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IS OPIOID-FREE GENERAL ANESTHESIA MORE SUPERIOR FOR POSTOPERATIVE PAIN VERSUS OPIOID GENERAL ANESTHESIA IN LAPAROSCOPIC CHOLECYSTECTOMY?

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ABSTRACT

Introduction: Opioid-free anesthesia (OFA) is a new anesthesiological technique, where the giving of opioids (fentanyl) is avoided in the intra- and post-operative period. This leads to reduction in the opioid-related side effects and lower pain scores in the postoperative period.

Materials and methods: In this randomized, single-blind clinical study, 60 patients scheduled for elective laparoscopic cholecystectomy were enrolled . Half of them (30 patients) received general balanced anesthesia with fentanyl (F group-FG), and the half received opioid-free general anesthesia (OFA group-OFAG). In the post-operative period, Visual Analogue Scale (VAS) scores were followed at rest and when coughing 1 hour, 4 hrs, 8 hrs, 12 and 24 hrs after surgery. Both groups were followed by opioid requirements in the postoperative period.

Results: In the postoperative period, patients in the fentanyl group (FG) have higher pain scores at rest and on coughing in all analyzed timeframes compared to patients from the OFA group, but statistically significant difference was approved 1 and 24 hours after surgery. In the OFA group 24 hours after surgery none of the patients reported pain at rest and when coughing number 7, 8, 9 and 10 according to the VAS pain score. The total opioid requirement in the postoperative period was significantly higher in the fentanyl group (FG) at rest and when coughing, compared to the OFA group.

Conclusion: Opioid-free anesthesia as a part of multimodal analgesia and a new anesthesiology technique is a safe procedure, where opioid-related negative effects in patients undergoing elective laparoscopic cholecystectomy are avoided..

Keywords: opioid-free anesthesia, fentanyl, laparoscopic cholecystectomy, pain

INTRODUCTION

Opioid-free anesthesia is an anesthetic technique where opioids are not used in the intra-operative period (neither systematic, nor neuroaxially or intracavitary). In this type of anesthesia, opioids can be also avoided in the postoperative period, thereby the number of opioid-related adverse effects will be reduced, too. Opioids are still one of the major drugs that general anesthesia is based on. Also, they are essential in pain treatment in the intra- and postoperative period. However effective these drugs are, they are associated with numerous side effects: somnolence, dizziness, constipation, nausea and

vomiting, respiratory depression, itching, urinary retention, short muscular stiffness, weak pharyngeal musculature (hence breathing problems). Other side effects from the opioid use are hyperalgesia and opioid tolerance [1]. Hyperalgesia is defined as an increased response to painful stimuli, caused by exposure to the opioids. If we give more opioids in the intra-operative period, the more opioids will be needed in the postoperative period. This is called opioid tolerance. Patients who receive higher doses of fentanyl during surgery are continuously requiring higher doses of opioids in the postoperative period, compared with patients who receive lower doses of opioids [2]. Multimodal pain treatment has been shown to be the best way to reduce opioid consumption. Multimodal analgesia involves the use of sympatholytic drugs and nonopioide analgesics. These drugs can reduce or avoid the use of opioids in the postoperative period [3]. As a non-opioide analgesics, which can be given intravenously in the intra-operative period, are: alpha-2 agonists (clonidine and dexmedetomidine), beta blockers (esmolol), gabapentinoids (gabapentine and pregabaline), lidocaine (lidocaine hydrochloride), magnesium (magnesium sulfate), ketamine and dexasone (dexamethasone). It has been shown that all these drugs with their analgesic effect if given together are changing the pathophysiologic process that is involved in nociception. In that way, more effective intra-operative analgesia with fewer side effects is obtained [4]. This multimodal approach allows reduction of the dose of each individual drug, to exploit the synergistic effect among drugs, thereby reducing the side effects of the drugs. Although laparoscopic cholecystectomy is a minimally invasive surgical technique, some patients have significant discomfort in the first 24 to 72 hours in the postoperative period [5]. The pain on the day of surgery is diffuse abdominal pain, more expressed in the right upper quadrant and right shoulder. Several methods have been described that would reduce pain in the postoperative period such as: giving a local anesthetic at the site of the troacar, intraperitoneal injection of a local anesthetic, intermittent administration of non-steroidal anti-inflammatory drugs (NSAIDs) and opioids, pressure reduction in pneumoperitoneum and reducing the number of operating ports.

