Spare Opioid Use Protocol Improved the Outcomes of the Enhanced Recovery after Surgery Protocol for Patients Undergoing Laparoscopic Sleeve Gastrectomy for Morbid Obese Patients

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Abstract

Background: Obesity and intraoperative (IO) opioid are risk-factors during bariatric surgery and require certain manipulations to deal with. Enhanced recovery after surgery (ERAS) and spare-opioid use protocol (SOUP) might aid to bypass these risk factors

Objectives: Evaluation of the outcomes of ERAS protocol with SOUP application for morbid obese patients undergoing laparoscopic sleeve gastrectomy (LSG).

Patients and methods: 60 obese patients were allocated into Group-C received conventional opioid-based anaesthesia and postoperative (PO) analgesia and Group-E received the ERAS protocol with SOUP application. All patients received balanced sevoflurane anesthesia 2% in oxygen 100% and rocuronium and 4-ports LSG. The study outcome is the efficacy of the applied protocol to provide IO and PO opioid-free analgesia during major surgeries for risky patients.

Results: All surgeries were conducted without a shift to laparotomy or conventional opioid-based anesthesia. Group-E patients had significantly shorter PACU stays (P=0.035) and higher Aldrete scores at time of PACU discharge (P=0.023). Among Group-E patients, 5 required IO fentanyl shots and 3 patients received PO morphine shots. Group-E patients showed significantly lower PO nausea (P=0.032) and need for antiemetic therapy (P=0.005), earlier ambulation (P=0.020) and oral intake (P=0.034) and hospital discharge (P=0.014).

Conclusion: Implementation of ERAS with SOUP protocols is a feasible, effective and safe anesthetic policy for high-risk patients undergoing major surgeries. The applied SOUP spared the need for opioid analgesia in about 90% of patients. The applied anesthetic policy improved immediate surgical outcomes, and reduced times for PACU discharge, ambulation, oral intake and PO hospital stay with cost reductions.

Keywords: Enhanced recovery after surgery protocol; Spare Opioid Use Protocol; Morbid obesity; Laparoscopic sleeve gastrectomy.

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Introduction

Morbid obesity as defined as body mass index (BMI) of ≥40 kg/m^2 or >35 kg/m^2 with co-morbidity, deleteriously impacts the quality of life of the affected individual **(Yazdani et al, 2019)**. Morbid obesity is associated with multiple medical problems, especially diabetes mellitus (DM), hypertension, sleep obstructive apnea, non-alcoholic fatty liver, and alterations of cardiac structure and function **(Hatto et al, 2023; Oldervoll et al, 2023)**.

Bariatric surgeries are the most effective treatment of morbid obesity and multiple procedures were applied and compared to achieve the best outcome **(Coulman et al, 2023)**. However, laparoscopic sleeve gastrectomy (LSG) was found to be safe and effective as other proposed procedures but was advantageous for its shorter operative time and length of hospital stay (LOS) **(Ali et al, 2021)**.

Obesity has been associated with a higher risk of perioperative complications and this increased concern of anesthesiologists with the management of obese patients **(Zandomenico et al, 2023)**. Enhanced recovery after surgery (ERAS) is a multidisciplinary and multimodal perioperative care protocol **(Gao et al, 2023)** that improved short-term outcomes following surgical procedures in several surgical specialties **(Fair et al, 2023)** and made it possible to achieve surgery safety **(Higueras et al, 2022)**.

Bariatric surgery requires the implementation of anesthetic techniques allowing to reduce the incidence of complications and improve postoperative (PO) outcomes **(Khalil et al, 2023)**. Opioids are routinely used for intraoperative (IO) and PO analgesia and this alerted the attention to the opioid epidemic and renewed the need to focus on the dangers and drawbacks of opioids especially in the PO setting **(Tan et al, 2023)**.

The effects of opioid use during and after bariatric surgery are not fully studied **(Wilson et al, 2022)** and the special μ-receptor opioids' unwanted gastrointestinal side effects and respiratory depression increased the concerns for the provision of opioids for patients undergoing bariatric surgeries **(Lee et al, 2023)**. The standardized Spare Opioid Use protocol (SOUP) for PO analgesia could be an interesting alternative to conventional opioid-based analgesia (OBA) in patients undergoing bariatric surgery **(Ulbing et al, 2023)**. The study tried to evaluate the outcomes of ERAS protocol with SOUP application for morbidly obese patients undergoing LSG.

Patients and methods

Design: Prospective interventional study.

Setting: Departments of Anesthesia, Surgical ICU & Pain and General Surgery, Faculty of Medicine, Benha University

Patients: All patients with BMI≥35 kg/m^2 were eligible for evaluation for determination of demographic data including age, gender, weight, and height for calculation of BMI as weight divided by squared height in meters **(Khosla and Lowe, 1967)**. History taking insisted on queries about the presence of medical comorbidities, especially DM, hypertension, presence of night snoring or apnea that is only relieved on maintenance of a setting position or receiving oxygen inhalation, cardiac diseases, previous cardiac interventions, chronic kidney diseases, maintenance on dialysis, osteoarthritis, maintenance on steroid or non-steroid analgesia, receiving narcotic analgesia, and presence of liver disorders.

Inclusion criteria: Patients with BMI≥35 kg/m^2, with controlled medical problems if present and accepted to undergo the study protocol during and after surgery were included in the study.

Exclusion criteria: Patients with uncontrolled medical disorders, hiatus hernia, gastroesophageal reflux, coagulopathy, hemoglobin concentration <7 g/dl, maintenance on dialysis, liver endangerment or maintenance on narcotics for their osteoarthritis were excluded from the study.

Ethical approvals: The study protocol was presented for departmental approval in Dec 2020 and then approved by the faculty ethical committee. The protocol was discussed with the patients before enrolment and those accepted were asked to sign the written consent. After the completion of case collection, the final approval of the outcomes was obtained.

