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Effect of Dexmedetomidine versus Fentanyl on Postoperative Analgesic profile in Patients with Morbid Obesity Undergoing Laparoscopic Sleeve Gastrectomy: A Randomized Controlled Trial

Doha Mohammed Bakr [1]*, Rasha Behery Youssef [1], Maged Salah Mohamed [2], Moataz Salah Khalil [1]

[1]Anesthesiology, Surgical Intensive Care and Pain Management Department, Faculty of Medicine, Helwan University, Helwan, Egypt
[2]Anesthesiology, Surgical Intensive Care and Pain Management Department, Faculty of Medicine, Cairo University, Cairo, Egypt

Abstract

Laparoscopic sleeve gastrectomy (LSG) is considered to be a beneficial procedure for the management of obesity. Opioids provide an important option for postoperative pain control. However, side effects are reported. Dexmedetomidine (DEX) works by activating the α2 adrenergic receptor in the locus coeruleus. This causes anxiolysis, hypnosis, analgesia, and sedation. We conducted our research to compare the effects of fentanyl and DEX on the postoperative analgesic profile and postoperative nausea and vomiting (PONV) of morbidly obese patients after LSG**.** This randomized, double-blind study was conducted on 64 patients, who were equally divided into two groups. DEX group (group D): received an intravenous (IV) loading dose of DEX (1µg/kg) over 15 minutes prior to the induction of anesthesia. Then, DEX infusion was delivered at a rate of 0.5 µg/kg/h. The patients assigned to the fentanyl group (group F) were administered fentanyl (1µg/kg) IV over 60 seconds with anesthetic induction. Following intubation, a continuous infusion of fentanyl was maintained at a rate of 1µg/kg/hr. Visual analogue pain scores were significantly decreased in group D compared to group F at the post-anesthesia care unit and at 2 hours postoperatively (p values = 0.015 and 0.017, respectively). The opioid dose consumed in the first 12 hours after surgery was significantly decreased in group D compared to group F. Significantly more patients in group F developed PONV. For morbidly obese patients undergoing LSG, intraoperative DEX is a good choice to obtain better postoperative analgesia and to decrease the incidence of PONV.

Keywords: Dexmedetomidine, fentanyl, analgesia, Morbid Obesity, Laparoscopic Sleeve Gastrectomy

Full length article **Corresponding Author*, e-mail: doha.bakr@med.helwan.edu.eg

1. Introduction

According to the World Health Organization, obesity is a persistent metabolic issue that results from excessive fat accumulation and causes serious diseases that lower quality of life [1]. Complications like sleep apnea, high blood pressure, stroke, joint pain, diabetes mellitus, and even tumor diseases are linked to obesity [2]. Laparoscopic sleeve gastrectomy (LSG) is considered to be a beneficial procedure for the management of obesity [3]. Laparoscopy, compared to open surgery, has the advantage of being less invasive with a shorter operation time, allowing for better recovery [4]. Opioids provide an important option for postoperative pain control. However, side effects like respiratory depression, drowsiness, vomiting, and nausea are reported [5]. So, alternative analgesics are needed for obese patients to improve their postoperative management and obtain better analgesia with minimal side effects. Dexmedetomidine (DEX) works by activating the α2 adrenergic receptor in the locus coeruleus. This causes anxiolysis, hypnosis, analgesia, and sedation [6]. We conducted our research to compare the effects of fentanyl and DEX on the postoperative analgesic profile and postoperative nausea and vomiting (PONV) in morbidly obese patients after SG. Our primary outcome was the visual analogue pain (VAS) scores at arrival to the post-anaesthesia care unit (PACU). Secondary outcomes included VAS scores after discharge from PACU, opioid dose after surgery, incidence of PONV, and other side effects.

