

Research Article

Multimodal Anesthesia/Analgesia Model in Obese Patients Undergoing Open Abdominal Surgery

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Abstract

Background: Patients with concomitant obesity show increased sensitivity to opioid-induced sedation and respiratory depression. To reduce the perioperative opioid load in bariatric surgery, various multimodal anesthetic techniques are used. The purpose is to check the effectiveness of our own perioperative multimodal anesthesia/analgesia protocol for obese patients undergoing open abdominal surgery.

Materials and methods: A prospective, single-centered study included 54 patients with BMI>30 kg/m² divided into two groups. In group 1 (MAA-group, n=30), a multimodal anesthesia/analgesia protocol was used (inhaled anesthesia with sevoflurane + epidural analgesia with lidocaine/bupivacaine + low doses of ketamine + low doses of clonidine + fentanyl). In group 2 (TIVA-group, n=24) total intravenous anesthesia was performed with propofol and fentanyl, and trimeperidine was used for postoperative analgesia. Endpoint comparative values included intraoperative hemodynamic stability, extubation time, general intra- and post-operative need for opioid analgesia, mobility of patients, return to enteral feeding and degree of analgesic comfort. Statistical analysis was carried out by software Statistica for Windows version 6.0.

Results: Intraoperative patients in MAA-group were more likely to use phenylephrine than in TIVA-group patients (18 cases vs 2 cases, p<0.05), but less fentanyl (0.8 (0.6-0.9) mg vs 1.3 (1.1-1.5) mg respectively, p<0.05). Extubation time in MAA-group was 13 (10-15) minutes, and in the TIVA-group - 35 (20-45) min. (p<0.05). After surgery, patients in MAA-group required less trimeperidine than patients in TIVA-group (30 (20-60) mg versus 60 (40-80) mg, respectively, p<0.05), earlier activated and began to consume food (24 h vs 48 h, respectively, p <0.05). In MAA-group, 100% of respondents showed satisfaction with the obtained analgesic regimen at the "excellent-good" level, while in TIVA-group, 15 (62.5%) of respondents noted the level of comfort as "good-satisfactory" and three patients (12.5%) of this group were completely dissatisfied with postoperative analgesia (p<0.05).

Conclusion: Multimodal anesthesia/analgesia based on low flow anesthesia with sevoflurane, thoracic epidural analgesia with lidocaine, intravenous ketamine and clonidine proved to be an effective method of perioperative pain management in obese patients undergoing open abdominal surgery, that decreases the need for post-operative opioid use and improves the analgesic patients' comfort.

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Introduction

Patients with concomitant obesity show increased sensitivity to opioid-induced sedation and respiratory depression. Many of them develop Obstructive Sleep Apnea (OSA) and are more likely to suffer from airway obstruction and desaturation in the postoperative period, especially when prescribed opioids [1,2]. To reduce the perioperative opioid load in bariatric surgery, various multimodal anesthetic techniques are used. [3,4]. According to Jan P. Mulier (2016), the principle of Opioid-Free Anesthetics (OFA) in obese patients is the following: the use of drugs that directly (clonidine, dexmedetomidine, β -blockers) or indirectly (nicardipine, lidocaine, MgSO₄, inhalation anesthetics) cause a sympathetic blockage; intraoperative saturation with "multimodal" non-opioid analgesics (small doses of ketamine, dexmedetomidine, lidocaine, diclofenac, paracetamol) to reach the peak of their activity after awakening; the use of neuroaxial techniques and regional blockades [3]. Based on these data and having experience in multimodal anesthesia for pancreatic laparotomy [5], and also given the lack of unambiguous recommendations on OFA in literature, we decided to check the effectiveness of our own multimodal protocol for perioperative anesthesia/analgesia in obese patients undergoing open abdominal surgery.

Materials and Methods

After Zaporozhye State Medical University Ethics Committee approval (protocol №5, 04.06.2015) the prospective single-centered study was carried out at the "Vita Center" clinic, Zaporizhzhia, Ukraine. Having submitted their written consent, patients with a body mass index (BMI) of more than 30 kg/m², who were scheduled for an open abdominal surgery, were consistently included into the study. Group 1 included patients undergoing Multimodal Anesthesia/Analgesia (MAA) as shown in Table 1 and described below. In the presence of contraindications or allergy to any of the drugs of the standard protocol, or if anesthesia/analgesia was rejected for any reason from the standard protocol, patients were excluded from this group.

