2)记录患者术后 24、48、72 小时的恶心呕吐的发生例数、术后胃复安的用量;(3)抽取手术当日清晨 7 点(T₀)、术后 24 小时(T₁)和术后 72 小时(T₂)患者静脉血,送至医院检验科检测红细胞计数、血红蛋白、白细胞计数、血糖和血清皮质醇浓度;(4)记录术后一周内患者伤口的感染情况。

1.4 统计学分析

应用 SPSS11.0 统计软件包进行统计分析,计量资料中皮质醇浓度以 $\bar{x} \pm \text{sem}$ 表示,其余计量资料以 $\bar{x} \pm s$ 表示,两组计量资料比较采用 t 检验,计数资料比较采用 Fisher 确切概率法,以 P<0.05 为差异有统计学意义。

2 结果

2.1 两组一般资料的比较

两组患者在年龄、体重、有无吸烟、麻醉时间、手术时间、围术期芬太尼和林格氏液用量等方面均无统计学差异(P>0.05)。对照组术后吗啡的用量高于实验组,但差异无统计学意义(P>0.05),见表 1。

表 1 两组患者一般资料的比较($\bar{x} \pm s$, n=80)

Table 1 Comparison of the general information between two groups($\bar{x} \pm s$, n=80)

	Experimental group (n=80)	Control Group (n=80)
Age (years)	52.1 ± 11.4	53.0 ± 10.5
Weight (kg)	60.2 ± 13.3	63.7 ± 15.2
History of smoking a	9 (11.3%)	11 (13.8%)
Intraoperative fentanyl (μg)	335.3 ± 41.5	332.7 ± 43.2
Duration of anesthesia (min)	176.5 ± 44.2	182.4 ± 40.3
Duration of surgery (min)	153.4 ± 36.2	160.8 ± 33.3
Intraoperative LR's requirement (ml)	1233.4 ± 436.1	1173.2 ± 326.3
Postoperative morphine consumption (mg)	6.2 ± 3.4	7.8 ± 4.3

Note: a Data are number (%) of patients. LR's = Lactated Ringer's solution.

2.2 两组术后恶心呕吐发生情况的比较

术后第一天,实验组患者的恶心发生率显著低于对照组,差异有统计学意义(P<0.05)。术后第二天和第三天,两组的恶心发生率比较无统计学差异(P>0.05)。术后第一天和第二天,实验组患者的术后呕吐发生率均显著低于对照组,差异有统计学意义(P<0.05)。术后 3 天内,实验组有 2 例患者给予胃复安镇吐治疗,对照组有 10 例,两组比较差异有统计学意义(P<0.05),见表 2。

2.3 两组术前和术后血清皮质醇水平的比较

两组患者术前清晨 7 点(T₀)血清皮质醇浓度比较差异无统计学意义(P>0.05)。与本组 T₀ 比较,对照组血清皮质醇浓度各

时间点无统计学差异,实验组术后 24 小时(T₁)时点明显降低,有显著统计学差异(P<0.001)。两组组间比较,在 T₁ 时点实验组血清皮质醇浓度显著低于对照组,差异有统计学意义(P<0.001)。至术后 72 小时(T₂)时点,两组组间无统计学差异(P>0.05),见表 3。

2.4 两组术前和术后血糖水平的比较

两组患者血糖基础值(T₀)比较无统计学差异(P>0.05)。与本组 T₀ 比较,对照组各时间点血糖水平均无统计学差异,实验组术后 24 小时(T₁)时点有所升高,但无统计学差异(P>0.05)。两组组间比较,各时点血糖水平均无显著差异(P>0.05),见表 4。

表 2 两组术后恶心呕吐发生情况的比较
Table 2 Comparison of the incidence of PONV between two groups

	Nausea		Vomiting	
	Experimental group (n=80)	Control group (n=80)	Experimental group (n=80)	Control group (n=80)
1 st day	4 (5.0%)*	11 (13.8%)	4 (5.0%)*	12 (15.0%)
2 nd day	1 (1.3%)	3 (3.8%)	1 (1.3%)*	7 (8.8%)
3 rd day	1 (1.3%)	1 (1.3%)	1 (1.3%)	0
Rescue antiemetics			2 (2.5%)*	10 (12.5%)

Note: Data are number (%) of patients. *P<0.05 compared with control group.