2. Materials and Methods

The present study was a double blind, randomized controlled trial conducted at Helwan University Hospitals from July 2021 to May 2023. The study was performed on 64 patients of both genders, aged between 20 and 50 years. The participants were required to meet certain inclusion criteria, which included having a body mass index (BMI) of 35 kg/m2 or more as well as an American Society of Anesthesiology (ASA) physical status of II-III. In addition, it was planned that all participants would have a laparoscopic sleeve gastrectomy (LSG). All participants signed informed consent. Patients with allergy to α2 -adrenergic agonist, kidney, liver, neuromuscular disorders, and cardiac disease, or patients on opioid medications, were excluded. The participants were assigned to two groups of equal size (32 patients in each group) by the use of computer-generated numbers and sealed opaque envelopes. The participants allocated to the DEX group (Group D) received an intravenous loading dose of DEX (1 μg/kg) over 15 minutes prior to the anesthetic induction. Following the intubation procedure, a maintenance infusion of DEX was delivered at a rate of 0.5μg/kg/h. The infusion was discontinued upon the removal of the trocars. The patients assigned to the fentanyl group (Group F) were administered fentanyl (1μg/kg) that was given intravenously slowly over 60 seconds with induction of anesthesia as a loading dose. Following intubation, a continuous infusion of fentanyl was administered at a rate of 1μg/kg/hr. The infusion was discontinued upon the removal of the trocars. Patients didn't know the type of drug had been given; anesthetic management and study solution administration were performed by anesthesiologists not involved in data collection or outcome assessment. Another anesthesiologist, blinded to the patient group assignment, assessed and recorded the postoperative outcomes. In both groups, standard monitors were applied to each patient, including an automated blood pressure cuff (NIBP), temperature probe, 5-lead electrocardiogram (ECG), capnography, and pulse oximetry. All the baseline parameters were recorded and observed. Adjusted body weight was the basis for the calculation of all drug doses except atracurium, which was calculated according to lean body weight. Preoxygenation for 3-5 minutes was done through a well-fitting face mask. The administration of general anesthesia was initiated with lidocaine at a dose of 1.5 mg /kg, propofol at a dose of 1-2mg/kg, and atracurium at a dose of 0.5mg/kg. The procedure of intubation was performed using an appropriately sized cuffed endotracheal tube (ETT). The ETT was secured and confirmed by auscultation, chest expansion, and the appearance of consistent waves in the capnogram. The padding of all pressure points was done in a satisfactory manner. The lung was ventilated using a volume-controlled mode, setting a tidal volume of 6-8 ml/kg (ideal body weight). The inspiratory-expiratory ratio was set at 1:2, and normocapnia was achieved by adjusting the respiratory rate setting. Positive end-expiratory pressure was adjusted to 5-10 mmHg to maintain spo2 ≥ 95%. All patients received 1 g paracetamol IV, 8 mg dexamethasone IV, and 60 mg ketorolac IV infusion after induction.

Anesthesia was maintained by isoflurane 1-MAC adjusted according to patient blood pressure (maintaining MAP within 20% of the baseline value); atracurium increments were given if needed. The pneumoperitoneum was kept at a pressure 12-14 mmHg. At the conclusion of the suturing procedure, the administration of isoflurane was discontinued, and the muscle relaxant was counteracted with neostigmine (0.05 mg/kg) and atropine (0.02 mg/kg). When the extubation requirements were met, the extubation was done. Patients were then transferred to the PACU with oxygen support and a head-up 45º for close monitoring and assessment of pain and side effects. Patients were instructed to report their pain intensity using a VAS from 0 to 10 cm (0: no pain, 10: the worst pain). It was assessed in PACU and every 2 hours for 12 hours postoperatively. Patients with VAS of 4 or greater received IV morphine at a dose of 2-4 mg. The time of the first analgesic request and the total opioid dose consumed during the first 12 hours postoperatively were recorded. The incidence of nausea and vomiting (PONV) and postoperative respiratory complications like apnea or hypoxemia were recorded.

2.1. Sample size justification

Our primary outcome was VAS values on arrival at PACU. Based on a pilot study, an effect size of 0.78 was obtained using the G Power program. Setting alpha error 0.05 and beta error 0.2 (power of study 80%), a sample size of 54 cases (27 in each group) was revealed. To compensate for dropouts, 20% was added. A total of 64 cases (32 in each group) were recruited.

2.2. Statistical analysis

The data analysis in this study was conducted using SPSS v27 (IBM, Armonk, NY, USA). The normality of the data distribution was assessed using histograms and the Shapiro-Wilks test. The quantitative parametric data, given as mean ± SD, was examined using unpaired student t-tests. The chi-square or Fisher's exact test was used to examine the qualitative variables, which were expressed as frequencies in percentage form. A significance level of less than 0.05 for a two-tailed P value was deemed statistically significant.

