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Effect of multimodal intervention on postoperative nausea and vomiting in patients undergoing gynecological laparoscopy

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Abstract

Objective: Postoperative nausea and vomiting (PONV) is a common complication in patients undergoing gynecological laparoscopic surgery, and achieving good results is difficult with a single antiemetic method. This study investigated whether multimodal intervention can reduce PONV in patients undergoing gynecological laparoscopic surgery.

Methods: A total of 153 patients who underwent gynecological laparoscopic surgery were randomized into the control group and multimodal group. Patients in the multimodal group received dexmedetomidine 1 μg/kg intravenously 15 minutes before induction of anesthesia. A bilateral transversus abdominis plane block was performed with 0.375% ropivacaine 30 mL after induction of anesthesia. Scores of postoperative nausea and vomiting, the visual analog scale, and the Bruggemann comfort scale (BCS) were assessed 24 hours postoperatively.

Results: Nausea and vomiting scores were significantly lower at 2, 6, and 24 hours in the multimodal group compared with the control group. BCS scores were significantly higher at 0 to 24 hours in the multimodal group compared with the control group.

Conclusions: Multimodal intervention improves PONV and increases patients' comfort. The multimodal approach can also enhance recovery after gynecological laparoscopic surgery.

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Introduction

Postoperative nausea and vomiting (PONV) is a common complication, which causes wound dehiscence, patient's discomfort, a longer discharge time, and high costs.[1] The incidence of PONV is as high as 80% in gynecological laparoscopic surgery with high-risk patients.[2] Vomiting is a type of complex nerve reflex, mainly involving the four following pathways that activate vomiting: (1) area postrema; (2) forebrain; (3) gut vagal afferent fibers; and (4) vestibular input. Stimulation of one of these afferent pathways may activate the sensation of vomiting through cholinergic (muscarine), dopaminergic, histamine, or 5-serotonergic receptors.[3–5]

At present, a single drug treatment or traditional acupuncture treatment is still unable to control the high incidence of PONV in gynecological laparoscopic surgery. In recent years, international management PONV guidelines have recommended multimodal intervention that can effectively prevent PONV.[6] Because several systems are involved in the pathogenesis of PONV that act on different receptors, multiple pathways are required for combined treatment of PONV.

Postoperative pain management mainly depends on opioids and use of opioids postoperatively has a significant effect on the incidence of PONV.[7] Apfel et al.[8] found that the use of postoperative opioids may be the strongest predictor of PONV. Transversus abdominis plane (TAP) block has a good analgesic effect and can reduce the use of postoperative opioids. Dexmedetomidine combined with TAP block has a better analgesic effect.[9,10] Dexmedetomidine also has the effect of preventing PONV.[6] As a 5-hydroxytryptamine 3 (5-HT3) receptor antagonist, ondansetron is commonly used to prevent PONV. The mechanisms of dexmedetomidine, ondansetron, and TAP block in preventing postoperative nausea and vomiting are different. Therefore, multimodal antiemetic intervention with TAP block combined with dexmedetomidine and 5-HT blockers were used in this study. We aimed to provide an effective method for preventing PONV by investigating the incidence of nausea and vomiting after patients had gynecological laparoscopic surgery.

Materials and methods

This study was approved by the Ethics Committee of Yijishan Hospital of Wannan Medical College (no: [2015] 73). The data were submitted as a registered project to chictr.org (ChiCTR-IPR-15007359). Written informed consent was obtained from all patients participating in the study.

A total of 160 patients were recruited who underwent general anesthesia in gynecological laparoscopic surgery in Yijishan Hospital of Wannan Medical College from June to December in 2015. Inclusion criteria were as follows: American Society of Anesthesiologists I–II, aged 18 to 65 years, and not taking hormones, opiates, or antihistamine antiemetic drugs 24 hours

before the operation. Exclusion criteria were as follows: nausea or vomiting 24 hours before surgery, drug or alcohol abuse, refusal to accept TAP block, unable to communicate, allergy to a local anesthetic, uncontrolled hypertension, and atrioventricular block above the second degree. According to the random number table method, the patients who met the criteria were randomly divided into two groups of the control group and the multimodal group.

