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Case report

PRACTICING OPIOID-FREE ANESTHESIA FOR LAPAROSCOPIC CHOLECYSTECTOMY OPIOID-FREE ANESTHESIA

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Abstract

***Introduction**: Opioid free anesthesia (OFA) is an anesthesiological technique, which uses non-opioid analgesics, such as paracetamol, dexamethasone, lidocaine, ketamine, and magnesium sulfate instead of opioids. In this case, the report about patient who after previous surgeries experienced opioid side effects is followed by a narrative review; we present the OFA method for laparoscopic cholecystectomy. **Case report**: We present a case of a 55-year-old woman with a history of controlled hypertension and asthma, planned for laparoscopic cholecystectomy. Previously she underwent two surgical interventions; bilateral radical mastectomy performed separately with a three year gap. Both anesthesias were complicated, postoperatively with nausea, vomiting, dizziness, and respiratory depression. Based on the previous postoperative complications, we hypothesized that nausea, vomiting, dizziness, and respiratory depression were caused by opioids, and we decided to perform OFA. Before the induction the patient received dexamethasone 8 mg and paracetamol 1 gr intravenously, followed by induction with midazolam 3 mg, lidocaine hydrochloride 78 mg, propofol 160 mg, ketamine hydrochloride 39 mg and rocuronium bromide 60 mg. After tracheal intubation, continuous intravenous infusion with lidocaine hydrochloride 2 mg/kg/hr and magnesium sulfate 1.5 gr/hr was started. Anesthesia was maintained by using sevoflurane MAC 0.7–1. At the end of the surgery, 2.5 gr of metamizole was given intravenously. Postoperative recovery was uneventful. **Conclusion**: In our patient, OFA eliminated opioid-related side effects (nausea, vomiting, dizziness, and shortness of breath), and provided satisfying postoperative analgesia.*

***Keywords:** opioid free anesthesia; laparoscopic cholecystectomy; pain; nausea vomiting*

Introduction

The opioid-free anesthesia (OFA) technique is characterized by perioperative opioid omittance[1]. Although opioids are still the mainstay analgesics used for the treatment of moderate to severe pain, opioid avoidance leads to less opioid-related side effects in the postoperative period, such as respiratory depression, postoperative nausea, and vomiting (PONV), dizziness, and constipation. We present a case of a patient with previous experience of opioid-mediated side effects, who underwent laparoscopic cholecystectomy with perioperative OFA application.

Case report

A 55-year-old woman (height 165 cm, weight 78 kg) was scheduled for laparoscopic cholecystectomy under general anesthesia. The patient had a history of hypertension treated with an angiotensin converting enzyme inhibitor and asthma which was treated with a bronchodilator (aminophylline). The patient had a bilateral mastectomy, left radical mastectomy was done five years before and right radical mastectomy two years before. After previous surgeries, postoperative recovery was complicated with nausea, vomiting, dizziness and respiratory depression (SpO_2 was 88–90% with an oxygen mask and respiratory rate of 8 breaths per minute), which necessitated the intensive care unit

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admission. The decision was made that for this surgery, an OFA technique is suitable. The day before surgery, the patient was trained to use the Numeric Rating Scale (NRS) score (0 means no pain at all, and the number 10 means the worst imaginable pain).

The patient was premedicated with 5 mg of diazepam orally two hours before the operation. In the operating room, the patient was placed on continuous hemodynamic monitoring, including electrocardiography (ECG), heart rate (HR), non-invasive blood pressure measurement (NIBP) every 5 minutes, saturation with oxygen by pulse oximetry (SpO_2%) and capnography. The preinduction vital signs were: NIBP: 157/92 mmHg, HR: 88/min, RR: 16/min, SpO_2 = 93%. Before the induction to general anesthesia, dexamethasone 8 mg as an antiemetic agent and paracetamol 1 gr intravenously (i.v.), were given. The induction into general anesthesia included midazolam 3 mg, lidocaine hydrochloride 78 mg, propofol 160 mg, ketamine hydrochloride 39 mg, and rocuronium bromide 60 mg. After tracheal intubation continuous intravenous infusion of lidocaine hydrochloride 2 mg/kg/h was started, and magnesium sulfate ($MgSO_4$) 1.5 gr/h. Anesthesia was maintained by using sevoflurane MAC 0.7–1 to maintain mean arterial pressure with a value of +/- 20% of the baseline value. The patient was mechanically ventilated with PCV-VG ventilation mode, with a breath volume of 6–8 ml/kg from a mixture of gases in proportion to 50% oxygen and 50% air, I:E ratio = 1:2, the number of respirations were customized according to $EtCO_2$ between 35–45 mmHg, PEEP 5 cm H_2O. An oral-gastric tube and sequential compression device were placed, and normothermia was maintained with a warming blanket. During the laparoscopy, the intra-abdominal pressure was 12 mmHg with continuous insufflation of CO_2. The operation lasted for one hour and was uneventful. After the gallbladder removal, the continuous infusion of lidocaine and magnesium sulfate was discontinued, and 2.5 gr of metamizole was given intravenously. At the end of the operation, the gastric tube was removed, and the residual neuromuscular blockade was antagonized with neostigmine 0.05 mg/kg and 0.02 mg/kg of atropine i.v. And the patient was extubated.