3. Results and discussion

In this research, the eligibility of 77 patients was evaluated; 7 patients were not eligible, and 6 declined to participate in the trial. The rest of the patients were randomized into two groups (32 patients each). All patients were statistically analyzed and followed up. (Figure 1)**.** There was no significant difference observed in the duration of operation or demographic data between the two groups. (Table 1)**.** As regard the visual analogue score, comparison between both groups revealed a significant decrease in VAS in PACU and 2 hours postoperatively in group D compared to group F (p value = 0.015 and 0.017, respectively), but there were no statistically significant changes between both groups at 4 h, 6 h, 8 h, 10 h, and 12 h postoperatively (Table 2). Concerning time to first opioid requirement in both groups, the mean values were 2.13 ± 1.68 hours and 1.38 ±1.48 hours in group D and group F, respectively, which showed a statistically insignificant difference between both groups (p value > 0.05), while the total dose of morphine consumption as rescue analgesia showed a significant decrease in group D compared to group F (P < 0.05) with mean values of 5.75 ± 2.20 mg in group D and 8.00 ±2.38 mg in group F. (Table 3)**.**

The incidence of nausea and vomiting was significantly lower in group D (9.4%) than in group F (34.4%). On the other hand, the incidence of desaturation was statistically insignificant between both groups, and no patients developed apnea in both groups. (Table 3)**.** The American Society of Anaesthesiologists advocates for a limitation of narcotic usage in individuals with obesity during the perioperative phase due to the potential for significant adverse effects related to opioids [7]. Anesthetists should depend on additional analgesic modalities to decrease the opioid requirement in obese patients [8]. In our study, VAS scores were significantly lower in the DEX group than in the fentanyl group when measured in the PACU and 2 hours after surgery. However, until 12 hours after surgery, there was no statistically significant difference between the two groups on other VAS score recordings. In agreement with our study, Greiss et al. [9] performed a study on 82 cases who were scheduled for laparoscopic surgery and allocated into two groups, the DEX versus fentanyl group, with 1µ/kg loading and 0.2-0.7µ/kg/h maintenance dose for both study drugs (rate of infusion adjusted according to intraoperative hemodynamics). They found that VAS scores were significantly decreased in DEX group on arrival in the PACU until 4 hours postoperatively. Also, a previous study conducted by Al Bahar et al. [10] compared opioid-free anesthesia (OFA) and opioid general anesthesia (OA) for morbidly obese patients undergoing laparoscopic cholecystectomy. Fentanyl (1µg/kg) loading dose and (1µg/kg/h) maintenance dose were the analgesic method in the OA group; the other group (OFA) received DEX (1µg/kg/h over 10 min), ketamine (0.25mg/kg), and lidocaine (1.5 mg/kg), and then DEX (0.5µg/kg/h as a maintenance) as anesthetic adjuvant and analgesic. They demonstrated that VAS values showed a significant decrease in the OFA group compared to the OA group for 24 h postoperatively (p value<0.05). The synergistic effects of lidocaine and ketamine with DEX could explain this longer analgesic period postoperatively. Furthermore, El Sayed et al. [11] divided 56 patients who were planned for bariatric laparoscopic procedures into two groups: the DEX group received DEX 1 µg/kg as loading over 10 min and 0.4 µg/kg/h as maintenance until extubation, and the saline group received a similar volume and rate of 0.9%. Fentanyl boluses were given to both groups according to hemodynamics. They found that PACU VAS scores showed a statistically significant lowering in the DEX group compared to the saline group. Also, Park et al. [12] conducted a study on 42 patients scheduled for laparoscopic cholecystectomy and divided them into two groups. Their results revealed that VAS scores were significantly decreased in the DEX group compared with the saline group, but only for 1 h postoperatively, and there was a statistically insignificant difference between the two groups for the next 12 hours. Also, Soudi et al. [13] conducted a study on 60 patients who presented for laparoscopic bariatric surgeries and were divided into two equal groups. One group received traditional balanced anesthesia (TBA) with fentanyl analgesia, and the other group received opioid-free anesthesia (OFA) with ketamine and DEX analgesia. They revealed that the postoperative pain scores were significantly decreased in the OFA group until 24 hours postoperatively (p value <0.001). We think that the longer duration of pain relief was due to the fact that ketamine was used with DEX in their study, the DEX infusion lasted longer because it stopped after the skin was closed, and the DEX dose was higher because they calculated it based on TBW while we used ABW. As regard time to first opioid request postoperatively, our study revealed prolonged time to first analgesic request in the DEX group (2.13±1.68min) than in the fentanyl group (1.38±1.48 min); however, this difference was statistically insignificant (p value 0.062). It also showed a statistically significant decrease in total morphine dose consumed during the first 12 hours postoperatively in the DEX group (5.75±2.20mg) compared to the fentanyl group (8.00±2.38mg) with p value 0.001. Consistent with our findings, Al Bahar et al. [10] showed a statistically significant decrease in the total analgesic dose consumed on the first day postoperatively in the OFA group compared to the OA group (p value 0.038). Moreover, Greiss et al. [9] demonstrated that the time to the first analgesic request was insignificantly different between both groups. However, morphine consumption in the 24 hours after surgery showed a statistically significant decrease in the DEX group (p value 0.003). Moreover, Chilkoti et al. [14] conducted a study on 80 patients who were planned for laparoscopic cholecystectomy and were divided into two equal groups. One group received DEX infusion at a rate of 0.5 µ g/kg/h, and the other group received saline 0.9% at the same rate. They concluded that IV DEX was an effective analgesic as it resulted in a significant decrease in the analgesic dose consumed during the first day postoperatively (p value 0.012). However, against our study, Siddiqui et al. [15] conducted a study on 90 patients posted for laparoscopic cholecystectomy using DEX 1.0 µg/kg over 10 minutes, then infusion at 0.5 µg/kg/h IV in one group, and fentanyl 2.0 µg/kg over 10 minutes, then infusion at 1.0 µg/kg/h IV in the other group. Their results revealed a statistically significant reduction in time to first analgesic request in the DEX group (1.73±1.27 h) compared to the fentanyl group (2.88±1.14h) (p value<0.001). We owe this difference from our results to the higher loading dose of fentanyl used in their study (double our dose). Also, Aronsohn et al. [16] in their retrospective cohort study of obese patients planned for elective laparoscopic sleeve gastrectomy. Patients were given either OFA in the form of propofol (90-200 µg/ kg/ min), DEX (0.2-0.6 µg/ kg/ h), ketamine (5 µg/ kg/min), and lidocaine (0.5-2 mg /kg/ h) or opioid-based anesthesia (OBA) in the form of propofol (90-200 µg kg/min) and remifentanil (0.05-0.3 µg/ kg/min). Their results revealed an insignificant difference between both groups regarding total opioid consumption and time to the first analgesic request. This different result may be due to the different study design, as they used different drug doses and combinations. As regard PONV, our study showed a significant increase in PONV incidence in the fentanyl group compared to the DEX group (34.4% versus 9.4%) with p value 0.016 and no significant difference between both groups regarding the incidence of desaturation (SpO2 less than 90% on room air).