Clinical evaluation

1. Full general clinical examination with abdominal ultrasonography
2. Cardiac examination, estimation of systolic and diastolic blood pressures (SBP & DBP), ECG and Echocardiography
3. Determination of baseline forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1) and peak expiratory flow rate (PEFR) using a Microlab 3000 series bedside spirometer (Micro Medical Ltd, Rochester, England).
4. Capillary hemoglobin oxygen saturation (Sp_{O2}) was measured using a Datex Cardiocap pulse oximeter (Datex, Helsinki, Finland).

Laboratory investigations

1. Estimation of random blood glucose levels and the percentage of glycated hemoglobin A1c.
2. Estimation of serum levels of urea, creatinine, liver enzymes, total bilirubin and albumin
3. Complete blood count to determine baseline hemoglobin concentration, platelet and white blood cell counts
4. Coagulation profile including bleeding and clotting time and prothrombin time and concentration

Randomization and Grouping

Patients were randomly allocated into two study groups using computer software with a 1:1 sequence that was translated as letters C and E by a blinded assistant and were provided to the anesthetist in charge to apply the anesthetic procedure. Group-C patients received conventional opioid-based anesthesia and PO analgesia and Group-E patients received the ERAS protocol with SOUP application.

Preoperative preparation

Patients received individualized perioperative management according to the presence of associated comorbidities. Diabetic patients were maintained on subcutaneous injection of regular insulin 6-hourly according to regular urine examination for glucose to achieve and maintain fasting blood glucose levels at <160 mg/dl, with no ketonuria. Hypertensive patients were maintained on Ca-channel blockers and β-adrenergic agonists to adjust and maintain SBP and DBP at ≤130 and ≤90 mmHg, respectively. Patients who had chronic obstructive pulmonary disease (COPD) were maintained on bronchodilators and β-adrenergic agonists. All patients with medical diseases were continued postoperatively on the same lines of treatment applied preoperatively.

The ERAS Protocol with SOUP

According to **(Khosla and Lowe, 1967)**, the main components of the ERAS program during bariatric surgeries include:

1. Perioperative fluid management using 6% hydroxyethyl starch in saline (6% HES 130/0.4; Voluven) as an initial dose of 3 ml/kg over 10 minutes and Lactated Ringer's (LR) solution in a dose of 5 ml/kg/h throughout operative time. Fluid therapy was adjusted to maintain the central venous pressure (CVP) at 8-10 cmH_2O, mean arterial blood pressure (MAP) ≥75 mmHg and urine output (UOP) at >0.5 ml/kg/h. During the 1st 24-h postoperative (PO), all patients received LR solution at a rate of 1.5ml/kg/h to maintain UOP at >0.5ml/kg/h and MAP >75 mmHg until oral fluid intake was allowed.
2. The prevention of aspiration during induction of anesthesia and prophylactic management for PO nausea and vomiting (PONV) by pre-induction injection of dexamethasone (8 mg) with ondansetron (8 mg) as previously documented **(Wang et al, 2020)**.
3. A standardized anesthetic protocol with airway management and monitoring of anesthetic depth.
4. The laparoscopic surgical procedure to minimize wounds and tissue damage to reduce the PO catabolic phase

According to **(Gabriel et al, 2019)**, the SOUP was provided as IO analgesia at the time of induction of anesthesia in the form of an intravenous (IV) dexmedetomidine (DEX) as a loading dose of 1 µg/kg diluted by 10-ml saline and injected through 10-20 min followed by DEX infusion starting at a rate of 0.2 µg/kg/h and increased by 0.1 µg/kg/h according to requirements up to 0.7 µg/kg/h **(Peng et al, 2017)**. Synchronously, a lidocaine (LID) IV loading dose of 1.5 mg/kg was given and followed by an LID infusion adjusted at a rate of 1 mg/kg/h **(Chu et al, 2020)**. For PO multimodal analgesia (MMA), acetaminophen was given as 1g in 100 ml saline at 20-min before the end of surgery and was repeated as an IV dose of 650 mg/6h **(Shimia et al, 2014)**, IV ketorolac injection as 15 mg/6h **(Eftekharian and Pak, 2017)** and the continued IO infusions as DEX infusion at a rate of 0.2-1 µg/kg/h according to requirements **(Wang et al, 2018)**, and LID infusion as 1-2 mg/kg/h to achieve a therapeutic level of 0.5-5 µg/kg **(Chu et al, 2020)**.

Anesthetic procedure

Before anesthetic manipulations, bilateral open venous lines were prepared, and under local infiltration anesthesia, a central venous line was inserted in the internal jugular for invasive monitoring of central venous pressure (CVP). Mean arterial pressure (MAP), heart rate (HR), end-tidal (ET) capnography and pulse oximetry were recorded non-invasively. For patients of Group C, anesthesia was induced by fentanyl 1 µg/kg/min and propofol 1.5-2 mg/kg and for patients of Group E; anesthesia was induced using bolus doses of DEX and LID. For all patients, rocuronium 0.5 mg/kg was injected and an endotracheal tube of appropriate size was inserted with the aid of fiberoptic laryngoscopy and patients were mechanically ventilated to keep ET_{CO2} in the range of 30-35 mmHg. After endotracheal intubation, Foley's urinary catheter was inserted to register UOP. Anesthesia was maintained for patients of both groups by sevoflurane 2% in oxygen 100% and rocuronium (0.15 mg/ kg) according to the requirements. Intraoperative analgesia was provided as fentanyl infusion (2µg/kg/h) and DEX and LID infusions for patients of groups C and E, respectively. In patients of Group E, fentanyl injection in a dose of 25-50 µg/h was provided if required as rescue

IO analgesia **(Soleimanpour et al., 2017)**.