The patient was pain-free (VAS score 1), no nausea, vomiting, or dizziness complaining. She was transferred to the PACU and stayed there for 60 minutes. Postoperative analgesia plan included 1g of paracetamol for NRS score from 4 to 6, or 100 mg of tramadol for NRS score from 7 to 10, while ketonal 100 mg was used as a rescue analgesic. The pain at rest and on movement and PONV were recorded at 1, 4, 8, 12, and 24 hours after the surgery. One hour after the surgery, the patient reported pain on NRS to score one at rest, and NRS score two on movement, no PONV, no respiratory depression or dizziness. She said that she felt very good like she wasn't operated and she was transferred to the ward. Postoperative pain was well controlled with NRS score 2 at rest, and NRS score 3 on movement at the fourth hour, and NRS score 3 at rest, and, NRS score 3 on movement on the eighth hour, without PONV. Paracetamol 1 gr was used for the pain management following 12 hours and 24 hours (NRS score 5 at rest, and NRS score 6 on movement and NRS 3 at rest and NRS 4 on movement, respectively), without PONV. Patient felt very comfortable during her stay in the hospital; she slept well without nightmare complaints.

Discussion

Here we present the case of a patient who was perioperatively managed with OFA as an example that this method is reasonably used in patients with previously experienced opioid's side effects. Although opioids are the strongest analgesics and an essential part of most general anesthesias, they have numerous side-effects, short and long term consequences[2], including respiratory depression[3], nausea[4], vomiting[5], dizziness[6], sedation[7], ileus[7], delirium[8], pruritus[4], urinary retention[7], hyperalgesia[7,9], opioid tolerance[7], opioid-induced immunosuppression[10], and sleep disorders[11].

Opioids can be avoided by intraoperative using multi-modal non-opioid analgesics such as paracetamol, dexamethasone, lidocaine, ketamine and magnesium sulfate, medications acting on receptors centrally and peripherally in the pain pathway[12]. Paracetamol given before the induction to anesthesia leads to lower requirements of opioids during the operation[13]. Dexamethasone has effective antiemetic effects given in a lower dose. Moreover intermediate doses (0.1–0.2 mg/kg) of dexamethasone have an opioid-sparing effect and has bene-

ficial effects on postoperative pain[14]. Lidocaine is local anesthetic and has an analgesic, antihyperalgesic and anti-inflammatory effect, and given intravenously reduces perioperative opioid consumption, provides better pain control and faster return of the bowel function[15]. Ketamine is a unique intravenous anesthetic with an analgesic effect, opioid-sparing effect, acting on N-methyl D-aspartate (NMDA) receptors through blocking potassium to exit outside of the cell[16]. Magnesium sulfate acts on NMDA receptors by blocking the entrance of calcium and sodium inside the cell and given as a continuous infusion in the intra-operative period leads to low pain scores and less nausea and vomiting in the postoperative period[17]. The occurrence of PONV after laparoscopic cholecystectomy ranges from 46% to 75%[18]. Apfel et al. created risk score for PONV with an aim to implement preventive strategy for PONV[19]. This score is consisted of four highly predictive risk factors: female gender, non-smokers, history of previous PONV or motion sickness and expected administration of postoperative opioids. Dexamethasone given in intermediate doses (0.1–0.2 mg/kg) has antiemetic effects, and better efficacy if given preventively[20]. It is also indicated in patients with asthma because it improves the efficacy of bronchodilator therapy[21]. Ketamine also has a bronchodilator effect and is suitable for induction and maintaining of anesthesia in patients with asthma[22]. Anesthetics dose of ketamine has an emetic effect and leads to nausea, but sub-anesthetic dose (< 0.5 mg/kg) reduces nausea and vomiting, probably because of his opioid-sparing effect[23]. The strategies for PONV reduction are regional anesthesia and total intravenous anesthesia – TIVA with propofol[24], volatile anesthetics avoidance, or use of sevoflurane and desflurane[25], adequate hidration[26], administration of dextrose[27], multimodal postoperative pain control (using regional anesthetic techniques, paracetamol, NSAID, other non-opioid adjuvants)[28], administration of antiemetics[29]. Pre-operative administration of midazolam in dose 0.04 mg/kg has shown significantly reduced PONV in the first 24 hours after intra-abdominal or ambulatory surgery[30].

