The Effect of Intraoperative Tramadol on Post-Operative Opioid Requirements After Laparoscopic Sleeve Gastrectomy for Morbidly Obese Patients: A Retrospective Multicentric Cohort Study

Original Article

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ABSTRACT

Background: This study aimed to compare the efficacy and safety of combined intraoperative tramadol with pethidine versus pethidine alone and to assess their impact on post-operative pethidine requirements after laparoscopic sleeve gastrectomy (LSG).

Methods and Results: This multicenter cohort research included 400 patients with morbid obesity who had LSG between January 2021 and December 2022. The patients included in the study were allocated to one of two treatment groups that were not randomized. Group A received only 1 mg/kg of pethidine before extubation. , while Group B got 1 mg/kg tramadol given when the surgeon started a gastric division with 1 mg/kg of pethidine before extubation. Doses were based on the patient's ideal body weight.The mean VAS pain score at 1, 3, 6, 12, and 24h after LSG was significantly reduced in group B (4.2, 2.89, 2.03, 1.69, and 0.26, respectively) compared to group A (5.1, 4.16, 3.21, 2.78, and 0.44). Post-operative nausea and vomiting (PONV) were higher in group A at 3 and 6 h after LSG. Opioid consumption in the post-operative period was less in Group B than in Group A. There was a significant reduction in the requirement for on-demand metoclopramide and ondansetron in group B. Oxygen desaturation (<92) significantly developed in group A after surgery and was managed using an oxygen mask. Post-operative bradycardia was significantly observed in group B after LSG.

Conclusion: Intraoperative tramadol with pethidine provides superior post-operative analgesia and safety over Intraoperative pethidine alone.

Key Words: Laparoscopic sleeve gastrectomy, multiple analgesia protocol, obesity, post-operative nausea and vomiting, post-operative pain. tramadol.

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INTRODUCTION

Obesity-related comorbidities [obstructive sleep apnea (OSA), cardiac diseases, type 2 diabetes, fatty liver disease, gastroesophageal reflux disease, and hypertension] are rising as the worldwide obesity rate increases. The only treatment that can help morbidly obese patients lose weight and gradually lessen comorbidities linked with obesity is bariatric procedures. Laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic sleeve gastrectomy (LSG) are the most widespread surgical operations[1-3].

Post-operative pain remains a common and unsatisfactory event, particularly in morbidly obese patients, and may be associated with obstructive sleep apnea. Bariatric surgery patients must get safe and efficient analgesia, which is essential given that up to 45% of patients report substantial pain in the first two days following surgery. In routine surgical patients, parenteral opioids like morphine or fentanyl are frequently used to treat immediate post-operative pain. When opioids are provided in the recommended doses for the patients, the prevalence of opioid-related side effects, such as post-operative nausea and vomiting (PONV), pulmonary complications, or drowsiness, is minimal. Obese people are more susceptible to the side effects of opioids due to certain anatomical and physiological features[4-7].

Enhanced recovery after surgery (ERAS) protocols are well proposed for the care of the surgical patient. Strong evidence and suggestions to use multimodal analgesia to lessen opioid usage were found in the current ERAS bariatric surgery protocol. Furthermore, severe restrictive syndrome brought on by obesity and atelectasis brought on by lying flat contribute to decreased respiratory function following bariatric surgery. Additionally, perioperative opioids encourage upper airway obstruction, possibly resulting in post-operative hypoxemia[8, 9].

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In morbidly obese patients undergoing LSG, the dose of intra- and post-operative opioid administration should be minimized. To reduce opioid-related adverse events (ORAE), a multimodal analgesia approach should be used to decrease opioid consumption. There are few studies in the literature showing the effect of tramadol on post-bariatric surgery courses as regards the opioid requirements. Tramadol is a synthetic pain killer having opioid, noradrenergic, and serotoninergic properties. Its opioid and nonopioid analgesic properties work together synergistically to produce potent analgesia with few severe side effects[10, 11]. This study hypothesized that the combined tramadol with pethidine would be more effective and safer than pethidine alone and reduce post-operative pethidine requirements after LSG for morbidly obese patients.

PATIENTS AND METHODS

Patients and characteristics

Study design

This multicenter cohort research included patients with morbid obesity who had LSG between January 2021 and December 2022. The age range for LSG was 16 to 65 years, and the eligibility requirements included morbid obesity [defined as a body mass index (BMI) of more than 40 or more than 35 with at least one comorbidity].

The study's exclusion criteria were: patients below the age of 16 or over 65 years, with pregnancy or inflammatory bowel disease, and those with BMI more than 60, patients with a history of alcohol or drug addiction, chronic opioid use, uncontrolled hypertension, a first-degree heart block, allergies to pethidine, and patients developed post-operative complications that required re-exploration. All patients completed an informed permission form after being informed about the procedure and any potential post-operative morbidities. Data were prospectively recorded in a computer file. The Institutional Review Board (IRB) approved the study protocol, code R.23.01.2008, and all patients agreed to our research's terms after we explained each intervention's benefits and possible drawbacks. And clinical trial reg. : ClinicalTrials.gov ID: NCT05696886.

This study followed the STROBE statement and provided a complete STROBE checklist.