All patients were fasted 8 hours before surgery with no preoperative medication. Peripheral vein access was provided after entering the operation room. Continuous monitoring of an electrocardiogram, heart rate, non-invasive arterial blood pressure, pulse oxygen saturation, and end-tidal carbon dioxide was performed by an HXD-1 monitor machine (Heilongjiang Huaxiang Co. Ltd., Harbin, China).

Patients in the multimodal group received dexmedetomidine 1 μg/kg 15 minutes before induction. The two groups were induced by intravenous midazolam 0.08 mg/kg, propofol 2 mg/kg, fentanyl 4 μg/kg, and rocuronium 0.6 mg/kg before tracheal intubation. After induction of anesthesia, the bilateral TAP in patients in the multimodal group was blocked under ultrasound by researchers who did not participate in the monitoring and postoperative follow-up. For blocking, the patients were placed in the supine position and their abdominal skin was sterilized. A linear ultrasonic scanning probe (S8; SonoScape Corp. LP, Shenzhen, China) was placed in the midpoint of the iliac crest and subcostal margin. An axial scan was performed along the vertical axillary line, followed by identification of the external oblique muscle of the abdomen, and oblique and transverse abdominal muscles. Puncture was administered by the ultrasonic in-plane technique on the inside or outside of the probe, and then 0.375% ropivacaine 30 mL was injected (multimodal group). Anesthesia and muscle relaxation were maintained by intraoperative continuous infusion of propofol and remifentanil, and intermittent injection of vecuronium in the two groups.

The depth of anesthesia was monitored by Narcotrend (MonitorTechnik, Bad Bramstedt, Germany), and values of patients were maintained between 37 and 46. Flurbiprofen axetil 50 mg and ondansetron 8 mg were provided by intravenous drip before the end of the surgery. Patients in the two groups were asked whether they required a postoperative analgesic pump before surgery. If the patient required an analgesic pump, a patient-controlled analgesia (PCA) intravenous analgesia machine (Henan Tuoren Medical Instrument Group Co. Ltd., Xinjiang, Henan, China) was turned on at the end of the operation. Analgesic drug formulation included sufentanil 100 μg, which was diluted with saline to 100 mL, with a background infusion of 1 mL/hour, a PCA dose of 2 mL, and a lock time of 8 minutes. If patients complained of wound pain (visual analog scale [VAS] score > 3) postoperatively, flurbiprofen axetil 50 mg was dripped intravenously.

With regard to outcome measures, participants were followed up by one researcher who did not participate in the anesthesia procedure at 2, 6, and 24 hours after surgery. Nausea and vomiting scores, the VAS score, and the Bruggemann comfort scale (BCS) score were recorded.[11] Adverse postoperative effects and the number of additional analgesics were also recorded.

Nausea and vomiting was classified into 10 levels as follows: a score of 0 was no nausea or vomiting; a score of 1 to 2 was mild nausea, but no vomiting; a score of 3 to 4 was obvious nausea; a score of 5 was mild vomiting; a score > 5 was frequent nausea and vomiting; and a score of 10 was intolerable vomiting. Antiemetic drugs were provided if the patient had a score > 5.

If patients complained of persistent nausea (>1 hour) or vomiting (>2 times), antiemetic drugs, such as intravenous granisetron 3 mg, were also provided. The BCS was scored as follows: 0, persistent pain; 1, no pain when quiet, but severe pain with deep breathing or coughing; 2, no pain when quiet, but mild pain with deep breathing or coughing; 3, painless when deep breathing; and 4, no pain when coughing.

Statistical analysis

On the basis of our pretest result, we expected a PONV event rate of approximately 55% in the control group and a reduction of 25% in the multimodal group. A sample size calculation (Power and Sample Size Calculation, version 3.1.2; Vanderbilt University, Nashville, TN, USA) showed that 148 patients were required to achieve a power of 0.8 with a two-tailed α level of $P = 0.05$. We planned to include a total of 160 patients to compensate for dropouts.

Continuous variables are expressed as the mean ± standard deviation. Normally distributed continuous variables were compared between the two groups using the Student's t test. Categorical variables were compared using the chi-square test. $P < 0.05$ was considered to indicate a statistically significant difference. Statistical analyses were performed using SPSS software (version 16; SPSS, Chicago, IL, USA).

