ISSN 1857-9345
UDC: 616.348-031.4-089.85-089.5

# OPIOID FREE ANESTHESIA FOR LAPAROTOMIC HEMICOLECTOMY: A CASE REPORT

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## ABSTRACT

Opioid free anesthesia (OFA) is deffined as anaesthesiological technique where opioids are not used in the intraoperative period (systemic, neuroaxial or intracavitary). Anaphylaxis caused by opioids (fentanyl) is very rare, and the reaction is presented with hypotension and urticaria. When we have proven allergy to fentanyl, patients' refusal of placing epidural catheter and refusal of receiving bilateral ultrasound guided transversus abdominis plane block (USG TAPB), we must think of using multimodal nonopioide analgesia. The concept of multimodal balanced analgesia is consisted of giving different analgesic drugs in purpose to change the pathophysiological process which is included in nociception, in way to receive more effective intraoperative analgesia with less adverse effects. This is a case report of a 60-year-old male patient scheduled for laparotomic hemicolectomy, who previously had proven allergy to fentanyl. We have decided to give him an opioid free anaesthesia. Before the induction to anaesthesia, the patient would receive dexamethasone (dexasone) 0.1 mg/kg and paracetamol 1 gr intravenously. The patient was induced into general endotracheal anesthesia according to a standardized protocol, with midazolam 0.04 mg/kg, lidocaine hydrochloride 1 mg/kg, propofol 2 mg/kg and rocuronium bromide 0.6 mg/kg. Anaesthesia was maintained by using sevoflurane MAC 1 in order to maintain mean arterial pressure (MAP) with a value of +/- 20% of the original value. After tracheal intubation, the patient had received ketamine hydrochloride 0.5 mg/kg (or 50 mg ketamine) in bolus intravenously and a continuous intravenous infusion with lidocaine hydrochloride (lidocaine) 2 mg/kg/hr and magnesium sulfate ($MgSO_4$) 1,5 gr/hr. At the end of surgery the continuous intravenous infusion with lidocaine and magnesium sulfate was stopped while the abdominal wall was closed and 2.5 g of metamizole (novalgetol) was given intravenously. VAS score 2 hours after surgery was 6/10 and 1 gr of paracetamol was given and the patient was transferred to the Department. Over the next 3 days, the patient had a VAS score of 4-6 / 10 and only received paracetamol 3x1g and novalgetol 3x1 gr daily, every four hours.