Preoperative assessment

All patients had LSG surgery following a diagnostic workup that included recording demographic data (age, sex, comorbidities, and BMI) and a routine physical examination. Complete laboratory tests, endocrine assessment, investigation of the heart, pulmonary function testing, and psychiatric assessment were conducted. Upper GIT endoscopy, abdomen ultrasonography, and chest X-rays were standard procedures. Before surgery, each patient was received a prophylaxis dose of 40 mg SC enoxaparin once daily and continued for 21 days postoperatively and had both lower limbs compressed with an elastic bandage.

Anesthesia and analgesia protocol

The usual ASA monitoring tools were used. Anesthesia was induced using propofol (2 mg/kg), fentanyl (1 μg/kg), and lidocaine (1 mg/kg). Rocuronium (0.6-1.2 mg/kg) was administered to help with tracheal intubation. Sevoflurane 2% and a combination of oxygen and air (FiO2 = 50%) were used to maintain anesthesia. Additional fentanyl (50 μg), dexamethasone (8 mg IV), ondansetron 4 mg and metoclopramide 10 mg IV as antiemetic prophylaxis, and paracetamol (1 g) were given to all patients following induction. Tramadol (1 mg/kg) was given when the surgeon started a gastric division for the tramadol group. At the end of the operation, 1 mg/kg of pethidine was given before extubation.

The patients included in the study were allocated to one of two treatment groups that were not randomized. Group A received only 1 mg/kg of pethidine before extubation, while Group B got 1 mg/kg tramadol given when the urgeon started a gastric division with 1 mg/kg of pethidine before extubation. Doses were based on the patient's ideal body weight.

Surgical technique

The patient was given general anesthesia for the LSG operation. The creation of pneumoperitoneum required up to 15 mmHg of CO_2. Depending on the surgeon's discretion, three to five ports were positioned. Above the pylorus, devascularization of the larger omentum using sealing devices started, moving on to the cardio-esophageal junction, revealing the left crus of the diaphragm. A 36-French calibration tube was used, after which the gastric division was carried out. Depending on the surgeon's choice, the antral was either preserved or resected. The gastric division was followed by gastropexy. The staple line could be checked after Methylene Blue was injected into the sleeved tube.

Post-operative management

Along with daily reports, vital signs, VAS for pain, nausea, and vomiting, pethidine requirement, oxygen saturation, oxygen requirement, and intravenous fluid were documented. After six h following surgery, clear oral fluid started to flow. Patients were discharged if there were no complaints. The patients were advised to take vitamins, an anticoagulant, and a proton pump inhibitor (PPI) for two months and drink lots of water.

Outcomes

Primary outcome

The primary outcome was post-operative pethidine requirements and total dose of pethidine consumption at 24 h. The pain's visual analog scale (VAS) was recorded upon arrival at the post-anesthesia care unit (PACU) and repeated at predetermined intervals. On a scale of 0 to 10, with 0 meaning no pain and 10 meaning the greatest agony possible, all patients were questioned about VAS of pain. Post-operative analgesia was given according to the patient's requirement and pain level (VAS). If the VAS pain score was over 4, post-operative pethidine medication was given in 1 mg/ideal body weight increments in both groups. In addition, if the VAS pain score was more than 2, post-operative paracetamol (1 g) medication was given in both groups. In addition, pethidine was administered if intravenous paracetamol did not offer adequate pain relief.

Secondary outcomes

Secondary outcomes included hemodynamic vital signs during and after the surgery, time to release from PACU, the frequency of itching, nausea, and vomiting, respiratory problems in the PACU, and the quality of recovery using quality of recovery -40 score (QoR-40) at 24 h. The QoR-40 has been verified as an accurate instrument to evaluate the post-operative quality of recovery and contains 40 questions relating to five areas where 1 = very poor and 5 = excellent. It measures five dimensions : pain (35 points), physical comfort (60 points), emotional state (45 points), psychological support (35 points), and physical independence (25 points), with total scores ranging from 40 to 200[12-14].

A modified Aldrete score was utilized to discharge the patient from the PACU. The Modified Aldrete score included five items (Breathing, consciousness, SPO2, physical activity, and circulation) A score of "0", "1", or "2" is given for each category, two representing the ideal condition. A score of 8 is required to be discharged from the PACU[15]. In addition, for the first 15 min after arriving in the PACU, hemodynamic values, VAS for pain, and modified Observer's Assessment of alertness/Sedation Scale (OAA/S) scores were documented every 5 min. Thereafter, until transfer to the ward, these measurements were taken at 15-min intervals. The MOAA/S ranges from 0 to 5, with a score of 5 defined as awake or minimally sedated and 0 defined as general anaesthesia[16].

The presence of nausea and vomiting, emesis attacks, and the requirement for rescue antiemetic medication were noted. Patients received antiemetics postoperatively according to the patient's needs, including intravenous ondansetron 4 mg and metoclopramide 10 mg. Metoclopramide (10 mg) was intravenously administered to patients who reported only nausea. A frequency of oxygen desaturation occurrences of 92% for 10 s despite oxygen delivery, blockage demanding chin lift or jaw push or nasopharyngeal airway, and the necessity for reintubation were documented as respiratory problems. One month following discharge, patients were contacted by phone and questioned to score their level of satisfaction with their surgical experience overall using the VAS scale.