Surgical procedure

After completion of anesthetic procedure and stabilization of patients' hemodynamic and respiratory variate, and with patients in the supine position, pneumoperitoneum is created using an optical 12-mm optiview trocar inserted about 10-cm sub-xiphoid with a gradual elevation of abdominal pressure till 14 mmHg and then reverse Trendelenburg position was attained and a nasogastric tube was inserted for gastric emptying and decompression. Using the 4-port procedure, the greater omentum was dissected from the greater gastric curvature by dividing the gastro-colic and -splenic ligaments up to the esophagogastric junction, and fine adhesions between the posterior stomach wall and pancreas were divided to free the lesser sac. Then, the left side of the esophagogastric junction was cleared of fat with complete exposure of the left diaphragmatic crus. The linear cutting stapler (60 cm long, 4.1-mm staple-height, and green cartridge; endoGastro-Intestinal-Anastomosis; Endo-GIA) was introduced through a right trocar, placed at the point of the initial dissection on the greater curvature to create a vertical cut on the gastric wall. Then a 36-Fr bougie was inserted down to the pylorus and using sequential firings of the Endo GIA with 60 mm -3.5 mm linear staplers are applied over it up to the esophagogastric junction leaving about 1 cm of the fat pad along the lesser curvature to assure adequate blood supply on the lesser curvature for the sleeve. The stable line was commenced was reinforced by interrupted monofilament absorbable sutures to avoid the risk of postoperative bleeding and leakage. Both vagi were preserved for normal gastric emptying, the resected greater curvature was extracted, the nasogastric tube is left in place and wound drainage if required is applied.

The collected intraoperative data included MAP, HR and CVP measures and UOP monitoring for adjustment of fluid requirements. The frequency of Group-E patients who required the standby fentanyl and the dose given is recorded. Operative time, intraoperative complications and the need for a shift to open surgery were registered.

Postoperative monitoring

After the end of the surgery, patients were transferred to the PACU and were cared for in a semi-setting position. Oxygen saturation was monitored and at a saturation level of ≤95%, oxygen (6L/min) supply was provided via a facemask. Patients were discharged from PACU at Aldrete recovery score **(Ghai et al, 2005)** of ≥8, time till PACU discharge was recorded.

Immediately after transfer to PACU, 30-min, 1, 2 and 3-h thereafter sedation score was determined using Ramsey Sedation score (RSS) **(Sessler et al, 2008)** and PONV were rated using a 4-point score for nausea (0-3) and 3-point score (0-2) vomiting scores **(Watcha and White, 1992)**, and IV ondansetron 8 mg was given for patients who had nausea (score 3) or vomiting (score 1).

The numeric rating; 0-10 points scale (NRS) was used to assess PO pain **(Williamson and Hoggart, 2005)**. NRS scores were determined at the time of PACU discharge, every 1-h for 4 hours and then each 4 hours for 24-hr. PO analgesia was provided for Group-C patients at an NRS score of 4, as morphine 10 mg diluted with saline up to 10 ml to give a concentration of 1 mg/ml and given as IV 2-ml shots till the pain disappears. For Group-E patients, the SOUP was applied immediately after PACU discharge, while rescue PO analgesia, if an NRS

score of 4 was reached despite SOUP, was provided with morphine IV 2-ml shots. The number of patients required and the dose of rescue analgesia were recorded

The nasogastric tube was removed on the 1st PO day after a normal upper GI series with gastrographin to ascertain the competence of the anastomotic line and oral soft fluids were allowed if there was no PONV. Time till 1st ambulation and 1st oral intake was registered.

The spirometric estimation of FVC, FEV1 and PEFR at 4-, 24 and 48-h PO was presented as the percentage of change about baseline measures.

Fluid therapy was stopped, urinary and wound drainage catheters were removed and patients were home-discharged starting after taking oral fluids and were able to ambulate. A liquid diet was instructed for four weeks; the duration of the PO hospital stay was recorded.

Surgeons' and patients' satisfaction with the study outcomes was evaluated using a visual analog scale of 0-100 with the higher score and the higher satisfaction **(Aitken, 1969)**.

Study outcomes

1. The primary outcome is the efficacy of the applied ERAS protocol with SOUP to provide IO and PO opioid-free analgesia during major surgeries for risky patients.
2. The secondary outcomes include
   - The failure rate of the applied protocol is judged by the incidence of the shift to opioid analgesia whether during or after surgery.
   - The PO outcomes of patients of both groups
   - Surgeons' and patients' satisfaction rates by the applied protocol.

Statistical analysis

The results were analyzed using an IBM software program (Ver. 27, 2020, IBM, USA) by the paired t-test for comparisons of dependent variate, One-way ANOVA test for independent variate and Chi-square test for the observed percentage. The used P value as cutoff point for significance of the differences was at <0.05.

Results

Seventy-three women were evaluated for inclusion criteria; 5 patients had uncontrolled medical problems, 3 patients had reflux disease, 2 patients were maintained on regular dialysis, 2 patients had HCV-hepatic fibrosis and one patient was maintained on narcotic analgesia. These thirteen patients were excluded from the study and 60 patients were randomly allocated into the study groups (**Fig. 1**). The inclusion criteria and preoperative data of patients of both groups are shown in (**Table .1**) and insignificant differences were observed between these data.