表 3 两组术前和术后血清皮质醇水平的比较($\mu\text{g/dL}$)($\bar{x} \pm \text{sem}$, n=80)
Table 3 Comparison of the serum cortisol level before and after operation between two groups($\mu\text{g/dL}$)($\bar{x} \pm \text{sem}$, n=80)

Group	Cases	T ₀	T ₁	T ₂
Experimental group	80	17.04 $\pm$ 1.55	5.42 $\pm$ 1.87*** ^{###}	15.99 $\pm$ 2.03
Control group	80	17.23 $\pm$ 1.31	19.52 $\pm$ 1.53	16.74 $\pm$ 1.16

Note: ***P<0.001 compared with control group, ^{###}P<0.001 compared with T₀.

表 4 两组术前和术后血糖水平的比较(mmol/L)($\bar{x} \pm \text{s}$, n=80)
Table 4 Comparison of the blood glucose level before and after operation between two groups

Group	Cases	T ₀	T ₁	T ₂
Experimental group	80	5.6 $\pm$ 1.2	6.4 $\pm$ 1.8	6.0 $\pm$ 1.3
Control group	80	5.5 $\pm$ 1.3	6.0 $\pm$ 1.2	5.9 $\pm$ 1.4

2.5 两组术后出血情况的比较

术前(T₀时点),两组患者红细胞计数和血红蛋白水平比较均无统计学差异(P>0.05)。与本组 T₀比较,实验组和对照组在

T₁时点的红细胞计数和血红蛋白水平均显著下降,差异有统计学意义(P<0.05),但组间比较无统计学差异(P>0.05)。两组患者均未出现严重贫血接受输血治疗,见表 5。

表 5 两组术前和术后红细胞、血红蛋白和白细胞水平的比较($\bar{x} \pm \text{s}$, n=80)
Table 5 Comparison of the levels of RBC, Hb and WBC after operation between two groups($\bar{x} \pm \text{s}$, n=80)

Index	Group	Cases	T ₀	T ₁	T ₂
RBC ($\times 10^{12}/\text{L}$)	Experimental group	80	4.51 $\pm$ 0.62	3.96 $\pm$ 0.57 [#]	4.33 $\pm$ 0.47
	Control group	80	4.49 $\pm$ 0.57	3.98 $\pm$ 0.68 [#]	4.32 $\pm$ 0.58
Hb (g/L)	Experimental group	80	130.7 $\pm$ 12.2	112.8 $\pm$ 16.4 [#]	128.2 $\pm$ 15.7
	Control group	80	129.8 $\pm$ 11.7	114.1 $\pm$ 17.3 [#]	127.9 $\pm$ 17.1
WBC ($\times 10^9/\text{L}$)	Experimental group	80	7.63 $\pm$ 1.92	8.98 $\pm$ 2.49	8.23 $\pm$ 2.11
	Control group	80	7.71 $\pm$ 2.02	8.86 $\pm$ 2.64	8.22 $\pm$ 2.33

Note: [#]P<0.05 compared with T₀.

2.6 两组术后感染情况的比较

两组患者术前和术后各时点白细胞计数组间比较均无统计学差异(P>0.05,见表 5)。观察术后 1 周内两组患者伤口的感染情况:实验组 5 例(6.3%),对照有 4 例(5.0%),两组伤口感染的发生率比较无统计学差异(P>0.05)。伤口感染的患者均接受了抗生素治疗并痊愈。

3 讨论

以往的研究报道未接受止吐药物治疗的女性乳房术后患者 PONV 的发生率可高达 60~80%^[4]。严重的 PONV 可导致伤口裂开、吸入性肺炎、水电解质和酸碱平衡紊乱、术后恢复延迟、甚至医疗费用的增加^[1]。地塞米松已被广泛地单独或联合用