Statistical analysis

Descriptive statistics were stated as numbers and percentages for categorical variables, while mean and standard deviation were used to describe continuous variables. All statistical evaluations were performed using SPSS 17 (SPSS Inc., Chicago, IL, USA). *P-values* less than 0.05 were considered statistically significant. The student T-test was used for continuous variables and the Chi-square test for categorical variables. Factorial ANOVA analyzes in which repeated measures (continuous and normally distributed variables measured at different times) and the difference between groups were evaluated together.

RESULTS

Patient characteristics

A total of 400 patients who underwent LSG were included in this study. The mean age of the participants was 31.58 ± 1.63 years (range, 16-60). Of these, 148 (37%) were males, and 252 (63%) were females. The patients in the trial were assigned to one of two non-randomized treatment groups. However, they were classified based on the time of surgery: Between January 2021 and December 2021, Group A received pethidine alone (n=200 patients), whereas Group B received Tramadol plus Pethidine between January 2022 and December 2022 (n=200 patients). Both groups were well matched regarding baseline demographics, comorbidities, operative time, anesthetic time, and PACU duration, except for a higher preoperative hemoglobin and blood sugar in group A (Table 1). OSA was presented in 128 (64%) patients in Group A and 129 (64.5%) patients in Group B.

Vital signs

Both groups have A non-significant difference regarding preoperative and intraoperative heart rates and blood pressures (Table 1). Severe hypotension (systolic blood pressure ≤ 90 mmHg) did not happen in either group. A repeated measures ANOVA with a Greenhouse-Geisser correction found that the mean systolic blood pressure differed significantly among different time points $F(1.73, 692.2) = 520.4$, $p < .0001$. There was a statistically insignificant interaction between both groups and systolic blood pressure at different time points, $F(1.73, 692.2) = 0.39$, $p = 0.65$). Factorial ANOVA with a Greenhouse-

Geisser correction determined that the mean pulse rate differed significantly among different time points F(2.03, 808.6) = 19.84, $p < 0.0001$). There was a statistically significant interaction between both groups and pulse rate at different time points, F(2.03, 808.6) = 4.13, $p = 0.016$ (Fig 1). Post-operative bradycardia(heart rate below 50 bpm) was significantly observed in group B at PACU and 3 h after LSG (Table 2).

Oxygen saturation

A repeated measures ANOVA with sphericity assumed determined that the mean oxygen saturation differed significantly between time points F(2, 796) = 223.9, $p=0.0001$). There was a statistically insignificant interaction between both groups and oxygen saturation at different time points, F(1.83, 731.89) = 1.82, $p = 0.16$). Oxygen desaturation (<92%) developed significantly in group A at PACU and 3 h after surgery and was managed by an oxygen mask. No patient needed chin lift/jaw thrust maneuvers or was re-intubated in PACU (Table 2).

The quality of recovery

The modified Aldrete score was significantly higher in group A compared to group B (8.73 versus 9.23, $P= 0.0001$, respectively). A repeated measures ANOVA with a Huynh-Feldt correction determined that the mean of the observer's assessment of the alertness/sedation scale (OAA/S) differed significantly between two-time points (F(1, 398) = 749, $p < .0001$). There was a statistically significant interaction between both groups and OAA/S at different time points, F(1, 398) = 22.7, $p = 0.0001$ (Fig 2). The results showed no significant difference in the post-operative quality of recovery between the two groups 24 h after surgery (Table 2).

Post-operative pain scores

A repeated measures ANOVA with a Huynh-Feldt correction determined that the mean VAS pain score differed significantly among different time points (F(3.2, 1277.1) = 323.24, $p < .0001$). There was a statistically significant interaction between both groups and VAS pain score at different time points, F(3.2, 1277.1 = 5.99, $p = 0.0001$ (Fig 3). The average VAS pain score at PACU, 3, 6, 12, and 24 h after LSG was significantly decreased from (5.1, 4.16, 3.21, 2.78, 0.44, respectively) in group A (4.2, 2.89, 2.03, 1.69, and 0.26, respectively) compared to group B ($p = 0.0001$) (Table 3).

Opioid requirements

The opioids administered in the post-operative period (PACU, 3, 6, 12, and 24 h after LSG) were significantly reduced in group B relative to group A (Table 3). The paracetamol administered in the post-operative period (PACU, 6, 12, and 24 h after LSG) was significantly reduced in group B compared to group A (Table 3). Time to first pethidine administration was not significantly different between groups (group A 7.65 ± 8.77 min vs. group B 7.42 ± 8.66 min, respectively). Patients in group B required an average of 51.5 ± 85.31 mg pethidine compared to 91.38 ± 51.52 mg in group A ($p = 0.0001$). There was a significant reduction in the dose of paracetamol when comparing group A (2400 ±1051.4 mg) to group B (2105 ± 1372.4 mg) ($p = 0.02$) (Table 3).

PONV and antiemetic requirements

There were no differences between the two groups in the intra-operative administration of metoclopramide, ondansetron, or dexamethasone. PONV was significantly more in group A at 3 and 6 h after LSG. Ondansetron injection was reduced significantly from 70 (35%) patients in group A to 46 (23%) patients in group B.