Results

General characteristics

A total of 78 patients were included in the multimodal group and 75 patients were included in the control group because open surgery was adopted or there was loss to follow-up. There was no significant difference in baseline characteristics between the two groups (Table 1).

Incidence of nausea and vomiting

The nausea and vomiting scores in the multimodal group were significantly lower at 2 ($P < 0.05$), 6, and 24 hours after the operation (both $P < 0.01$). The incidence of nausea and vomiting was significantly lower in the multimodal group than in the control group (both $P < 0.01$). Patients required additional antiemetics significantly less frequently in the multimodal group than in the control group ($P < 0.01$, Table 2).

The VAS and BCS scores

The VAS score in the multimodal group at 24 hours postoperatively was not significantly different between the groups. There was no significant difference in the rate of additional analgesics required after the operation between the two groups. However, the amount of times that the PCA pump was pressed was significantly

Table 1. Demographic data and characteristics of the two groups.

Group	n	Age (years)	BMI (kg/m^2)	ASA (n, I/II)	Smoking (n, %)	History of motion sickness or PONV (n, %)	Duration of anesthesia (minutes)	Dosage of intraoperative fluid infusion ($mL \cdot kg^{-1} \cdot hour^{-1}$)	Dosage of analgesic pump ($mL \cdot kg^{-1} \cdot hour^{-1}$)
C	75	42 ± 9	23 ± 3	36/39	3 (4.0)	51 (68.0)	91 ± 38	14 ± 4	32 (42.6)
M	78	41 ± 8	22 ± 3	34/45	3 (4.0)	40 (51.2)	81 ± 40	14 ± 5	28 (35.8)

Data are mean ± standard deviation. C: control; M: multimodal; BMI: body mass index; ASA: American Society of Anesthesiologists; PONV: postoperative nausea and vomiting

Table 2. Incidence of nausea and vomiting in patients in the two groups after the operation

Group	n	2 hours after the operation	6 hours after the operation	24 hours after the operation	Nausea (n, %)	Vomiting (n, %)	Additional antiemetic drugs (n, %)
C	75	1.0 ± 1.7	2.1 ± 2.2	2.4 ± 2.2	52 (70.1)	37 (48.7)	38(50.8)
M	78	0.3 ± 1.4^a	0.8 ± 2.0^b	1.0 ± 1.8^b	25 (32.6)[b]	11 (14.6)[b]	17 (21.7)[b]

Data are mean ± standard deviation. C: control; M: multimodal. [a]$P < 0.05$, [b]$P < 0.01$, compared with the C group

Table 3. Postoperative VAS and BCS scores in the two groups

Variable	C group (n = 75)	M group (n = 78)
VAS score		
2 hours after the operation	1.6 ± 1.1	1.3 ± 1.3
6 hours after the operation	1.7 ± 1.2	1.6 ± 1.3
24 hours after the operation	1.6 ± 1.1	1.2 ± 1.2
Press times of the PCA pump	6.7 ± 1.2	1.6 ± 1.1 [b]
Additional antiemetic drugs (n, %)	3 (4.0)	4 (5.1)
BCS score		
2 hours after the operation	1.9 ± 0.9	2.6 ± 0.8^b
6 hours after the operation	1.7 ± 0.9	2.3 ± 0.8^b
24 hours after the operation	2.2 ± 0.8	2.7 ± 0.7^a

Data are mean ± standard deviation. C: control; M: multimodal; VAS: visual analog scale; BCS: Bruggemann comfort scale; PCA: patient-controlled analgesia. [a]$P < 0.05$, [b]$P < 0.01$, compared with the C group

less in the multimodal group than in the control group ($P < 0.01$). The BCS score was significantly higher in the multimodal group at 2, 6 (both $P < 0.01$), and 24 ($P < 0.05$) hours after the operation (Table 3).

Discussion

The overall incidence of nausea in PONV is approximately 50%, but in high-risk groups, it is as high as 80%.[6,12] The risk factors of PONV include female sex, a history of PONV or motion sickness, no smoking, age (<50 years), inhalation anesthesia, postoperative opioids, anesthesia time, gynecological surgery, and laparoscopic surgery.[13,14] According to Apfel's PONV risk rating scale, gynecological laparoscopic surgery is a highly dangerous category of PONV.[2] The patients in the current study underwent gynecological laparoscopic surgery.