**Keywords**: opioid free anesthesia, multimodal analgesia, laparotomic hemicolectomy

## CASE REPORT

A 60-year-old male patient with permanent abdominal pain was planned for surgical treatment as an elective case for open surgery of right colon carcinoma (laparotomic colectomy). The patient had previous history of hypertension, which was well controlled with antihypertensive therapy. Five years ago, the patient was operated for Meningeoma cerebri. Then, following an induction to anaesthesia, an anaphylactic reaction with a generalized rash throughout the body and hypotension was manifested, before the surgical incision. The operation was delayed and the patient was transferred to the Intensive Care Unit. After one week, allergic tests of anaesthetics were made and the test was positive for fentanyl, with a recommendation not to use this drug during surgery. The patient was operated without using fentanyl. Now the patient refused to receive an epidural catheter for intra- and postoperative pain treatment and refused applying bilateral ultrasound guided transversus abdominis plane block (USG TAPB). In the preoperative anaesthesiology visit, the visual analogue scale (VAS) for pain was explained to the patient. Two hours before surgery, the patient was premedicated with 5 mg of valium (diazepam) orally. After being transferred into the operating room, the patient was placed on continuous haemodynamic monitoring, followed by: electrocardiographic record (ECG), heart rate (HR), measurement of non-invasive blood pressure every 5 minutes, saturation with oxygen by pulse oximetry (SAT%), capnography (measurement of the concentration of $CO_2$ in the end expiratory air - $EtCO_2$). Two intravenous cannulas and a crystalloid infusion solution were placed, with a rate of 12-15 ml/kg/hr during surgery. Before the induction to anaesthesia, the patient would receive dexamethasone (dexasone) 0.1 mg/kg and paracetamol 1 gr intravenously. After preoxygenation with 100% oxygen of 6 L/min for three minutes, the patient was induced into general endotracheal anesthesia according to a standardized protocol, with midazolam 0.04 mg/kg, lidocaine hydrochloride 1 mg/kg, propofol 2 mg/kg and rocuronium bromide 0.6 mg/kg. After tracheal intubation, 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. Anaesthesia was maintained by using sevoflurane MAC 1 in order to maintain mean arterial pressure (MAP) with a value of +/- 20% of the original value. A nasogastric tube was placed and we kept the patient warm with air-warm blanket to avoid intra-operative hypothermia and anti-embolic pumps on the legs. Immediately after intubation, the patient had received ketamine hydrochloride 0.5 mg/kg (or 50 mg ketamine hydrochloride) in bolus intravenously and a continuous intravenous infusion with lidocaine hydrochloride (lidocaine) 2 mg/kg/hr and magnesium sulfate ($MgSO_4$) 1.5 gr/hr. At the end of surgery the continuous intravenous infusion with lidocaine and magnesium sulfate was stopped while the abdominal wall was closed and 2.5 g of metamizole (novalgetol) was given intravenously. The operation lasted for 2 hours. The residual neuromuscular blockade was antagonized with neostigmine (prostigmin) 0.05 mg/kg and atropine 0.02 mg/kg, and when the patient had regular breathing, tracheal extubation was performed. The patient was immediately transferred to the Post Anaesthesia Care Unit (PACU) with no complain of pain in the immediate post-operative period. In PACU was followed the VAS score at rest and at coughing. If the VAS score is above 4, 1 gr of paracetamol will be given, and if the VAS score is above 7, 100 mg of tramadol will be given. VAS score 2 hours after surgery was 6/10 and 1 gr of paracetamol was given and the patient was transferred to the Department. Over the next 3 days, the patient had a VAS score of 4-6 / 10 and only received paracetamol 3x1g and novalgetol 3x1 gr daily, every four hours. Tramadol was not given during the post-operative period.

## DISCUSSION

Opioid Free Anaesthesia (OFA) is defined as an anaesthetic technique in which opioids are not used in the intra-operative period (not systemic, neuroaxial or intracavitary). It is a new approach to general anaesthesia in which opioids are replaced with non-opioid analgesics in the intra- and post-operative period. Opioids are ideal drugs to block the sympathetic response to surgical pain [1]. Multimodal analgesia is consisted of administration of local anaesthetic and other drugs systemic, in order to use the synergistic effect among these drugs, thereby reducing the possibility of occurrence of adverse effects [1, 2].

Currently, the opioids are the basis of intra-operative pain management. The use of opioids however is effective it can result in numerous intra-operative and post-operative side effects. These side effects are one of the main reasons why opioids are not included or minimized in ERAS (Enhanced Recovery After Surgery) protocols [3]. Patients treated with opioids had prolonged hospital stay and increased hospital costs [4]. The most common complications or side effects of the use of opioids are: delayed healing, somnolence, dizziness, ileus, nausea and vomiting, respiratory depression, weakness of pharyngeal muscle (and thus breathing problems), itching, urinary retention, tolerance from desensitization, reduced cardiac output, short central muscle stiffness. Opioids can lead to acute tolerance, which means that the more opioids are given intra-operatively, the more is the need for opioids for reduction of postoperative pain. Also, opioids lead to hyperalgesia, which is defined as an increased response to a painful stimulus, which is caused by exposure to opioids leading to a state of nociceptive hypersensitization. It is a phenomenon that can be seen in patients treated with opioids and they have increased susceptibility to the nociceptive (painful) stimuli [5]. Evidence now is showing that opioid-induced immune system suppression may affect the outcome of the operation, including the increased risk of infection and the increased risk of metastasis in the cancer population [6].

Anaphylaxis caused by using opioids (fentanyl) is a very rare occurrence, which is manifested by hypotension and urticaria [7].

In the past, the opioids were ideal drugs that blocked the sympathetic response to surgical pain. Today there are other drugs available for this purpose. A direct central or peripheral sympathetic block can be achieved using α-2 agonists (clonidine and dexmedetomidine) and β-blockers [8, 9, 10]. Indirect sympathetic block can be achieved by using calcium blockers, lidocaine, magnesium sulfate and inhaled anaesthetics [11, 12]. Multimodal treatment of pain is the best way to reduce opioid consumption [8, 13]. Intra-operative use of multimodal non-opioid analgesics allows pre-emptive blocking of receptors in the complex pain pathways, both centrally and peripherally. Stable anaesthesia can be achieved by using a multimodal approach of sympathicolytic drugs and non-opioid analgesics [8].