Patients in group B required an average of 1.88 ± 3.49 mg of ondansetron compared to 3.2 ± 4.74 mg in group A ($p = 0.03$). There was a significant reduction in the metoclopramide dose from 20.5 ± 13.25 in group B to 11.4 ±9 .87 mg in group A ($P=0.0001$) (Table 3).

Table 1: Demographic and operative data

Variables	Pethidine alone	Tramadol with pethidine	*P value*
Age (years)	31.5±8.7	31.66±9.07	*0.86*
Sex Male Female	 73 (36.5%) 127 (63.5%)	 75 (37.5%) 125 (62.5%)	 *0.46*
Preoperative weight (KG)	127±13.4	126.7±12.3	*0.86*
Preoperative BMI	47.3±4.6	47.2±4.7	*091*
Preoperative excess weight (KG)	62.9±12.9	63.4±11.03	*0.67*

Co-morbidites			
Diabetes meltities	44 (22%)	43 (21.5%)	*0.5*
Hypertension	49 (24.5%)	46 (23%)	*0.41*
Sleep apnea	128 (64%)	129 (64.5%)	*0.91*
Dyslipidemia	45 (22.5%)	44 (22%)	*0.9*
Mean preoperative blood sugar(mg%)	97.92±26.8	91.5±12.74	*0.002*
Mean Preoperative hemoglobin level(gm/dl)	13.45±1.35	12.95±1.32	*0.0001*
Baseline systolic blood pressure (mmHg)	130.2±16.79	128.5±15.38	*0.29*
Baseline diastolic blood pressure (mmHg)	67.5±8.5	67.7±8.8	*0.9*
Baseline preoperative heart rate (bpm)	83.8±9.8	83.3±9.9	*0.56*
Intraoperative systolic blood pressure (mmHg)	122.21±16.79	120.05±15.39	*0.29*
Intraoperative diastolic blood pressure (mmHg)	62.5±7.5	62.7±7.8	*0.91*
Intraoperative heart rate (bpm)	88.8±9.4	88.3±9.5	*0.9*
Operative time (min)	59.28±13.86	58.97±12.26	*0.81*
Anesthetic time (min)	78.52±12.78	77.76±11.29	*0.48*
PACU duration (min)	52.97±9.17	57.97±12.51	*0.0001*

Data is expressed as mean and standard deviation or as percentage and frequency.. ***P*** is significant when < *0.05* **BMI**….body mass index, **bpm** beats per minute, **min**….minutes, **PACU**….. Post-Anesthesia Care Unit

Table 2: Post-operative course, vital signs and quality of recovery data

Variables	Pethidine alone	Tramadol with pethidine	*P value*
Pulse rate at PACU			
Normal	162 (81%)	144 (72%)	
Bradycardia	11 (5.5%)	30 (15%)	0.007
Tachycardia	27 (13.5%)	26 (13%)	
Pulse rate after 3 hours			
Normal	177 (88.5%)	162 (81%)	
Bradycardia	10 (5%)	26 (13%)	0.02
Tachycardia	13 (6.5%)	12 (6%)	
Pulse rate after 12 hours			
Normal	191 (95.5%)	179 (89.5%)	
Bradycardia	6 (3%)	16 (8%)	0.07
Tachycardia	3 (1.5%)	5 (2.5%)	
			Partial Eta Squared 0.047
Baseline preoperative heart rate (bpm)	83.8±9.8	83.3±9.9	Main effect
Pulse rate at PACU (bpm)	83.86±11.86	80.52±15.28	F(2.03, 808.6) = 19.84, *p < 0.0001*)
Pulse rate after 3 hours (bpm)	82.28±9.17	79.54±12.43	Interaction effect
Pulse rate after 12 hours (bpm)	81.71±7.65	77.55±11.07	F(2.03, 808.6) = 4.13, *p = 0.016*)
			Pairwise comparison *P= 0.003*
			Partial Eta Squared 0.58
Baseline preoperative systolic blood pressure (mm Hg)	130.2±16.79	128.5±15.38	Main effect
The mean systolic blood pressure at PACU (mm Hg)	140.21±16.79	138.5±15.38	F(1.73, 692.2) = 520.4, *p < .0001*)
The mean systolic blood pressure after 3 hours (mm Hg)	124.25±15.98	122.28±15.79	Interaction effect
The mean systolic blood pressure after 12 hours (mm Hg)	118.35±9.95	117.27±9.75	F(1.73, 692.2)) = 0.39, *p = 0.65*)
			Pairwise comparison *P= 0.19*
			Partial Eta Squared 0.53
Baseline preoperative diastolic blood pressure (mm Hg)	67.5±8.5	67.7±8.8	Main effect
The mean diastolic blood pressure at PACU (mm Hg)	76.55±8.51	76.65±8.84	F(1.83, 731.89) = 463.1, *p < .0001*)
The mean diastolic blood pressure after 3 hours (mm Hg)	72.27±9.93	72.3±9.79	Interaction effect
The mean diastolic blood pressure after 12 hours(mm Hg)	70.81±9.34	72.07±9.96	F(1.83, 731.89) = 1.02, *p = 0.36*)
			Pairwise comparison *P= 0.68*
			Partial Eta Squared 0.36
O2 saturation at PACU (%)	95.11±2.14	95.35±1.95	Main effect
O2 saturation after 3 hours (%)	96.54±2.23	97.22±2.56	F(2, 796) = 223.9, *p = 0.0001*)
O2 saturation after 12 hours (%)	97.65±1.74	98.31±2.05	Interaction effect
			F(1.83, 731.89) = 1.82, *p = 0.16*)
			Pairwise comparison *P= 0.013*
O2 saturation > 92% at PACU	35 (17.5%)	15 (7.5%)	002
O2 saturation > 92% after 3 hours	24 (12%)	10 (5%)	0.01
O2 saturation > 92 %after 12hours	9 (4.5%)	4 (2%)	0.16