Because of triggering of receptors, anesthetics and opioids may be the cause of PONV. The cause of nausea and vomiting may be associated with drug sympathomimetic action or its effect on the adrenal receptor, excitability of sympathetic nerves, and high circulating catecholamine levels in the vomiting center. A variety of hormones are secreted when the body is stimulated. Previous studies have shown that animal hormones are secreted when anesthetic is injected into the vein, such as arginine vasopressin, gastrin, thyrotropin-releasing hormone, and angiotensin II.[15] These substances can act on the vomiting center in various ways. Analgesic drugs stimulate the body to produce chemical 5-HT, which can activate receptors in the medulla

oblongata vomiting center, and this triggers and increases sensitivity of the vestibular response to movement. The 5-HT3 receptor is distributed in the gastrointestinal tract and may also cause anesthetic stimulation, which results in vagal impulses and activates the emetic center.

Single use of drugs affects prevention of PONV, but the incidence of PONV is still high in high-risk patients who have a gynecological laparoscopic operation.[16] On the basis of analysis of a large number of studies, PONV international management guidelines recommend that the method of combination therapy should be used to prevent PONV with moderate- and high-risk factors for adults.[17–20] Therefore, in this study, we adopted a multimodal antiemetic intervention combined with TAP block with dexmedetomidine and a 5-HT receptor blocker. The dose of dexmedetomidine and ondansetron were based on international management PONV guidelines, and the dose of ropivacaine in the TAP block was based on previous studies.[6,9]

TAP block refers to occlusion of the abdominal intercostal nerve, including T_7 to T_{12}, ilioinguinal and iliohypogastric nerves, and dorsal branches of $L_{1–3}$ nerve conduction. TAP block can be effectively applied to laparoscopic, inguinal hernia, abdominal hysterectomy, and abdominal surgeries. TAP has a precise effect on postoperative analgesia.[21] In our study, the number of times that the analgesic pump was pressed in the multimodal group was significantly less than that in the control group. Previous studies have shown that reducing use of opioids may reduce the risk of PONV, but pain itself is also a possible cause of PONV.[22,23]

Dexmedetomidine has analgesic, sedative, and sympathetic block effects, and does not cause respiratory depression. Dexmedetomidine activates presynaptic alpha 2 receptors, inhibits norepinephrine release, inhibits postsynaptic membrane alpha 2 adrenergic receptors, makes cells hyperpolarized, and inhibits pain transmission to the brain. Dexmedetomidine reduces sympathetic tension by acting on alpha 2 receptors centrally or at other sites, and catecholamines are released. Elevated plasma catecholamine levels are one of the factors contributing to PONV, and this may be the mechanism of dexmedetomidine for preventing PONV.[24] The 5-HT3 receptor is located in the chemical and sensory area of the upper digestive tract with vagal afferents on 5-HT3 receptors. The mechanism of 5-HT3 receptor antagonists on nausea and vomiting involves blocking 5-HT with high selection. The 5-HT3 receptors block or inhibit the vomiting reflex induced by the vagus nerve to achieve a dual antiemetic effect centrally and peripherally.[25] Drugs with different mechanisms can optimize antiemetic drugs' efficacy for PONV. Drugs with different mechanisms can enhance the preventive effect of PONV for the population who is above average in risk.

In the current study, the scores of nausea and vomiting in the multimodal group were lower than those in the control group at each time point (2–24 hours) after the operation. Through a combination of different mechanisms and different methods, which acted on the target of different pathophysiological mechanisms and different times, we achieved the best curative effect to reduce vomiting and adverse reactions.

In summary, TAP block combined with dexmedetomidine and 5-HT blockers can effectively improve the postoperative analgesic effect and reduce the occurrence of PONV. This improves patients' comfort and increases patients' satisfaction with anesthesia. Therefore, multimodal intervention can provide significant improvement in PONV, increase patients' comfort, and enhance recovery after gynecological laparoscopic surgery.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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