于防治化疗和手术后的恶心呕吐^[5,6],其止吐机制可能包括:抑制前列腺素的合成、促进内源性阿片样物质的释放、抑制外周和中枢 5-羟色胺的合成和释放^[7]。本研究结果显示,在术后第一天和第二天,接受单次剂量地塞米松治疗的实验组 PONV 的发生率显著低于对照组,提示单次剂量地塞米松可有效预防 PONV 的发生,这与以往研究结果一致^[8,9]。本研究中 PONV 的发生率为 5.0~15.0%,这可能与使用丙泊酚全凭静脉麻醉相关^[10],提示多模式止吐方案可有效缓解 PONV。

现有研究证实 PONV 的发生与患者因素^[11](女性、既往 PONV 病史或晕动病史、非吸烟人群和年龄)、手术因素^[12](手术时间和类型)、麻醉因素^[13](麻醉时间、麻醉方式和术后镇痛药物的使用)等密切相关。Porhomayon J 等提出不同的气道建立方

式(如喉罩、气管导管等)可能影响术后恶心呕吐的发生率^[4]。为了避免麻醉因素导致的偏倚,本研究中所有患者都接受全身麻醉(喉罩),机械通气模式为间歇正压通气(IPPV),将围麻期因喉罩放置困难或对位不良致漏气而改为气管内插管的患者列为排除对象。同时,在本研究实施过程中严格限制了手术类型(单侧乳癌改良根治术)和麻醉方式(丙泊酚联合瑞芬太尼的全凭静脉麻醉、补液种类和新斯的明肌松拮抗剂量等)。本研究的结果显示两组 PONV 相关危险因素(年龄、既往吸烟史、麻醉和手术时间、围术期芬太尼和林格氏液用量等)组间比较差异无统计学意义。因此,地塞米松预防用药可能是导致两组间 PONV 显著性差异的主要原因。

近年来,有学者对地塞米松的使用安全性提出质疑。Mackenzie J 等学者指出,大剂量的外源性糖皮质激素能抑制下丘脑-垂体-肾上腺皮质(HPA)轴分泌皮质醇^[5],显著提高患者术后高血糖、出血、伤口感染和肾上腺皮质功能不全的发生率^[6,17]。地塞米松的效价是皮质醇的 25 倍,对 HPA 轴的抑制作用长达 48~72 小时^[18,19]。本研究结果也显示给予 8 mg 地塞米松的实验组患者术后 24 小时血清皮质醇浓度显著降低(从术前 $17.04 \pm 1.55 \mu\text{g/dL}$ 将至 $5.42 \pm 1.87 \mu\text{g/dL}$, $P < 0.001$),术后 72 小时血清皮质醇恢复至术前水平。此外,本研究结果显示术前单次给予地塞米松 8 mg 不增加患者术后发生高血糖、出血和感染的风险。因此,单次剂量的地塞米松可安全用于 ASA I ~ II 级浅表手术的患者,并有效预防 PONV 的发生。但抗呕吐剂量的地塞米松能否安全用于危重或重大手术患者,还有待于进一步的临床研究^[20]。

总之,本研究表明地塞米松可安全有效地预防乳腺癌改良根治术患者的 PONV,短暂抑制术后内源性皮质醇水平,且不增加患者术后高血糖、出血和感染的风险。

参考文献(References)