Modified **Aldrete** score	9.23±0.95	8.73±0.69	0.0001
OAA/S observer's assessment of alertness/sedation scale arrival to PACU	3.98±0.47	3.7±0.59	Partial Eta Squared 0.65 Main effect F(1, 398) = 749, *p < .0001*)
OAA/S observer's assessment of alertness/sedation scale at 60 minutes	4.75±0.43	4.78±0.41	Interaction effect F(1, 398) = 22.7, *p = 0.0001*) Pairwise comparison *P= 0.0001*
Quality of recovery score-40	158.12±7.95	159.25±7.48	0.14
Quality of recovery score comfort	44.79±3.37	44.63±4.17	0.66
Quality of recovery score emotional state	33.33±2.42	33.46±2.53	0.61
Quality of recovery score psychological support	31.64±2.1	32.07±1.7	0.03
Quality of recovery score physical independence	18.76±1.76	19.05±1.7	0.08
Quality of recovery score pain	29.59±2.09	30.04±1.68	0.02
Hospital stays (days)	1.91±0.51	1.86±0.47	0.31

Data is expressed as mean and standard deviation or as percentage and frequency. ***P*** is significant when < *0.05*, **bpm** beats per minute, **PACU**….. Post Anesthesia Care Unit

Table 3: post-operative pain and pethidine requirement.

Variables	Pethidine alone	Tramadol with pethidine	*P value*
VAS immediate post-operative PACU	5.1±2.21	4.2±2.31	Partial Eta Squared 0.45
VAS at 3 hours post-operative	4.16±2.76	2.89±2.39	Main effect
VAS at 6 hours post-operative	3.21±2.19	2.03±2.13	F(3.2, 1277.1) = 323.24,
VAS at 12 hours post-operative	2.78±2.14	1.69±1.84	*p < .0001*
VAS at 24 hours post-operative	0.44±1.1	0.26±0.84	Interaction effect F(3.2, 1277.1 = 5.99, *p = 0.0001* Pairwise comparison *P= 0.0001*
Number of patients with pain immediate post-operative PACU	200 (100%)	200 (100%)	1
The need of pethidine post-operative PACU (patients)	95 (47.5%)	72 (36%)	0.02
The need of paracetamol postoperative PACU (patients)	185 (92.5%)	141 (70.5%)	0.0001
Number of patients with pain at 3 hours post-operative	157 (78.5%)	129 (64.5%)	0.002
The need of pethidine at 3 hours post-operative (patients)	99 (49.5%)	51 (25.5%)	0.0001
The need of paracetamol at 3 hours post-operative (patients)	138 (69%)	126 (63%)	0.21
Number of patients with pain at 6 hours post-operative	132 (66%)	109 (54.5%)	0.019
The need of pethidine at 6 hours post-operative (patients)	43 (21.5%)	25 (12.5%)	0.017
The need of paracetamol at 6 hours post-operative (patients)	128 (64%)	92 (46%)	0.001
Number of patients with pain at 12 hours post-operative	105 (52.5%)	91 (45.5%)	0.16
The need of pethidine at 6 hours post-operative (patients)	27 (13.5%)	9 (4.5%)	0.002
The need of paracetamol at 6 hours post-operative (patients)	117 (58.5%)	88 (44%)	0.004
Number of patients with pain at 24 hours post-operative	34 (16.5%)	20 (10%)	0.06
The need of pethidine at 24 hours post-operative (patients)	3 (1.5%)	2 (1%)	0.65
The need of paracetamol at 24 hours post-operative (patients)	18 (9%)	8 (4%)	0.04
Postoperative analgesic (mg)			
Pethidine (mg)	91.38±51.52	51.5±85.31	0.0001
Paracetamol (mg)	2400±1051.4	2105±1372.4	0.02
Nausea and vomiting immediate post-operative PACU	97 (48.5%)	83 (41.5%)	0.16
Nausea and vomiting at 3 hours post-operative	157 (78.5%)	105 (52.5%)	0.0001
Nausea and vomiting at 6 hours post-operative	162 (81%)	135 (67.5%)	0.002
Nausea and vomiting at 12 hours post-operative	25 (12.5%)	26 (13%)	0.88
Nausea and vomiting at 24 hours post-operative	16 (8%)	16 (8%)	1
Postoperative antiemetic (mg)			
Metoclopramide (mg)	20.5±13.25	11.4±9.87	0.0001
Ondostrone (mg)	3.2±4.74	1.88±3.49	0.0001