The pre-emptive pain control is an issue that has been resolved in recent years. If the analgesics are given regionally or systemically before the onset of the surgical procedure (which prevents the central sensitization of the pain pathways), all of these leads to a decrease in the amount of given analgesics and to a decrease in the need for analgesics [14].

Paracetamol is a centrally acting drug, which inhibits the prostaglandins and cyclooxygenase synthesis (COX) in the nervous system. Pathways that are based on the spinal serotonergic mechanism of action of other central mechanisms may be involved in the mechanism of action of paracetamol. In clinical practice, paracetamol does not cause side effects that are typical of other non-steroidal anti-inflammatory drugs (NSAIDs) that occur due to inhibition of peripheral COX-1 (gastric bleeding and anti-platelet activity). Paracetamol given intravenously at a dose of 1 gr has analgesic activity in moderately severe postoperative pain similar to that of 30 mg ketorolac, 75 mg diclofenac and 10 mg of morphine [15].

Dexamethasone (dexasone) is a strong corticosteroid without mineralocorticoid effects. It is recognized as effective anti-emetics if given at a dose of 50 μg / kg in an anaesthetic introduction. For doses higher than 100 μg / kg, it was found that they further reduced the need for analgesics in the postoperative period [16, 17]. It has been shown to have reduced pain scores, as well as reduced postoperative nausea and vomiting, even up to 24 hours in the postoperative period. This can be explained by its anti-inflammatory effect on the wound itself, with less edema leading to less pain [1].

Ketamine hydrochloride (ketamine) is the only intravenous anaesthetic with analgesic properties. It is an in-competitive NMDA-glutamate receptor antagonist, preventing the release of potassium from the cell, thereby blocking depolarization and transmission of the pain impulse [18]. It has been shown that the single preoperative dose of ketamine reduces opioid needs and VAS pain scores in the first 24 hours in the postoperative period [19]. Ketamine in a small dose of 0.1-0.2 mg / kg has been shown to have an opioid sparing effect [20].

Lidocaine hydrochloride (lidocaine) is an amide local anaesthetic and as a blocker of sodium channels in the neural cascade given intravenously provides a great reduction in pain. It has an analgesic, anti-hyperalgetic and anti-inflammatory effect [20]. Peri-operative infusions with lidocaine are associated with better postopera-

tive control of resting pain, coughing and up to 6 hours movement. Lidocaine reduces the need for opioids by reducing the side effects of opioids. Faster return of the intestinal function (faster than 24 hours), the reduction in postoperative nausea and vomiting, and the reduction of days of hospital stay show significant benefits after abdominal surgery [12, 21]. Lidocaine can be given as a bolus dose of 1-2 mg / kg with a continuous infusion of 1-2 mg / kg / hr [13].

Magnesium sulfate acts as an in-competitive NMDA-glutamate receptor antagonist. Pain impulses activate the NMDA receptors causing Ca++ to enter the cell and trigger central sensitization [22]. Magnesium blocks NMDA receptors by blocking the entrance of Ca++ and Na++ into the cell (ketamine receptors prevent the release of K+), thereby preventing depolarization and transmission of the pain impulse [23]. In one study, low pain scores were reported in the first 48 hours, the intra-operative need for neuromuscular blockers was reduced, and also was reduced postoperative nausea and vomiting [24]. Magnesium can be given in premedication with bolus doses of 3-4 gr for 5 minutes and then can be continuited with a dose of 1-2 g/hr as a continuous infusion.

The multimodal anaesthetic approach may include other drugs such as α-2 agonists (clonidine and dexmedetomidine), β-blockers (esmolol), gabapentinoids (gabapentin and pregabalin).

Opioid free anaesthesia (OFA) is already a reality in many places in the world and in some countries it is already used in a routine practice. A recent presentation of the Meeting of the American Association of Anesthesiologists (ASA) in New Orleans suggests using a postoperative infusion with ketamine hydrochloride 100mg + dexmedetomidine 100 μg + lidocaine hydrochloride 100 mg + magnesium sulfate 5 g in 1 L saline and via PSA (patient controlled analgesia) pump or infusion pump to flow to 12 ml/hr (no clinically controlled boluses or boluses given by the patient are allowed) [25]. In Bruges (Belgium) the use of anaesthesia and analgesia without opioids (OFA) increased patient satisfaction with less pain in the postoperative period, better sleep in the first postoperative night and decreased opioid-related side effects [1].