Table 1. Duration of surgery and demographic data of the studied groups

		Dexmedetomidine group (n=32)	Fentanyl group (n= 32)	P value
Age (years)		35.09 ± 8.35	34.91± 7.45	0.925
Sex	**Male**	11 (34.4%)	10 (31.3%)	0.790
	Female	21 (65.6%)	22 (68.8%)	
BMI(Kg/m^2)		43.77 ± 4.67	42.63 ± 4.41	0.318
Duration of surgery (min)		77.09 ± 21.00	70.16 ± 10.73	0.101

Data are presented as mean ± SD or frequency (%), BMI: Body mass index.

Table 2. Comparison of VAS score in both groups

	Dexmedetomidine group (n=32)	Fentanyl group (n=32)	P value
VAS at PACU arrival	3.16±1.59	4.19±1.71	0.015*
2h	2.91±1.30	3.88±1.81	0.017*
4h	3.81±1.45	3.38±1.36	0.218
6h	2.75±1.27	2.5±1.19	0.420
8h	3.09±1.51	3.5±1.61	0.301
10h	2.66±1.45	2.56±1.50	0.800
12h	2.13±1.26	1.97±1.09	0.599

Data are presented as mean ± SD,*: Significant when $P \leq 0.05$
VAS: visual analogue scale, PACU: post-anesthesia care unit