The aim of this study is to determine the effect of opioid-free versus opioid general anesthesia on postoperative pain in patients scheduled for elective laparoscopic cholecystectomy and to determine the overall need for opioids in the postoperative period in both groups.

MATERIALS AND METHODS

This is a prospective, randomized, single-blind clinical study where 60 patients scheduled for elective laparoscopic cholecystectomy are included. The study was prepared with the approval of the Ethical Committee for Clinical Research. Randomization of patients was done by selecting one envelope from 2 offered envelopes. Inside the envelope the group to which the patient belongs is written (fentanyl or opioid-free anesthesia group), and hence which drugs will be used during the anesthesia. Inclusion criteria for the study were: patients who were hospitalized for elective laparoscopic cholecystectomy between the ages of 25 and 60 with American Association of Anesthesiologists (ASA) classification 1, 2 and 3. Exclusion criteria for participating to this study were: patients with ASA classification 4 and 5, allergy to opioids (fentanyl and tramadol), lidocaine, magnesium, ketamine, paracetamol, ketonal and metamizole; patients who chronically use benzodiazepines or opioids; patients who are pregnant or are breastfeeding; patients with chronic pain; patients with cardiac, renal and hepatic failure; patients with diabetes and psychiatric illness. Also, patients from the OFA group will be excluded from the study if during the surgery they have a sympathetic response to pain by increasing blood pressure and heart rate more than 20% from the initial value, without any blood loss and if the patient is sweating during surgery. In this occasion, opioids will be given in the intra-operative period, and the patient will be excluded from the OFA group. In the preoperative visit the Visual Analogue Scale for Pain (VAS score) from 0 to 10 was explained to the patients, where the number 0 means absence of pain, and the number 10 indicates the greatest imaginable pain.

Each patient was placed on continuous haemodynamic monitoring (Datex-Ohmeda S/5 Avance 1009-9002-000, Helsinki Finland): electrocardiographic record (ECG), heart rate, measurement of non-invasive blood pressure every 5 minutes, oxygen saturation from pulse oximetry, capnography (measurement of the concentration of CO2 in the terminal expiratory air) and fraction of inspired oxygen. Patients from the OFA group (OFAG) before induction to general anesthesia received dexasone (dexamethasone) 0.1 mg/kg and 1 g paracetamol intravenously (i.v.) as a preemptive analgesia. The induction to general endotracheal anesthesia was followed by administration of midazolam 0.04 mg/kg, lidocaine 1 mg/kg, propofol 2 mg/kg and rocuronium bromide 0.6 mg/kg. After tracheal

intubation, ketamine 0.5 mg/kg was given and intravenous continuous infusion with lidocaine 2 mg/kg/hr and magnesium sulphate 1.5 g/hr was started. Patients from the Fentanyl group (FG) were introduced into general endotracheal anesthesia with midazolam 0.04 mg/kg, opioid (fentanyl) 0.002 mg/kg, propofol 2 mg/kg and rocuronium bromide 0.6 mg/kg. All patients were mechanically ventilated with ventilation mode PVC-VG, with a volume of 6-8 ml/kg and mixture of gases in proportion 50% oxygen and 50% air, with respiratory rate adapted according to EtCO2 to range between 35-45 mmHg, PEEP 5 cm H2O. Anesthesia was maintained with volatile anesthetic (sevoflurane) 0.7-1 MAC, in order to maintain mean arterial pressure (MAP) +/- 20% of the baseline value. During laparoscopy intra-abdominal pressure was adjusted to 12 mmHg by continuous CO2 insufflation. During the surgery, patients from Fentanyl group received fractionated bolus doses of fentanyl. After removal of the gallbladder, continuous i.v. infusion with lidocaine and magnesium sulphate was stopped in OFA group and 2.5 g metamizole was given intravenously. The residual neuromuscular blockade was antagonized with prostigmine 0.05 mg/kg and atropine 0.02 mg/kg, and when the patient had regular spontaneous breathing, tracheal extubation was performed. Then patients were transported to the Post-Anesthesiological Care Unit (PACU) and their heart rate and oxygen saturation from pulse oxymetry were monitored. In PACU the VAS score of pain at rest and when coughing was followed; if the VAS score was 4, 5 or 6, 100 mg of the ketoprofen was given, and if the VAS score was 7, 8, 9 or 10, 100 mg of trodon was given. Apart from the intensity of pain, the occurrence of nausea and vomiting in the postoperative period was followed also, and if necessary 4 mg of odansetron was given. The first analysis was carried out 1 hour after surgery, in the PACU. After that, the patients were sent to the Department of Digestive Surgery where further analysis was performed. The second analysis was 4 hours after surgery, the third analysis-8 hours after surgery, the fourth-12 hours after surgery, and the fifth analysis was 24 hours after surgery.