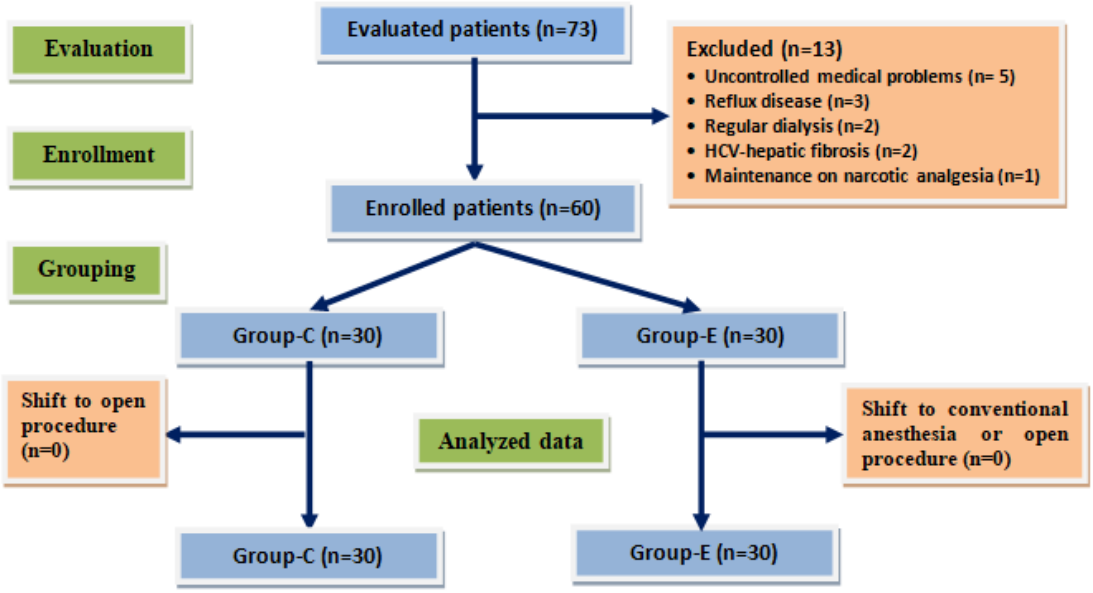

Fig.1. Study flow chart

Table 1. Demographic, clinical and laboratory data of the studied groups

Data / Group			C (n=30)	E (n=30)	P
Age (years)			35.2±7.9	36.3±8.3	0.601
Gender	Males		7 (23.3%)	9 (30%)	0.559
	Females		23 (76.7%)	21 (70%)	
ASA grade	II		9 (30%)	6 (20%)	0.524
	III		19 (63.3%)	20 (66.7%)	
	IV		2 (6.7%)	4 (13.3%)	
Co-morbidities	No		14 (46.6%)	13 (43.3%)	0.808
	Yes	Diabetes mellitus	5 (16.7%)	7 (23.3%)	
		Hypertension	6 (20%)	4 (13.3%)	
		COPD	2 (6.7%)	1 (3.4%)	
		Others	3 (10%)	5 (16.7%)	
Body mass index (kg/m^2)			39.6±1.9	40.2±2.5	0.335
Heart rate (beats/min)			83.8±5.1	84.5±3.1	0.522
Systolic blood pressure (mmHg)			126±12.6	124.3±11.9	0.594
Diastolic blood pressure (mmHg)			85±3	84.4±3.3	0.46
Glycemic status	Fasting blood glucose (mg/dl)		112.4±15.9	115.1±16.1	0.516
	Glycated hemoglobin A1c (%)		5.78±0.6	5.93±0.6	0.351
Kidney function tests	Serum urea (mg/ml)		35.6±8.4	37.1±9.5	0.519
	Serum creatinine (mg/ml)		1.27±0.13	1.295±0.12	0.448
Liver function tests	Serum AST (IU/ml)		26±4.8	25.3±7.9	0.679
	Serum ALT (IU/ml)		45.8±7.3	44.3±10.5	0.522
	Serum total bilirubin (mg/ml)		1.17±0.28	1.21±0.39	0.859
	Serum albumin (g/ml)		4.16±0.15	4.17±0.21	0.833

Complete blood count	**Hemoglobin concentration (g/dl)**	11.66±0.69	11.43±0.83	0.248
	Platelet count (10^3/cc)	279.7±12.3	275.2±13.4	0.181
	Total leucocytic count (10^3/cc)	4.2±0.53	4.05±0.4	0.221
Coagulation profile	**Bleeding time (min)**	2.12±0.19	2.1±0.2	0.689
	Clotting time (min)	4.9±0.25	4.8±0.3	0.169
	Prothrombin time (sec)	13±0.51	12.9±0.58	0.478
	Prothrombin concentration (%)	89.1±5.7	88.9±7.24	0.906

ASA: American Society of Anesthetists; Group C: Conventional opioid-based anesthesia; Group E: ERAS protocol with SOUP; COPD: Chronic obstructive pulmonary disorders; AST: Aspartate transaminase; ALT: Alanine transaminase; P indicates the significance of the difference between the data of both groups; P>0.05 indicates the insignificance

Anesthetic and surgical maneuvers induced significant hemodynamic changes, irrespective of the provided anesthetic procedure. The recorded HR measures at the time of intubation, 1 min after abdominal insufflation and up to 60 min during surgery were non-significantly lower, while other measures showed significantly lower in Group-E patients in comparison to Group-C patients. Further, Group-E patients showed non-significantly lower MAP measures at intubation, 1 min before abdominal insufflation and at extubation, while all other MAP measures were significantly lower than measures of Group-C patients. The estimated CVP measures were significantly lower at 1-min after insufflation, and at 30-min and 90-min IO, while other measures were non-significantly lower in patients of Group-E than Group-C patients.

The applied fluid therapy preserved tissue perfusion as shown by the non-significant differences between the amounts of UOP determined till 1 min after insufflation and then UOP was significantly increased till the end of surgery in comparison to preoperative UOP and with non-significantly higher UOP of Group-E than Group-C patients, except at 1-min after desufflation whenever, UOP was significantly higher in group E (**Table.2**).

Table 2. Intra-operative hemodynamic measures and UOP of patients of both groups

Parameter / Time	Group	HR (beats/min)		MAP (mmHg)		CVP (cmH2O)		UOP (ml/kg/h)	
		C	E	C	E	C	E	C	E
Preoperative	**Mean**	85.5±1.9	85.2±3.5	83.1±3.6	83.9±4.2	9.03±0.5	9±0.5	0.72±0.12	0.75±0.12
	P	0.679		0.428		0.814		0.361	
At intubation	**Mean**	91.8±2.2†	91±3.2†	92.2±3.8†	91.1±3.7†	9.47±0.6†	9.41±0.5†	0.7±0.1	0.72±0.12
	P	0.261		0.258		0.675		0.798	
1-min before insufflation	**Mean**	78.4±2.9†	76.7±3.1†	84.6±3.9*	78.5±2.1†	9.05±0.5*	8.85±0.4†	0.73±0.11	0.75±0.12
	P	0.034		<0.001		0.115		0.55	
1-min after insufflation	**Mean**	83.9±3*	84.1±2.8*	93.7±3.5†	85.7±3.5*	9.57±0.6	9.19±0.4†	0.71±0.09	0.74±0.1
	P	0.793		<0.001		0.0035		0.412	
30-min IO	**Mean**	75.4±3.5†	74.4±3.2†	81.6±3.7	77.9±1.6†	9.21±0.4	8.82±0.3*	0.74±0.1	0.78±0.1†
	P	0.225		<0.001		0.0002		0.131	
60-min IO	**Mean**	74±3.5†	72.6±4.2	78.6±2.8†	75.7±0.8†	8.95±0.3	8.78±0.5*	0.76±0.1*	0.8±0.1†
	P	0.168		<0.001		0.112		0.188	
90-min IO	**Mean**	72.8±3.2†	69.4±2.9*	77.8±1.8†	75.5±0.7†	8.94±0.4	8.57±0.4†	0.78±0.1†	0.82±0.09†