Preoperative preparation included fasting starting midnight and no fluid intake 2 hours prior to surgery, without the use of any medication premedication. On arrival in the operating room and setting up a standard monitoring care, group 1 patients received premedication as described in Table 1 and had the epidural space catheterized at the T10/11/12 level. In 13 cases, an ultrasound scanner Logiq e (GE, USA) was used to determine the point of the needle, its direction of insertion and the distance to the epidural space in the manner described earlier [6]. The initial dose of 1.0-1.2% of lidocaine solution was 8-10 ml with 0.1 mg of fentanyl. After development of the sensory block to the level of T4, induction of anesthesia was performed, consistently using fentanyl, atracurium and propofol in doses according to the Society for Obesity

Stage	Protocol
Premedication	pantoprazole 40 mg IV, metoclopramide 10 mg IV, diphenhydramine 10 mg IV, dexamethasone 8 mg IV, diclofenac 75 mg IM
Induction	diazepam 1.25-2.5 mg IV, fentanyl 0.1-0.2 mg IV, atracurium 0.4 mg/kg LBW IV (suxamethonium 1 mg/kg ABW IV), propofol 1-2 mg/kg LBW IV
Maintenance of anesthesia	sevoflurane 2-2.5 vol%, atracurium 0.2 mg/kg LBW IV (if required)
Intraoperative analgesia	lidocaine 1-1.2% 6.0-10.0 ml/h EA, bupivacaine 0,25% 6.0-8.0 ml EA at the end of surgery, ketamine 0.15 mg/kg IBW/h IV, fentanyl 0.1 mg IV (if required), clonidine 100 mcg IV titrated
IV fluid therapy	balanced crystalloid solution \geq 10 ml/kg ABW IV, balanced colloid solution (if required)
Recovery	neostigmine and atropine (if required)
Postoperative analgesia	bupivacaine 0.125% 6.0-8.0 ml/4-6 h EA, diclofenac 75 mg IM 2/24h, trimeperidine 20 mg IM (if required)

IV – intravenous, IM – intramuscular, vol% – volume percent, LBW – lean body weight, ABW – actual body weight, IBW – ideal body weight, EA – epidural analgesia, h –hour.

Table 1: Multimodal anesthesia/analgesia protocol.

and Bariatric Anaesthesia (SOBA) recommendations [7]. In 5 cases of anticipated difficult intubation a muscle relaxant suxamethonium was used. In 4 cases an awake intubation with laryngeal mask was used in the manner described earlier [8]. Shortly after induction and intubation 0.15 mg/kg of Ideal Body Weight (IBW) ketamine was injected and repeated bolus every 60 minutes during the surgery.

General anesthesia for group 1 patients was performed using sevoflurane and Low-Flow Anesthesia (LFA) on Neptun machine (Medec, Benelux N.V.). Myoplegy was supported by bolus administration of atracurium every 20-30 minutes if required accordingly clinical signs. Intraoperative anesthesia was achieved by combined use of epidural analgesia (EA: 1% lidocaine solution for 6-10 ml/h) and IV anesthesia (fentanyl: if required). For additional sympathetic nervous system blockade, clonidine was used in a total dose of 100 mcg during surgery. Fluid therapy included balanced solutions of crystalloids at a rate of 10 ml/kg for Actual Body Weight (ABW) and additional administration of balanced colloids/crystalloids according to circumstances. Hypotension was managed by phenylephrine.

At the end of the surgery group 1 patient were epidurally injected with 6.0-8.0 ml of 0.25% bupivacaine solution. After restoring muscle tone and consciousness endotracheal extubation was performed and patients were transferred to the postoperative ward. Subsequently diclofenac 150 mg/day and standard nurse-controlled EA with solution of bupivacaine (1.25 mg/ml at 6-8 ml every 4 to 6 hours) was used for analgesia. If patients needed “rescue” analgesia they were prescribed trimeperidine 20 mg IM.

The control group (group 2) consisted of patients who have received Total Intravenous Anesthesia (TIVA), where propofol was used for hypnosis, fentanyl for analgesia and atracurium for muscle relaxation. Dosage of drugs was determined by the clinical signs of the depth of anesthesia. For postoperative analgesia, diclofenac 150 mg/day and trimemperidine, if required, were used.

The quality of the proposed multimodal anesthesia/analgesia protocol was assessed by determining the intraoperative hemodynamic stability of patients, the extubation time, the overall intra- and post-operative need for opioids, the time of patients’ mobility and the return to enteral nutrition, the degree of analgesic comfort according to the following numerical scale: 4 (excellent) - without pain; 3 (good) - slight pain without the need for additional analgesics; 2 (satisfactory) - pain requiring additional analgesics; 1 (bad) - pain that did not diminish after the administration of additional analgesic.