RESULTS

In this study 60 patients were enrolled. Half of them (30 patients) received general anesthesia with fentanyl (Fentanyl group-FG), and half of them (30 patients) received opioid-free general anesthesia (Opioid-free anesthesia group – OFAG).

In terms of statistical analysis, the processing of data was made in the statistical program SPSS for windows 17.0. Quantitative data are displayed with average and standard deviation, qualitative with absolute and relative numbers. For comparison of both groups, the parametric Student t-test and non-parametric tests (Chi-square test, Mann-Whitney test) were used. The value of $p < 0.05$ was statistically significant.

The two groups of patients were homogeneous in terms of age; the average age of participants in the Fentanyl group (FG) was 52.9 ± 11.9 years, while the participants if the Opioid-free anesthesia group (OFAG) were 48.7 ± 9.8 years ($t = 1.5$ $p = 0.13$).

The two groups were homogeneous in terms of gender structure, with dominant participation in female subjects, 24 (80%) in the Fentanyl group (FG), and 20 (66.7%) in the opioid-free anesthesia group (OFAG) (Chi-square: 1.4, df = 1, p = 0,24).

An analysis of the comparison of the two groups according to VAS pain score in the first 24 hours postoperatively at rest showed that patients in the Fentanyl group (FG) at all analyzed time points had higher VAS scores, compared to patients from the Opioid-free anesthesia group (OFAG), but statistically significant difference was confirmed during the first hour after the surgery (p = 0.003), and 24 hours after the intervention (p = 0.002) (Table 1).

Table 1: *Distribution of the pain scores at rest during the study*

AT REST				
		VAS score		
time	Groups	mean ± SD	median (Q25 -Q75)	p-level
1 hour	FG	5.13 ± 2.7	5 (4-7)	Z = 2.929 p = 0.003 sig
	OFAG	3.27 ± 1.7	3 (2-5)	
4 hours	FG	3.87 ± 2.6	4 (2-6)	Z = 1.602 p = 0.11 ns
	OFAG	3.0 ± 1.7	3 (2-4)	
8 hours	FG	3.93 ± 2.6	4 (2-6)	Z = 1.739 p = 0.08 ns
	OFAG	2.90 ± 1.9	3 (2-4)	
12 hours	FG	2.63 ± 2.2	2 (1-4)	Z = 0.031 p = 0.97 ns
	OFAG	2.50 ± 1.9	2 (1-3)	
24 hours	FG	3.67 ± 2.3	4 (2-5)	Z = 3.049 p = 0.002 sig
	OFAG	1.90 ± 1.7	2 (0-3)	

The first hour postoperatively, the most of the patient from the Fentanyl group (FG) rated the intensity of pain with VAS score 5 (8 patients), while in the Opioid-free anesthesia group (OFAG)

the most common VAS pain score was 5 and 3 (7 patients).

The first day postoperatively (24 hours after the operation), the most common VAS score in the Fentanyl group (FG) was 4 (9 patients), while in the Opioid-free anesthesia group (OFAG) the most of the patients reported that they had no pain (9 patients). In the opioid-free anesthesia group (OFAG) 24 hours after the surgery none from the patients reported pain of 7, 8, 9 and 10 according to VAS pain score (Table 2).

hours) after the operation (p = 0.002, p = 0.004). In the remaining analyzed time points, when coughing, patients from the Fentanyl group (FG) had no-significantly higher scores on the VAS score scale, compared to patients from the Opioid-free anesthesia group (OFA) (Table 3).