	P	0.00006		<0.001		0.0005		0.08	
1-min before desufflation	**Mean**	79.4±3.7†	76.5±3	80.1±3*	79.9±2.1†	9.1±0.4	8.83±0.4	0.8±0.1†	0.85±0.09†
	P	0.0015		0.768		0.011		0.027	
At extubation	**Mean**	84.2±3*	81±2.7*	87±2.7†	83.4±2.2	9.26±0.3*	9.1±0.4	0.76±0.1*	0.77±0.1*
	P	0.00006		<0.001		0.119		0.833	
At PACU transfer	**Mean**	80.4±2.5†	76.5±2.7*	83.1±2.8	80±2.5†	8.98±0.4	8.75±0.4*	0.79±0.1†	0.8±0.08*
	P	<0.001		0.0003		0.034		0.712	

HR: Heart rate; MAP: Mean arterial pressure; CVP: Central venous pressure; UOP: Urinary output; IO: Intraoperative; PACU: Post-anesthetic care unit; Group C: Conventional opioid-based anesthesia; Group E: ERAS protocol with SOUP *: indicates significant differences versus preoperative measure at P<0.05; †: indicates significant differences versus preoperative measure at P<0.001; P indicates significance of the differences between both groups

All surgeries were conducted uneventfully without a shift to laparotomy or conventional opioid-based anesthesia. All Group-C patients received supplemental doses of fentanyl for IO analgesia, while only 5 of Group-E patients required supplemental analgesia with fentanyl shoots that were taken once and the mean used dose was 35±10.6; range 25-50 µg. Operative time and amount of IO blood loss showed non-significant differences between patients of both groups. At PACU admission, 6 patients (10%) required O_2 supplements with a non-significant difference between both groups. Group-E patients had significantly shorter PACU stay (P=0.035) and significantly higher Aldrete scores at the time of PACU discharge (P=0.023) with significantly (P=0.031) lower frequency of patients discharged at a score of 8 (**Table. 3**).

Table 3. Operative and PACU data of patients of both groups

Data Group			**C (n=30)**	**E (n=30)**	**P**
Operative data	**Shift to an open procedure**		0	0	-
	Shift to OBA		-	0	-
	Need for supplemental fentanyl	**Frequency**	-	5 (16.7%)	-
		Mean dose (µg)		35±10.6 (25-50)	-
	Operative time (min)		76±9.9	72.5±14.5	0.275
	IO blood loss (ml)		181±61.7	189±57.9	0.606
	Need for blood transfusion		0	0	-
PACU data	**Need for O_2 supplements at PACU**	**Yes**	4 (13.3%)	2 (6.7%)	0.389
		No	26 (86.7%)	28 (93.3%)	
	Time for PACU discharge (min)		14.2±2.7	12.4±3.7	0.035
	Aldrete score	**8**	17 (56.7%)	7 (23.3%)	0.031
		9	10 (33.3%)	18 (60%)	
		10	3 (10%)	5 (16.7%)	
	Mean Aldrete score		8.5±0.7	8.9±0.6	0.023

Group C: Conventional opioid-based anesthesia; Group E: ERAS protocol with SOUP; OBA: Opioid-based anesthesia; IO: Intraoperative; PACU: Post-anesthetic care unit; P indicates the significance of the differences between both groups; P<0.05 indicates the significant difference

Immediate and 30-min PO, no patient had RSS of one with non-significant differences between patients of both groups but in favor of Group-E. Thereafter, the frequency of patients who had lower RSS was significantly higher among those of Group E than Group C. During 24-h PO observation, only 3 patients (10%) of Group E required supplemental PO analgesia, while the remaining 27 patients passed their 1st PO day without pain sensation or with NRS scores of 1-3. Patients' distribution according to NRS scores showed significantly higher frequencies of Group-C patients among higher NRS scores in comparison to Group-E patients. Moreover, the collective mean NRS score was significantly lower at all times of estimations in Group-E patients compared to Group-C patients (**Fig. 2**).

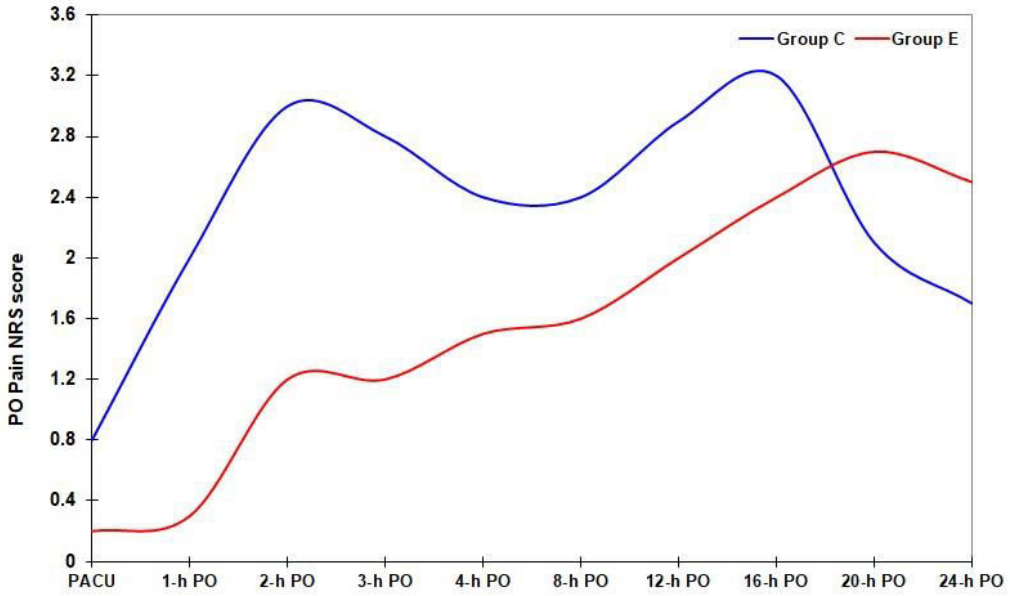

Fig.2. Mean collective NRS score of patients of both groups determined during 24-h PO