Data is expressed as mean and standard deviation or as percentage and frequency. ***P*** is significant when < *0.05*

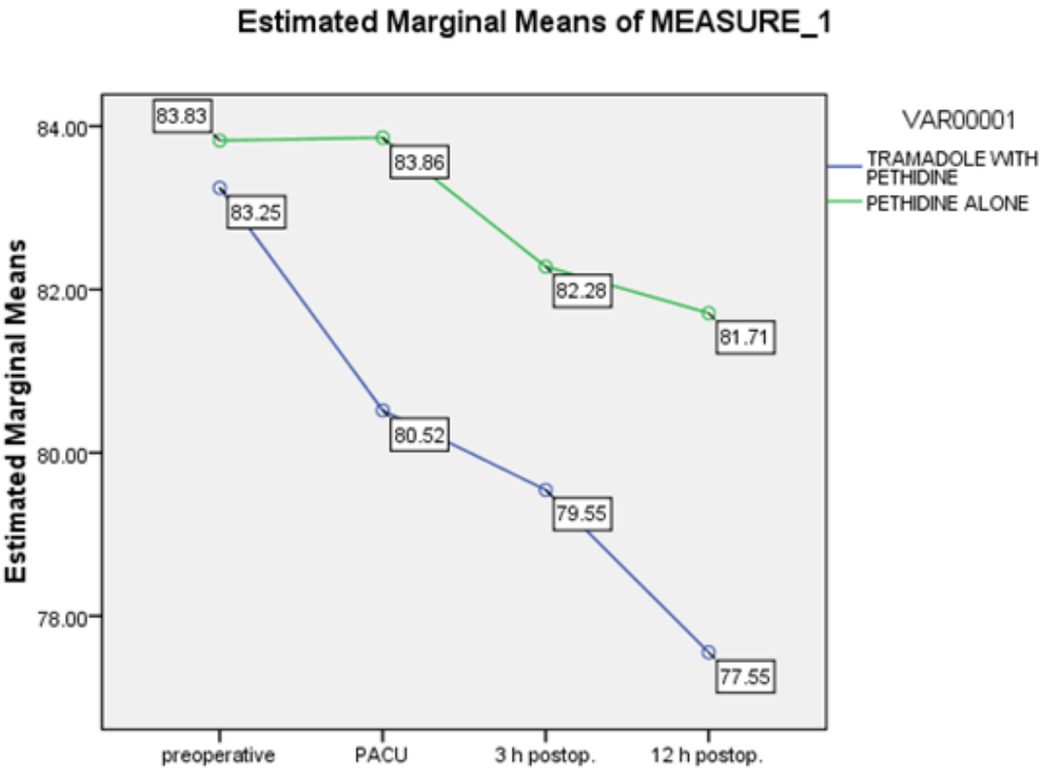

Fig 1: Effect of tramadol/pethidine and pethidine alone on pulse rate at different times post-operative