Statistical analysis was carried out using Statistica for Windows version 6.0. Quantitative variables are presented as mean \pm standard deviation with normal data distribution, median and quartile - with abnormal. Student’s t-test and Mann-Whitney U-test were used to compare them. Categorical variables were calculated as frequencies and

compared with the χ^2 test or the Fisher exact test. Data with a value of $p < 0.05$ were considered statistically significant.

Results

A total of 54 patients were analyzed, the characteristics of which are presented in Table 2. As can be concluded from Table 2, MAA-group includes 30 patients, and TIVA-group - 24 patients. There was no difference by demography, initial ASA status, presence of comorbidity or kind of laparotomy. However, with the same duration of surgery, in MAA-group the dosage of fentanyl and atracurium was almost twice lower than in TIVA-group ($p < 0.05$). This was probably due to the prolongation of the postoperative need for ventilation in TIVA-group patients on average up to 35 minutes, while patients from MAA-group were extubated on average 13 minutes after surgery ($p < 0.05$). It should also be noted that with the use of multimodal anesthesia, no patient needed recovery of neuromuscular conduction with neostigmine, but in the TIVA-group it was administered to all patients ($p < 0.05$). However, phenylephrine was significantly more commonly used in MAA-group to maintain hemodynamic stability than in TIVA-group ($p < 0.05$).

During the first hour after extubation of the trachea 71% of TIVA-group patients needed additional “rescue” pain relief with trimeperidine as they had a score of 4 on the numerical rating scale (Table 3). In MAA-group the opioid was administered to only one patient at the same time ($p < 0.05$). The overall consumption of trimeperidine in the first day after surgery was also lower in patients who followed multimodal anesthesia/analgesia protocol and averaged 30 mg. In the TIVA-group this figure was almost twice as high ($p < 0.05$). Perhaps for this reason, there was a statistically significant difference in the frequency and severity of Postoperative Nausea and Vomiting (PONV) between the study groups: in TIVA-group there was four times higher incidence of PONV than in MAA-group ($p < 0.05$). The above mentioned resulted in the fact that patients from MAA-group began to move independently in the ward and consume food starting from the end of the first post-operative day, whereas patients from TIVA-group did so only on the third postoperative day ($p < 0.05$).

An analysis of the patients’ assessment of the degree of analgesic comfort showed that it was significantly higher in the MAA-group, where 100% of the respondents reported satisfaction at the “excellent-good” level. In the TIVA-group, 15 (62.5%) respondents reported comfort levels as “good-satisfactory”, but three (12.5%) patients in this group were completely dissatisfied with post-operative analgesia ($p < 0.05$).

Discussion

Opiates are among the oldest known drugs in the world. In anesthesiology, they are traditionally used as part of a balanced anesthesia to ensure hypnosis and analgesia and reduction of the

Parameter	MAA-group (n=30)	TIVA-group (n=24)
Age, years	52.4±11.2	53.8±12.2
Sex, male/female	10/20	9/15
BMI, kg/m ²	38.5±5.2	36.7±6.1
ASA class I/II/III, n	2/15/13	3/11/10
Comorbidity:		
Diabetes mellitus, n (%)	16 (53.3)	12 (50)
Hypertension, n (%)	15 (50)	10 (41.7)
Ischemic heart disease, n (%)	2 (6.7)	2 (8.3)
Surgery types:		
Hemicolectomy, n (%)	8 (26.7)	5 (20.8)
Hernioplastics, n (%)	15 (50)	12 (50)
Choledochotomy, n (%)	7 (23.3)	7 (29.2)
Surgery duration, min	146 (122-175)	155 (125-168)
Intraoperative medication:		
Phenylephrine, n (%)	18 (60)	2 (8.3)*
Fentanyl, mg	0.8 (0.6–0.9)	1.3 (1.1-1.5)*
Atracurium, mg	55 (40–67)	140 (120-150)*
Neostigmine, mg	-	1,0 (0.5-1.5)*
Extubation time, min	13 (10–15)	35 (20-45) *

BMI – Body Mass Index, ASA – American Society of Anesthesiologists, *p<0.05.

Table 2: General patient information.