All Group-C patients required PO morphine after a mean duration of 2.9±0.8; range: 1-4 h. According to the time of 1st request of rescue analgesia, 7 patients (23.3%) requested analgesia at 4-h PO, 13 patients (43.3%) at 3-h PO, 9 patients (30%) at 2-h PO and only one patient required PO analgesia at 1-h PO. Twenty of the Group C patients (66.7%) requested morphine twice and received 10 mg, while 10 patients (33.3%) required three doses and received 15 mg. On the contrary, the three patients of Group E requested rescue analgesia at 16, 20 and 24-h PO two patients received 4 mg and the 3rd patient received only 2 mg (**Table. 4**).

Table 4.Post-operative sedation and pain data of patients of both groups

PO sedation according to Ramsey Sedation Score (RSS)						
Time	**Group**	**RSS=1**	**RSS=2**	**RSS=3**	**RSS=4**	**P**
Immediate PO	**C**	0	0	12 (40%)	18 (60%)	0.301
	E	0	0	16 (53.3%)	14 (46.7%)	
30-min PO	**C**	0	4 (13.3%)	12 (40%)	14 (46.7%)	0.466
	E	0	7 (23.3%)	13	10	

				(43.4%)	(33.3%)	
1-h PO	**C**	1 (3.3%)	7 (23.3%)	19 (63.3%)	3 (10%)	0.044
	E	5 (16.7%)	12 (40%)	13 (43.3%)	0	
2-h PO	**C**	7 (23.4%)	10 (33.3%)	13 (43.3%)	0	0.026
	E	14 (46.7%)	12 (40%)	4 (13.3%)	0	
3-h PO	**C**	10 (33.3%)	13 (43.3%)	7 (23.4%)	0	0.042
	E	17 (56.7%)	12 (40%)	1 (3.3%)	0	

PO pain score and treatment							
	Item	**NRS score**				**Collective score**	
Time	**Group**	0	1-3	4	P	Mean (±SD)	P
PACU discharge	**C**	16 (53.3%)	14 (46.7%)	0	0.0125	0.8±1	0.0025
	E	25 (83.3%)	5 (16.7%)	0		0.2±0.5	
1-h PO	**C**	0	29 (96.7%)	1 (3.3%)	<0.001	2±0.9	<0.001
	E	21 (70%)	9 (30%)	0		0.3±0.5	
2-h PO	**C**	0	21 (70%)	9 (30%)	0.0025	3±0.9	<0.001
	E	2 (6.7%)	28 (93.3%)	0		1.2±0.5	
3-h PO	**C**	3 (10%)	14 (46.7%)	13 (43.3%)	0.0001	2.8±1.3	<0.001
	E	1 (3.3%)	29 (96.7%)	0		1.2±0.5	
4-h PO	**C**	1 (3.3%)	22 (73.4%)	7 (23.3%)	0.01	2.4±1.1	0.0001
	E	1 (3.3%)	28 (93.4%)	1 (3.3%)		1.5±0.5	
8-h PO	**C**	3 (10%)	23 (76.7%)	4 (13.3%)	0.019	2.4±1.2	0.0012
	E	0	30 (100%)	0		1.6±0.6	
12-h PO	**C**	0	23 (76.7%)	7 (23.3%)	0.0048	2.9±0.8	<0.001
	E	0	30 (100%)	0		2±0.5	
16-h PO	**C**	1 (3.3%)	14 (46.7%)	15 (50%)	<0.001	3.2±1.1	0.0018
	E	0	29 (96.7%)	1 (3.3%)		2.4±0.6	
20-h PO	**C**	6 (20%)	15 (50%)	9 (30%)	0.001	2.1±1.5	0.044
	E	1 (3.3%)	28 (93.4%)	1 (3.3%)		2.7±0.7	
24-h PO	**C**	7 (23.3%)	18 (60%)	5	0.026	1.7±1.3	0.008

				(16.7%)			
	E	2 (6.7%)	27 (90%)	1 (3.3%)		2.5±1	

RSS: Ramsey Sedation Score; PO: Postoperative; PACU: Post-anesthetic care unit; NRS: Numerical Rating Scale; Group C: Conventional opioid-based anesthesia; Group E: ERAS protocol with SOUP P indicates the significance of the differences between both groups; P<0.05 indicates the significant difference

The frequency of patients who had nausea was significantly lower, while the frequency of patients who had vomiting was insignificantly lower and the consumption of antiemetic therapy was significantly lower among patients of Group E. Group-E patients showed significantly earlier time of ambulation, 1st oral intake and hospital LOS with significantly higher frequencies among earlier times (**Table .5 & Fig. 3**).