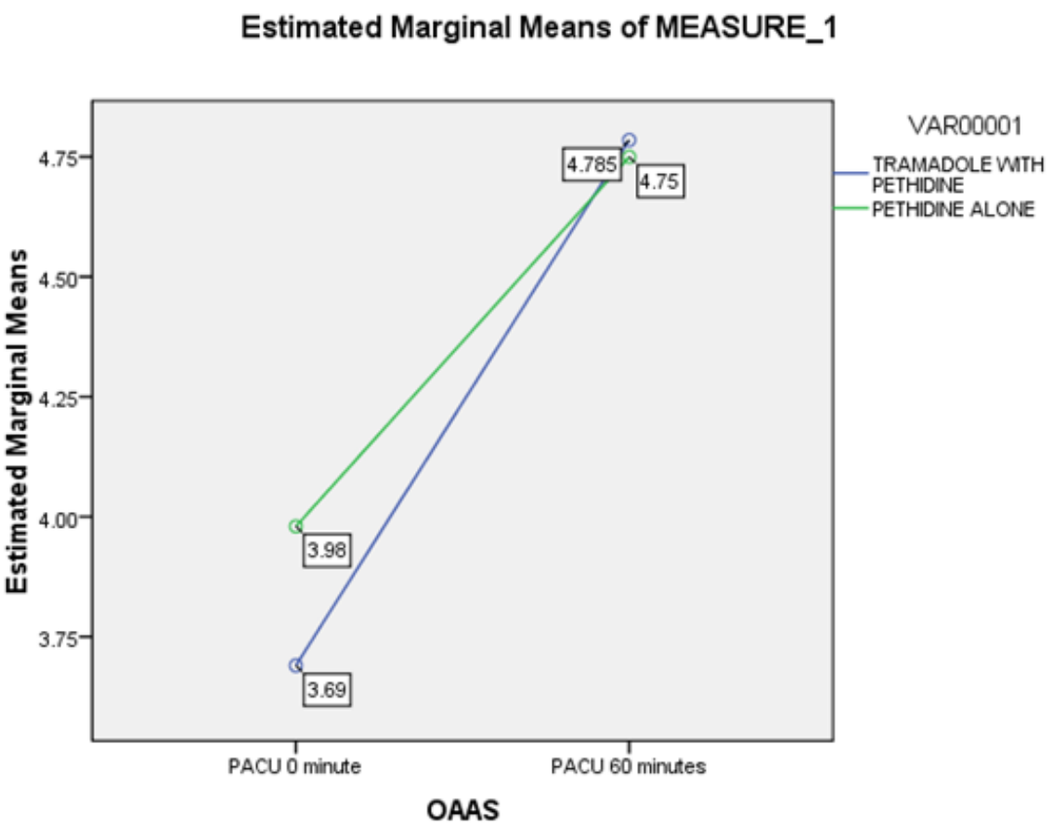

Fig. 2: Effect of tramadol/pethidine and pethidine alone on OAA/S observer's assessment of alertness/sedation scale at different times post-operative at PACU

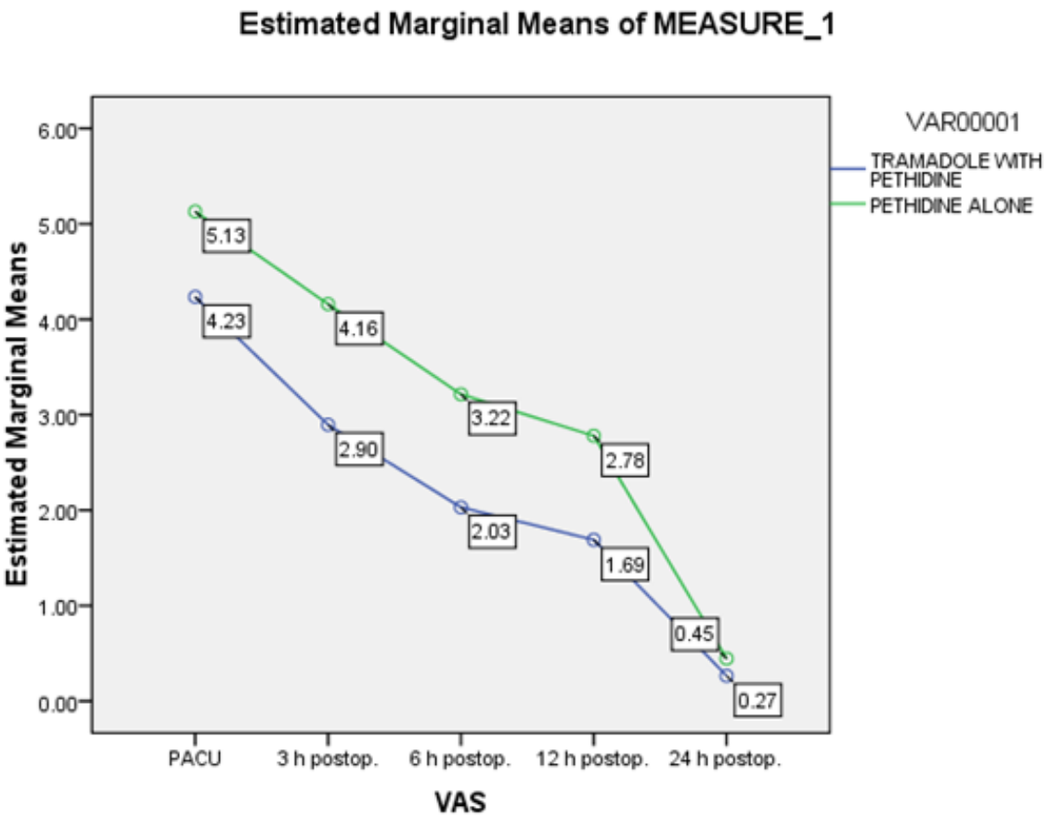

Fig. 3: Effect of tramadol/pethidine and pethidine alone on VAS of pain at different times post-operative.

DISCUSSION

Post-operative pain can affect recovery, breathing, hemodynamics, mental function, ambulation, bowel movement, and hospital stay. Additionally, opioid analgesia in obese individuals is linked to significant side effects, such as nausea, vomiting, ileus, hypoxemia, respiratory depression, sleepiness, delirium, and mortality. The most recent bariatric surgery protocol issued by ERAS contained convincing data and recommendations to employ a multimodal analgesia protocol (MAP) to reduce the use of opioids[17, 18]. The MAP targets various pain pathways to reduce perioperative opioid consumption and reduce opioid-related side effects that may impede patient recovery. The MAP may offer better effectiveness, fewer problems, and advanced fast-track bariatric surgical car[19-23].

Few studies in the literature show the effect of tramadol on post-bariatric surgery courses regarding opioid requirement[24, 25]. Tramadol is a synthetic painkiller having opioid, noradrenergic, and serotoninergic properties. Its opioid and nonopioid analgesic properties synergize to produce potent analgesia with few severe side effects. Bamgbade *et al*.[25] compared patients who had LSG who received morphine with those who received intraoperative tramadol and found that the tramadol group had better post-operative analgesia, a shorter stay in the PACU, a lower need for post-operative opioids, earlier ambulation, a shorter hospital stay, a lower incidence of post-operative hypopnea, and a lower need for doxapram. Hence, tramadol is appropriate, effective, safe, and correlated with the best perioperative consequences in bariatric surgery patients. Vomiting is the major adverse effect of tramadol. However, proactive multimodal antiemetic treatments may be successfully avoided[25]. Tramadol has also been demonstrated to be effective and secure when used as part of a multimodal analgesic strategy in patients undergoing bariatric surgery[21, 23, 24].