In the postoperative period, the patient was treated according to hospital protocol for postoperative analgesia with the total amount of given analgesics of 2 gr paracetamol during 24 hours after the surgery. Antiemetics and analgesics (tramadol and ketoprofen as a rescue analgesic) were not given during the post-operative period. No side effects were recorded during the postoperative period. Usually suggested medications for opioid-free anesthesia like alfa-2 agonists (clonidine and dexmedetomidine) were not registered in our country and therefore not used[2,12]. This case can serve as an example of OFA approach. Alfa-2 agonists have many pharmacological characteristics such as sedation, hypnosis, anxiolysis, analgesia, and sympatholysis.

OFA is indicated in patients with acute and chronic opioid addiction. It can be used in opioid-tolerant patients: patients with persistent non-cancer pain, cancer pain, a substance abuse disorder, and with acute opioid tolerance. Opioid-addicted patients planned for surgery have 30–100% increased intra-operative opioid requirements, compared to opioid-naive patients[31]. OFA is also indicated to avoid administration of opioids during the perioperative period.

Also, OFA can be used in obese patients scheduled for bariatric surgery, therefore serves for avoiding opioids as this group of patients are particularly in risk to develop respiratory depression[32]. Majority of obese patients have obstructive sleep apnoea syndrome (OSA) and they are prone to airway obstruction and desaturation in the perioperative period, especially if opioids are given. Mulier et al. evaluated the effect of OFA versus general opioid anesthesia in patients scheduled for elective laparoscopic bariatric surgery[2]. Patients who received OFA required fewer analgesics in the postoperative period, experienced less postoperative PONV and shivering, less postoperative hypertension and desaturation, and had an improved quality of recovery after surgery.

Samuels et al. compared postoperative opioid consumption in three groups of patients divided into three anesthesia regiments: the first group received opioid-sparing anesthesia (OSA), the second group received opioid-free anesthesia (OFA), and the third group received opioid anesthesia (OA)[12]. These patients were planned for various surgical procedures, including breast reconstructions, cochlear implants, stapedectomies, and mastoidectomies. In the postoperative period, 73% of the OFA patients didn't require opioids, compared to 52% of OA patients and 37% of OSA patients. OFA patients also had less nausea and vomiting compared with OSA and OA patients. OFA also

reduces PONV compared to patients who underwent general anesthesia with volatile anesthetics and opioids[33].

Additionally, cancer patients can benefit from OFA is also indicated in patients scheduled for cancer surgery opioids have immunosuppressive effects (inhibition of cellular immunity), and potentially can stimulate cancer cells growth and angiogenesis[34].

Based on the literature data, OFA is suggested for obese patients, patients with OSA, pulmonary disease (asthma, COPD, respiratory insufficiency), history of acute or chronic opioid dependence, hyperalgesia, history of chronic pain, immunodeficiency, oncologic surgery, and inflammatory diseases. Absolute contraindication for OFA is an allergy of any non-opioid adjuvant drug, while relative contraindications are cerebrovascular disease, disorders of autonomic failure, acute coronary ischemia, critical coronary stenosis, heart block, extreme bradycardia, non-stabilized hypovolemic shock, polytrauma patient, elderly patients on beta blockers.

Opioid-free postoperative analgesia has opioid-tolerant more than ten years[35], and the POFA trial is the first prospective, randomized, multicentric study evaluating the effects of OFA on severe postoperative opioid-related adverse events[36].

Conclusion

Opioid-free anesthesia technique leads to less opioid-related side effects such as PONV, dizziness, respiratory depression, and more satisfied patient. It's a safe and effective anesthetic technique, suggested for ambulatory surgery.

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