In the first hour postoperatively in the Fentanyl group (FG) the most of the patients (9 patients) reported pain when coughing with VAS score 5, while in the Opioid-free anesthesia group (OFAG) the most common VAS pain score when coughing was 2 (in 11 patients).

Table 2: *The level of pain (VAS scores) reported by the patients (N) at rest*

AT REST										
VAS score	1 hour		4 hours		8 hours		12 hours		24 hours	
	FG	OFAG	FG	OFAG	FG	OFAG	FG	OFAG	FG	OFAG
0	2	2	5	3	5	3	6	5	4	9
1	0	2	0	1	0	4	2	3	1	4
2	3	6	4	5	5	6	9	8	5	8
3	1	7	4	13	3	7	5	8	1	3
4	6	4	5	5	3	5	4	2	9	3
5	8	7	4	1	5	3	0	2	6	2
6	1	2	4	0	5	1	0	1	2	1
7	2	0	2	1	2	0	4	0	0	0
8	4	0	1	1	1	0	0	1	1	0
9	1	0	0	0	0	1	0	0	0	0
10	2	0	1	0	1	0	0	0	1	0

Table 3: *Distribution of the pain scores when coughing during the study*

WHEN COUGHING				
time	Groups	VAS score		p-level
		mean ± SD	median (Q25 - Q75)	
1 hour	FG	6.03 ± 2.5	0 – 10	Z = 3.046 p = 0.002 sig
	OFAG	4.17 ± 1.5	2 – 6	
4 hours	FG	4.87 ± 2.6	0 – 10	Z = 1. 811 p = 0.0 7 ns
	OFAG	3.93 ± 1.8	1 – 8	
8 hours	FG	4.87 ± 2.7	0 – 10	Z = 1. 412 p = 0. 1 6 ns
	OFAG	4.07 ± 2.03	1 – 10	
12 hours	FG	3.70 ± 2.6	0 – 10	Z = 0. 399 p = 0. 6 9 ns
	OFAG	3.40 ± 1.7	0 – 8	
24 hours	FG	4.57 ± 2.5	0 – 9	Z = 2.905 p = 0.004 sig
	OFAG	2.67 ± 1.9	0 – 6	

Statistically significant higher scores on VAS scale when coughing were observed in the Fentanyl group (FG) compared to Opioid-free anesthesia group (OFAG), the first hour and the first day (24

The first day postoperatively, the most common VAS pain score when coughing in the Fentanyl group (FG) was 6 (7 patients), while in the Opioid-free anesthesia group (OFAG) the most of the patients reported pain when coughing by number 3 (10 patients). Also when coughing, in OFAG 24 hours after the surgery none of the patients experienced pain with severity 7, 8, 9, and 10 on the VAS pain score (Table 4).

Table 4: *The level of pain (VAS scores) reported by the patients (N) when coughing*

	WHEN COUGHNING									
VAS	1 hour		4 hours		8 hours		12 hours		24 hours	
	FG	OFAG	FG	OFAG	FG	OFAG	FG	OFAG	FG	OFAG
0	1	0	3	0	3	0	4	1	3	6
1	0	3	0	1	0	1	0	1	1	2
2	5	11	1	3	2	7	5	7	2	5
3	0	3	5	13	6	6	7	12	5	10
4	6	4	5	4	2	4	6	1	1	1
5	9	9	4	4	4	5	4	3	6	2
6	0	0	4	2	5	5	0	4	7	4
7	0	0	3	0	3	0	0	0	1	0
8	3	0	3	3	2	1	1	1	2	0
9	2	0	0	0	1	0	2	0	2	0
10	4	0	2	0	2	1	1	0	0	0