Various drugs and techniques are used as a part of multimodal analgesia in order to improve the treatment of pain and reduce the consumption of opioids and opioid-related adverse effects [26]. The concept of multimodal balanced analgesia is consisted of providing several different analgesics to alter the pathophysiological process involved in nociception and thus to obtain more effective intra-operative analgesia with less side effects [8].

## CONCLUSION

Opioid free anaesthesia (OFA) represents the avoidance of opioids in the treatment of pre-, intra- and postoperative pain in an attempt to reduce opioid-related complications without compromising the patient's comfort. Another important benefit of this type of anaesthesia is the prevention of opioid-induced hyperalgesia, which results in increased pain and therefore requires use of a higher dose of opioids for adequate pain control.

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**Резиме**

## НЕОПИЈАТНА АНЕСТЕЗИЈА (OPIOID FREE ANESTHESIA) ЗА ЛАПАРОТОМИСКА ХЕМИКОЛЕКТОМИЈА: ПРИКАЗ НА СЛУЧАЈ

**Марија Толеска [1], Билјана Кузмановска[1], Андријан Карталов[1], Мирјана Шошолчева[2], Јасминка Нанчева[3], Александар Димитровски[1], Наташа Толеска[4]**

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Неопијатната анестезија (opioid free anesthesia-OFA) се дефинира како анестезиолошка техника во која не се користат опијати во интраоперативниот период (системски, невроаксијално или интракавитарно). Анафилаксата предизвикана од опијати (fentanyl) е многу ретка појава, која се манифестира со хипотензија и уртикарија. Кога имаме докажана алергија на fentanyl, одбивање од страна на пациентот за поставување епидурален катетер за аналгезија и одбивање за двостран transversus abdominis plane block (TAPB) воден под ултразвук, мора да се размислува за користење мултимодална неопијатна анестезија. Концептот на мултимодална балансирана аналгезија се состои од давање неколку различни аналгетици за да се измени патофизиолошкиот процес што е вклучен во ноцицепцијата и на тој начин да се добие поефективна интраоперативна аналгезија со помалку несакани ефекти. Прикажан е случај на 60-годишен маж предвиден за лапаротомиска хемиколектомија, со претходно докажана алергија на fentanyl. Одлучивме да му дадеме неопијатна анестезија. Пред воведот во анестезијата пациентот прими dexamethasone (dexasone) 0,1 mg/kg и paracetamol 1 gr интравенски. Пациентот беше воведен во општа ендотрахеална анестезија според стандардизиран протокол со midazolam 0,04 mg/kg, lidocaine 1 mg/kg, propofol 2 mg/kg и rocuronium bromide 0,6 mg/kg. Анестезијата се одржуваше со инхалациски анестетик sevoflurane со вредност на MAC 1, со цел да се одржува вредноста на средниот артериски притисок (MAP) +/- 20 % од првичната вредност. По ендотрахеалната интубација, на пациентот му дадовме ketamine 0,5 mg/kg (или 50 mg ketamine) интравенски во болус и континуирана интравенска инфузија со lidocaine 2 mg/kg/hr и magnesium sulfate ($MgSO_4$) 1,5 gr/hr. На крајот на операцијата ја прекинавме континуираната инфузија со lidocaine и magnesium sulphate, додека хирургот го затвораше абдоминалниот sид, и аплициравме интравенски 2,5 gr metamizole (новалгетол). Пациентот беше префрлен во собата за будење и не се пожали на никаква болка во раниот постоперативен период. Визуелната аналогна скала за болка, односно BAC-скорот за болка два часа по операцијата беше 6/10. Дадовме 1 g paracetamol и пациентот го пративме на оддел. Следните три дена пациентот имаше BAC-скор 4-6/10 и примаше paracetamol 3x1 g и novalgetol 3x1 g дневно на секои четири часа.

**Клучни зборови**: неопијатна анестезија, мултимодална аналгезија, лапаротомиска хемиколектомија