Table 5. Recovery and PO data of patients of both groups

Data Group			**C (n=30)**	**E (n=30)**	**P**
Nausea scoring	**0**		15 (50%)	21 (70%)	0.032
	1		4 (13.3%)	7 (23.3%)	
	2		6 (20%)	2 (6.7%)	
	3		5 (16.7%)	0	
Vomiting scoring	**0**		24 (80%)	28 (93.3%)	0.226
	1		4 (13.3%)	2 (6.7%)	
	2		2 (6.7%)	0	
Antiemetic therapy	**Yes**		11 (36.7%)	2 (6.7%)	0.005
	No		19 (63.3%)	28 (93.3%)	
Time to 1st ambulation	**Frequency**	**<6 h**	2 (6.7%)	9 (30%)	0.02
		6-12 h	25 (83.3%)	21 (70%)	
		>12 h	3 (10%)	0	
	Mean		8.6±2.5	6.5±1.7	0.0003
Time to 1st oral intake	**Frequency**	**<30 h**	14 (46.7%)	23 (76.7%)	0.034
		30-36 h	10 (33.3%)	6 (20%)	
		>36 h	6 (20%)	1 (3.3%)	
	Mean		32.6±4.3	29.5±3.3	0.0014
Length of hospital stay	**Frequency**	**48-60 h**	9 (30%)	17 (56.6%)	0.014
		>60-72 h	5 (16.7%)	8 (26.7%)	
		>72-84 h	13 (43.3%)	2 (6.7%)	
		>84-96 h	2 (6.7%)	3 (10%)	
		>96 h	1 (3.3%)	0	
	Mean		70.6±13	62±10.7	0.007

Group C: Conventional opioid-based anesthesia; Group E: ERAS protocol with SOUP; PO: Postoperative; P indicates the significance of the differences between both groups; P<0.05 indicates the significant difference

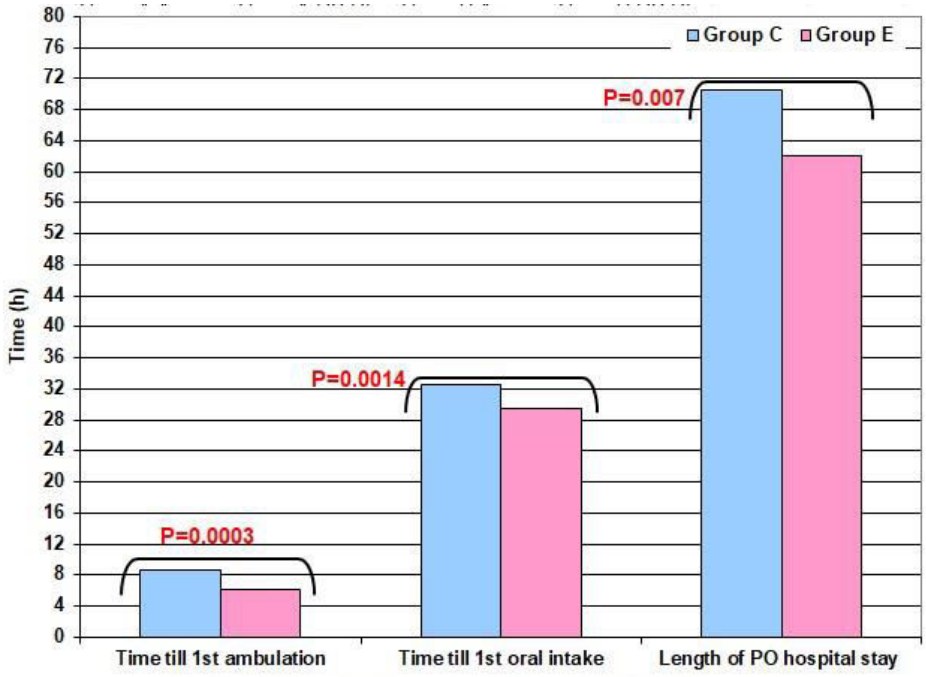

Fig.3. Post-operative recovery data of patients of both groups

Estimated pulmonary function tests till 48-h PO were significantly lower in patients of both groups in comparison to the corresponding preoperative measures. The estimated functions were non-significantly higher all through the 48-h PO in patients of E-group than in Group-C patients, apart from estimated FEV1 at 4-h PO and PEFR at 24-h PO were significantly (P=0.035 &0.046, respectively) than the corresponding measures of Group-C patients. The percentage of change in all measures about the preoperative measures showed non-significant differences between patients of both groups (**Table. 6**).

Table 6.Mean value of the estimated pulmonary function tests till 48-h PO and the percentage of change about the preoperative measures (*)

Function / Time		FVC		FEV1			PEFR
		Measure	%*	Measure	%*	Measure	%*
Preoperative measures	Group C	93.1±11	-	89.4±6.8	-	93.6±6.7	-
	Group E	94.5±8.7	-	92.5±8.2	-	96.3±8.9	-
	P	0.587	-	0.115	-	0.189	-
At 4-h PO	Group C	66.5±5	27.9±7.2	61.3±7.2	31.3±7	67.6±4.6	27.7±2.5
	Group E	68±6.1	28±2.5	64.9±5.7	29.8±0.4	68.7±6.6	28.6±3.3
	P	0.310	0.956	0.035	0.245	0.456	0.244
At 24-h PO	Group C	73.9±5.6	20.1±6.2	71.2±6.6	20.2±6.6	74.7±5	20.1±2.1
	Group E	74.4±5.5	21±3.2	72.4±5.7	21.6±2.7	78.2±8	18.8±3.8
	P	0.713	0.444	0.373	0.278	0.046	0.096

At 48-h PO	**Group C**	81.3±7	12.2±5.7	82.4±6.4	7.8±2.2	82.3±5	12±2.8
	Group E	84.8±7.4	10.2±1.9	84.5±7.5	8.6±1.8	84.7±7.8	11.9±4
	p	0.063	0.069	0.219	0.121	0.157	0.964

FVC: Forced vital capacity; FEV1: Forced expiratory volume 1-sec; PEFR: peak expiratory flow rate Group C: Conventional opioid-based anesthesia; Group E: ERAS protocol with SOUP; PO: Postoperative; P indicates the significance of the differences between both groups; P<0.05 indicates the significant difference

Discussion

Induction of anesthesia using bolus doses of DEX/LID with muscle relaxant attenuated the vasoactive reflexes to intubation similar to or better than with opioid-based induction. Similarly, **(Rajan et al, 2017)** found that trans-tracheal injection of LID or IV DEX provided comparable patient immobility and hemodynamic stability during intubation and for 10-min later during total parotidectomy with nerve stimulation. Also, **(Parikh et al, 2017)** compared pretreatment using DEX (0.5 or 1 µg/kg), esmolol, and LID versus saline during electroconvulsive therapy and reported a significant reduction of HR, MAP with DEX and esmolol than with LID and saline with comparable motor seizure duration. Thereafter, **(Seangrung et al, 2021)** documented the higher efficacy of DEX induction of anesthesia over LID/propofol in blunting the hemodynamic responses to intubation. Moreover, **(Zhang et al, 2023)** found IV sufentanil and DEX injection with topical LID allowed safe anesthesia induction, and awake fiberoptic nasotracheal intubation under a conscious state without any uncomfortable feeling.