Parameter	MAA-group (n =30)	TIVA-group (n =24)
NRS, score	2 (1–2)	5 (4–6)*
«Rescue» analgesia 60 min, n (%)	1 (3.3)	17 (71)*
Trimeperidine dose, mg/24h	30 (20–60)	60 (40–80)*
Nausea, n (%)	3 (10)	12 (50)*
Vomiting, n (%)	0 (0)	4 (9)*

NRS - Numerical Rating Scale, * p<0.05.

Table 3: Post-operative analgesia quality values.

sympathetic response to surgical aggression, being also the fundamental part of post-operative anesthesia in many situations. However, obese patients are particularly susceptible to respiratory depression due to the effect of opioids. Taylor et al. [2] found that the use of opioids alone was a risk factor for ventilation failure within the first 24 hours after surgery. Ahmad et al. [1] demonstrated that in 40 obese patients after laparoscopic bariatric surgery with desflurane and remifentanyl-morphine anesthesia, episodes of hypoxemia for the first 24 hours were commonplace, and 14 of them had more than five such episodes per hour, despite extra oxygen therapy.

How can an anesthetist avoid or reduce the use of opioids and at the same time provide a balanced anesthesia with hypnosis, analgesia, hemodynamic stability and satisfactory postoperative anesthesia? The first method is to combine general anesthesia with regional analgesia. This is why we have focused our attention on using EA, being the best “opioid-free” anesthetic technique for the abdominal cavity interventions [9]. In the absence of contraindications to EA, the only risk factor may be moderate hypotension, which is well managed by phenylephrine. In obese patients there may be some technical difficulties with the puncture of the epidural space due to the lack of clear anatomical landmark. But the use of ultrasound navigation makes it a lot easier to perform EA in most of these patients [6].

In addition to EA, another way to reduce the perioperative use of opioids is a combination of non-narcotic agents with volatile anesthetics or propofol [3]. This is the so-called OFA or opioid-free anesthesia technique. Plenty of research suggests that paracetamol, NSAIDs or COX-2 inhibitors, gabapentinoids, ketamine and α^2 -agonists, when used alone or in various combinations, including regional methods,

reduce postoperative need for opioids and relieve pain [10-13]. In our study as NSAIDs we used diclofenac in standard dosage for all patients, but in the MAA-group, ketamine and clonidine were additionally administered intraoperatively.

Ketamine is an N-methyl-D-aspartate-receptor antagonist with a strong anesthetic effect when administered in subanesthetic doses [14]. The use of ketamine has advantages in obese patients, since causes almost no respiratory depression in comparison with opioids. In our protocol, we used IBW to calculate the dose of ketamine, and used relatively low doses (0.15 mg/kg bolus followed by bolus administration of 0.15 mg/kg/h). This led to a low total dose of ketamine with an average value of 35 mg per patient (range 25-45 mg). Diazepam at a dose of 1.25 to 2.5 mg was administered at the time of induction to prevent any psychomelic reactions caused by ketamine. As a result, we did not observe any hallucinations, dysphoria or delayed restoration of consciousness after surgery in patients in the MAA-group.

According to the meta-analysis of Blaudzun et al. [11] perioperative administration of clonidine improves the quality of analgesia and reduces the use of opioids as well as the incidence of postoperative nausea. We included clonidine in a multimodal anesthesia/analgesia protocol at a dose of 100 mcg to prevent such negative effect of α^2 -agonists as hypotension. But, probably due to the combination of local (EA) and systemic (clonidine) sympathetic blockade, 60% of patients showed instability of hemodynamics, which required additional phenylephrine administration.

Our research has a number of limitations. This was a prospective observational study with a relatively small number of cases and a

multimodal anesthesia/analgesia protocol using multiple techniques together, which makes it impossible to analyze the quality of the isolated action of any of them and needs a different design of work - randomization and control (randomized controlled trial). The administration of trimeperidine for "rescue" analgesia through intramuscular injection only reflects the tendency of its use in patients. In order to accurately assess the need for opioids after surgery, all patients should have received patient-controlled analgesia with parenteral administration of opioids if required.

Modern abdominal surgery develops in the direction of minimally invasive surgery technique, especially in case of "problematic" patients, who include people with obesity. Nonetheless, such patients still have laparotomies performed, which requires improvement of the methods of perioperative "opioid-free" anesthesia, which is a promising perspective for further research.

Conclusion

Multimodal anesthesia/analgesia based on low flow anesthesia with sevoflurane, thoracic epidural analgesia with lidocaine, intravenous ketamine and clonidine proved to be an effective method of perioperative pain management in obese patients undergoing open abdominal surgery, that decreases the need for post-operative opioid use and improves the analgesic patients' comfort.

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