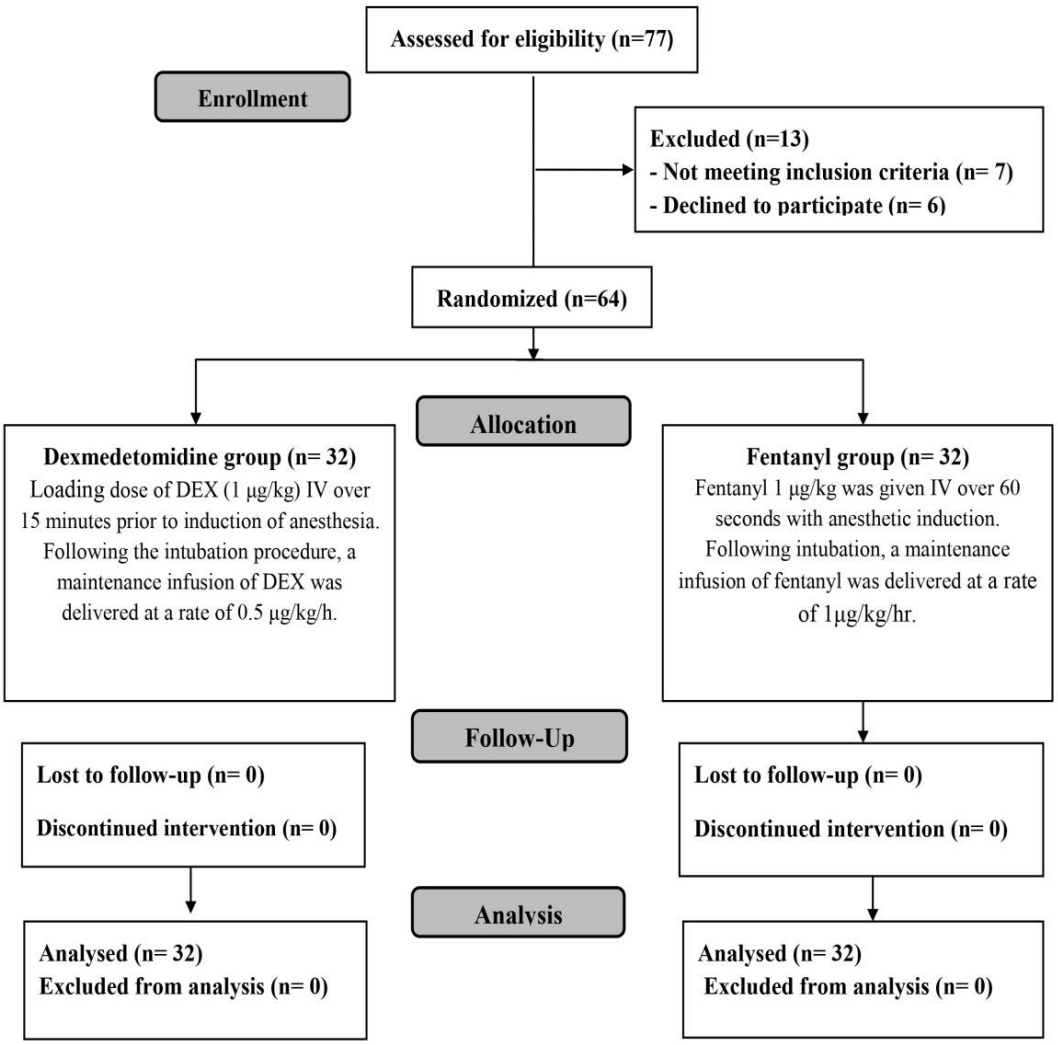

Figure 1. CONSORT flow chart of both groups

Table 3. Time to first opioid requirement, total dose of morphine consumption and side effects in both groups

	Dexmedetomidine group (n=32)	Fentanyl group (n=32)	P value
Time to 1st opioid requirement in h	2.13±1.68	1.38±1.48	0.062
Total dose of Morphine (mg) consumption	5.75±2.20	8.00±2.38	**0.001***
Nausea & vomiting	3 (9.4%)	11 (34.4%)	**0.016***
Desaturation	1 (3.1%)	3 (9.4%)	0.302

Data are presented as mean ± SD or frequency (%),*: Significant when $P \leq 0.05$.

Similar to our results, Mulier et al. [17] compared the role of OFA (using DEX, ketamine, and lidocaine) and OA (using sufentanil) in 50 cases planned for bariatric laparoscopic procedures. Their results revealed that OFA cases experienced fewer PONV episodes (3 patients) than the OA group (14 patients), with p value less than 0.001. Furthermore, Al Bahar et al. [10] demonstrated a significantly lower incidence of PONV in the DEX group (p value <0.05). Moreover, Beloeil et al. [18] conducted a study on 314 patients scheduled for non-cardiac surgery and divided them into 2 equal groups to receive either remifentanil infusion (0.1 to 0.25 µg/ kg /min) or DEX infusion (0.4 to 1.4µg/ kg /min). Their results revealed a significant decrease in the incidence of PONV in the DEX group compared to the remifentanil group. In disagreement with our study, Aronsohn et al. [16] showed an insignificant difference between the OFA group and the opioid-based anesthesia group with regard to PONV. The difference from our study can be attributed to the lack of a standardized OFA protocol in their study, as there was no loading dose of DEX given and they used a lower maintenance dose along with ketamine, which is known to have an emetic effect.

3.1. Limitation of the study

The recovery profiles of both drugs were not assessed.

4. Conclusions

For morbidly obese patients undergoing LSG, intraoperative DEX is a good choice to obtain better postoperative analgesia and to decrease the incidence of PONV.

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