Combining multiple analgesics, including tramadol and an opioid-based medication, seems to be associated with improved pain relief compared to single regimen therapy after LSG[23, 25]. Jun *et al*.[22] reported that post-operative pain release in the MAP group could be continued without the routine usage of opioids. These authors showed that the pain values (VAS) after LSG at 12 and 24 h were significantly decreased. The mean dose of opioid consumption after LSG was significantly decreased in the post-MAP group from 23.7 to 0.7 mg, with a significant increase in post-operative acetaminophen usage and tramadol usage. MAP

significantly reduced the ORAE from 33.3 to 8.8%[22]. Our study found effective post-operative pain relief can be sustained without routine opioids. We found that the pain VAS after surgery was significantly reduced in tramadol and pethidine groups. We also found a significant decrease in pethidine consumption after the application of the combined intraoperative tramadol and pethidine, which was attributed to significant pain relief with the reduction of post-operative opioids.

The prevalence of OSA in morbidly obese individuals is estimated to be between 40% and 90%. Opioid analgesia has been associated with an increased risk of OSA in patients undergoing LSG. This is because opioids can cause respiratory depression, leading to decreased oxygen reaching the lungs and increased carbon dioxide[6, 7, 21, 22]. Opioid use must remain minimal, particularly in obese individuals with obesity hypoventilation syndrome or OSA, who are at greater risk of respiratory depression[6]. In our study, Oxygen desaturation (< 92%) was significantly more developed when using pethidine alone. The severe restrictive condition caused by morbid obesity and atelectasis from resting flat contributes to lower respiratory function after LSG. Opioid analgesia has also been linked to decreased oxygen saturation levels after LSG. This is because opioids can cause a decrease in ventilation rate and tidal volume, which leads to a decrease in oxygen exchange between the lungs and the bloodstream[6, 7, 21, 22].

Intraoperative tramadol injection has been found to cause a decrease in both heart rate and blood pressure. This decrease is usually mild but can be more pronounced in certain individuals or when larger doses are administered. The decrease in heart rate is thought to be due to the drug's ability to reduce sympathetic nervous system activity, which helps to slow down the heart rate. The decrease in blood pressure is likely due to the drug's ability to reduce peripheral vascular resistance, which helps lower systemic vascular resistance[25]. In the current study, post-operative bradycardia was significantly observed when using combined intraoperative tramadol and pethidine at PACU and three h after LSG.

PONV is among the most common side effects after LSG, with prevalence ranging from 27% to 67%. Opioids are often used to treat pain after LSG, but their use can result in opioid-induced nausea and vomiting. Administration of opioids raises the risk of PONV through increased vestibular system sensitivity and direct stimulation of the mu and delta opioid receptors in the brain stem chemoreceptor trigger zone[26]. The PONV can result in problems such as aspiration, wound dehiscence, pneumothoraxes, and prolonged duration in PACU[26]. Several studies have suggested that preemptive analgesia using opioid-based regimens before surgery reduces the risk of PONV compared with delayed analgesia. Studies have also shown that multimodal preoperative analgesia regimens, including ketorolac, paracetamol, dexamethasone, and neostigmine, provide effective prophylaxis against PONV after LSG[8]. Overall, there is a lack of evidence regarding the most effective treatments for PONV following LSG. Systematic reviews suggest that multimodal pre-, intra-, and post-operative analgesic regimens may be more effective than single agents alone[27]. In this study, the prevalence of PONV was significantly reduced when using combined intraoperative tramadol and pethidine. These results may be attributed to a significant reduction of opioid administration when using combined intraoperative tramadol and pethidine.

The strengths of this study are its multicenter design and large sample size, as the sample size calculated for a prospective randomized study was 28 in each group[18, 23]. However, there is a limitation to this study, the retrospective nature of our research leads to confounding variables and biases. Data were prospectively entered into a computer file to reduce the influence of confounders.

CONCLUSION

Combined intraoperative tramadol with pethidine provides superior post-operative analgesia and safety over pethidine alone. PONV was significantly more in patients who received intraoperative pethidine alone after LSG. The opioid requirements in the post-operative period were significantly reduced in patients who received combined intraoperative tramadol with pethidine. There was a significant decrease in the necessity for on-demand antiemetic in the tramadol group. Oxygen desaturation significantly developed in patients who received intraoperative pethidine alone after surgery and was managed by an oxygen mask. Post-operative bradycardia was significantly observed in the tramadol group after LSG.

ABBREVIATIONS

laparoscopic sleeve gastrectomy (LSG).

Post-operative nausea and vomiting (PONV)

obstructive sleep apnea (OSA)

Enhanced recovery after surgery (ERAS)

opioid-related adverse events (ORAE)

body mass index (BMI)

visual analog scale (VAS)

post-anesthesia care unit (PACU)

quality of recovery -40 score (QoR-40)

CONFLICT OF INTEREST

There are no conflicts of interest.

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