- [1] Gan TJ, Diemunsch P, Habib AS, et al. Consensus guidelines for the management of postoperative nausea and vomiting[J]. *Anesth Analg*, 2014, 118(1): 85-113
- [2] Cowie BS, Allen KJ, Sais SA, et al. Anti-emetic doses of dexamethasone suppress cortisol response in laparoscopic cholecystectomy[J]. *Anaesth Intensive Care*, 2010, 38(4): 667-670
- [3] Percival VG, Riddell J, Corcoran TB. Single dose dexamethasone for postoperative nausea and vomiting - a matched case-control study of postoperative infection risk[J]. *Anaesth Intensive Care*, 2010, 38(4): 661-666
- [4] Gartner R, Kroman N, Callesen T, et al. Multimodal prevention of pain, nausea and vomiting after breast cancer surgery [J]. *Minerva Anesthesiol*, 2010, 76(10): 805-813
- [5] Song JW, Park EY, Lee JG, et al. The effect of combining dexamethasone with ondansetron for nausea and vomiting associated with fentanyl-based intravenous patient-controlled analgesia [J]. *Anaesthesia*, 2011, 66(4): 263-267
- [6] Jeon Y, Kim H, Kwak KH. Comparison of ramosetron, dexamethasone, and a combination of ramosetron and dexamethasone for the prevention of postoperative nausea and vomiting in Korean women undergoing thyroidectomy: A double-blind, randomized, controlled study[J]. *Curr Ther Res Clin Exp*, 2010, 71(1): 78-88
- [7] De Oliveira GSJ, Castro-Alves LJ, Ahmad S, et al. Dexamethasone to prevent postoperative nausea and vomiting: an updated meta-analysis of randomized controlled trials[J]. *Anesth Analg*, 2013, 116(1): 58-74
- [8] Wang B, He KH, Jiang MB, et al. Effect of prophylactic dexamethasone on nausea and vomiting after laparoscopic gynecological operation: meta-analysis[J]. *Middle East J Anesthesiol*, 2011, 21(3): 397-402
- [9] Fujii Y, Nakayama M. Reduction of postoperative nausea and vomiting and analgesic requirement with dexamethasone in women undergoing general anesthesia for mastectomy [J]. *Breast J*, 2007, 13(6): 564-567
- [10] Akkurt BC, Temiz M, Inanoglu K, et al. Comparison of recovery characteristics, postoperative nausea and vomiting, and gastrointestinal motility with total intravenous anesthesia with propofol versus inhalation anesthesia with desflurane for laparoscopic cholecystectomy: A randomized controlled study [J]. *Curr Ther Res Clin Exp*, 2009, 70(2): 94-103
- [11] Bakshi SG, Jibhake B, Sareen R, et al. Nausea and vomiting after breast cancer surgery, and relationship with tumor receptor status[J]. *J Anesth*, 2012, 26(2): 187-195
- [12] Eberhart LH, Geldner G, Kranke P. The development and validation of a risk score to predict the probability of postoperative vomiting in pediatric patients[J]. *Anesth Analg*, 2004, 99(6): 1630-1637
- [13] Li NL, Yu BL, Tseng SC, et al. The effect on improvement of recovery and pain scores of paravertebral block immediately before breast surgery[J]. *Acta Anaesthesiol Taiwan*, 2011, 49(3): 91-95
- [14] Porhomayon J, Wendel PK, Defranks-Anain L, et al. Do the choices of airway affect the post-anesthetic occurrence of nausea after knee arthroplasty? A comparison between endotracheal tubes and laryngeal mask airways[J]. *Middle East J Anesthesiol*, 2013, 22(3): 263-271
- [15] Mackenzie J. Guidelines and use of dexamethasone for postoperative nausea and vomiting[J]. *Anaesthesia*, 2013, 68(12): 1285-1286
- [16] Ho CM, Wu HL, Ho ST, et al. Dexamethasone prevents postoperative nausea and vomiting: benefit versus risk [J]. *Acta Anaesthesiol Taiwan*, 2011, 49(3): 100-104
- [17] Nazar CE, Lacassie HJ, Lopez RA, et al. Dexamethasone for postoperative nausea and vomiting prophylaxis: effect on glycaemia in obese patients with impaired glucose tolerance[J]. *Eur J Anaesthesiol*, 2009, 26(4): 318-321
- [18] White SM, Campbell DJ. Primary hypopituitarism and peri-operative steroid supplementation[J]. *Anaesthesia*, 2009, 64(3): 336-337
- [19] Yu Q, Gao L, Gu MH, et al. Antiemetic effects of combined methylprednisolone and tropisetron in mastectomy [J]. *Minerva Anesthesiol*, 2013, 79(2): 130-136
- [20] Ho KM. Dexamethasone for postoperative nausea and vomiting: time for a definitive phase IV trial[J]. *Anaesth Intensive Care*, 2010, 38(4): 619-620