Intraoperative analgesia provided as DEX/LID infusions provided significantly better control of hemodynamic changes induced by abdominal insufflation and desufflation and with extubation than OBA. Further, the applied protocol for IO analgesia spared the need for fentanyl supplements for 83.3% of Group-E patients and significantly reduced the dose of fentanyl required to achieve stable hemodynamics than that required by Group-C patients. These data go in hand with **(Singh et al, 2022)** who documented that DEX or LID can be useful IO pain relief adjuncts and **(Rekatsina et al, 2022)** compared the effect of induction of anesthesia and IO analgesia using DEX or LID versus placebo infusion on chronic neuropathic pain after abdominal surgery and reported that DEX was superior in reducing pain scores at 3-m PO and 6-m pain scores were non-significant between DEX and both of LID and placebo, while versus placebo the effect of LID was weakly significant. Also, **(Qin et al, 2023)** reported, in comparison to the control, significantly lower IO opioid consumption with IO infusion of DEX or LID.

On the contrary, the obtained result from **(Evrard et al, 2023)** retrospectively found using DEX/LID boluses for induction and DEX/LID infusions with morphine titration did not reduce IO opioid in comparison to OBA. This difference could be attributed to the low dose of DEX (0.4 µg/kg) used by **(Evrard et al, 2023)** for induction of anesthesia in comparison to the currently used dose (1 µg/kg).

The applied ERAS protocol allowed significantly shorter PACU time, higher Aldrete recovery score at the time of PACU discharge and significantly lower RSS of Group-E than Group-C patients. Regarding, PO surgical outcomes, Group-E patients had a significantly shorter time to 1st ambulation and oral intake with a significantly shorter duration of PO hospital stay than Group-C patients. Similarly, **(Qin et al, 2023)** reported a

significantly shorter time to first flatus and feces after elective colorectal surgery with LID infusion than placebo infusion. Also, **(Ulbing et al, 2023)** assured the obtained results regarding lower pain scores, less opioid consumption and improved PO recovery with no opioid anesthesia during bariatric surgery. Furthermore, **(Xu et al, 2023)** detected significantly higher quality of recovery scoring with induction and maintenance of anesthesia during a laparoscopic hysterectomy using either LID or DEX alone or LID/DEX than placebo, but highest scores, better sleep quality, lower pain scores and shorter PO hospital stay was with LID/DEX than either alone.

The findings of the current study assured the efficacy of ERAS implementation during bariatric surgery and go in hand with multiple prospective studies that reported significantly lower pain scores, decreased narcotic utilization and PONV, with significantly shorter time to first oral intake and hospital LOS with no change in adverse events or reduced complication and 30-d readmission rates **(Svetanoff et al, 2023; Papasavas et al, 2023)**. Further, a recent meta-analysis indicated the safety and feasibility of the implementation of ERAS protocol in perioperative management during minimally invasive bariatric surgery and compared with standard care, ERAS protocol significantly decreased hospital LOS, 30-day readmission rate, and hospitalization costs with no differences in PO complications and mortality **(Qin et al, 2023)**.

The applied SOUP spared PO opioid in 90% of Group-E patients who did not require morphine despite the early ambulation. Further, pain sensation reported by the three patients who had NRS of 4 responded to a minimal number of morphine shoots than corresponding Group-C patients on their 1st request of rescue analgesia. These data indicated the competence of SOUP to provide its target for opioid-sparing and go in hand with **(Muniz Da Silva et al, 2022)** who compared three protocols dependent on opioid induction and maintenance using opioid infusion, DEX infusion or MMA using IO infusions of DEX/LID/magnesium with methadone and reported that PO pain score and incidence of pain score >3 and PONV were the least with MMA than other protocols and were less with DEX than opioid infusions. Moreover, **(Wilson et al, 2022)** compared bariatric surgery using ERAS alone versus ERAS with SOUP protocols and found patients of the SOUP cohort showed lower pain scores, required significantly lower morphine supplements, and had shorter hospital LOS than patients of the ERAS cohort alone.

The results of the current study and multiple recent studies assured the effectiveness of DEX as a cornerstone for ERAS and various SOUP used for PO analgesia, where, **(Ibrahim et al, 2022)** found DEX/Ketamine induction and maintenance with DEX/Ketamine/LID significantly reduced PO pain and morphine consumption as well as time to oral fluid tolerance and readiness for discharge. Further, **(Shim et al, 2022)** found IO DEX/ketorolac significantly reduced IO and PO opioid consumption and PO pain scores after robot-assisted laparoscopic radical prostatectomy and **(Singh et al, 2022)** reported that DEX alone delayed 1st rescue analgesia and total analgesic consumption more than LID alone.

Conclusion

The implementation of ERAS with SOUP for PO analgesia is a feasible, effective and safe anesthetic policy for high-risk patients undergoing major surgeries. The applied SOUP spared the need for opioid analgesia in about 90% of patients. The applied anesthetic policy improved immediate

surgical outcomes, and reduced times for PACU discharge, ambulation, oral intake and PO hospital stay with subsequent cost reductions.

Limitation

The study is a single-center, the flow of patients requiring bariatric surgery is low and this reduced the number of cases. Also, the applicability of similar anesthetic policies for other bariatric surgical procedures is another limitation.

Recommendations

Evaluation of the impact of the applied anesthetic policy on perioperative immune and redox milieus of these high-risk patients is required and might be conducted through multicenter comparative studies to provide further support for the applied ERAS with SOUP anesthetic policy.

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