DISCUSSION

Pain is an important factor in the post-operative period in surgical patients and may lead to unwanted prolonged post-operative recovery, increased use of opioids in the post-operative period, prolonged hospital stay, and patient dissatisfaction. Even 75% of all surgical patients reported having had inadequate treatment of pain in the postoperative period, while they were in hospital [6]. The use of opioids in intra- and postoperative period is a standard anesthetic procedure, but more side effects are recorded from the use of opioids in the post-operative period as the occurrence of nausea and vomiting, respiratory depression, itching and sedation. The use of a large dose of opioids can cause acute tolerance and hyperalgesia, which further leads to worsening of the pain control [7]. Because of these side effects, opioids are not included or are minimized in Enhanced Recovery After Surgery protocols (ERAS protocols) [8]. As a result, the model of multimodal balanced anesthesia by using non-opioid drugs has been introduced, in order to reduce the giving of opioids in the postoperative period and to avoid opioid-related unwanted effects. The multimodal approach of intra-operative analgesia more drugs are included: alpha-2 agonists, lidocaine, magnesium sulfate, ketamine and dexamethasone. Lidocaine is a local anesthetic that has analgesic, anti-hyperalgesic, and anti-inflammatory effects. The continuous infusion of lidocaine in the intra-operative period leads to a reduced need for opioids, decreased postoperative nausea and vomiting, faster return of intestinal function, and a shortening of hospital stay [9]. Magnesium sulfate is an antagonist of N-methyl D-aspartate (NMDA) receptors, blocking the entry of calcium and sodium into the cell and thereby preventing the transmission of pain. Using magnesium in the intra-operative period leads to reducing the pain, nausea and vomiting in the post-operative period [10]. Ketamine is also an antagonist of the NMDA receptors, by blocking the release of potassium from the cell and thus prevents the transmission of painful impulses. Preemptive giving of ketamine has shown an opioid sparing effect in the intra-operative period and decreased need of opioids in the postoperative period [11]. Dexamethasone is a corticosteroid well-known for its antiemetic effect. Its anti-inflammatory effect on the wound with less creating of edema leads to less pain. This drug has the effect of saving the opioids, leading to reduced pain score at rest and during movement and it reduces PONV [12]. The purpose of all these

drugs given together in a non-toxic dose in the intra-operative period is to improve the treatment of pain, to reduce giving of opioids in the intra- and postoperative period, to reduce PONV, to shorten hospital stay and to have satisfied patients.

In our study it has been shown that in the postoperative period patients from the Fentanyl group (FG) at all analyzed time points have higher pain scores at rest compared to patients from the Opioid-free anesthesia group (OFAG), but statistically significant difference was confirmed during the first hour after the surgery ($p = 0.003$), and 24 hours after the surgery ($p = 0.002$). In the OFAG 24 hours after the surgery none of the patients felt pain at rest, according to the VAS pain score of 7, 8, 9 and 10. When coughing statistically significant higher VAS pain scores in the Fentanyl group (FG) were registered, compared to OFAG, in the first hour and 24 hours after the surgery ($p=0.002$, $p=0.004$). In the OFAG when coughing 24 hours after the surgery none of the patients felt pain by intensity of 7, 8, 9 and 10 on the VAS pain score. The total need for opioids in the postoperative period was significantly greater in FG at rest and when coughing, compared to the OFA group. It was also noted that patients from the OFA group after surgery are waking up without pain, do not complain about nausea and vomiting and have a brighter look. In contrast, patients from the Fentanyl group wake up with complaints that they have pain, have nausea and vomiting and respiratory depression (make long breathing pause). No side effects were observed in patients from both groups during the postoperative period.

Opioid-free anesthesia can be used as a reliable anesthesiological technique in patients scheduled for laparoscopic cholecystectomy as a one day outpatient (ambulatory) surgery.

REFERENCES

1. Velayudhan A, Bellingham G, Morley-Forster P. Opioid-induced hyperalgesia. Continuing education in Anaesthesia Critical Care & Pain 2014; 14(3): 125–129.
2. Chia Y, Liu K, Wang JJ, Kuo MC, Ho ST. Intraoperative high-dose fentanyl induces postoperative fentanyl tolerance. Can J Anesth 1999: 46 (9); 872.
3. Mulier J. P. Why and how to give opioid free anaesthesia (OFA). The Bruges approach. American Society of Anesthesiologists Annual Meeting, New Orleans 2016 .
4. White PF. The role of non-opioid analgesic techniques in the management of pain after ambulatory surgery. Anesthe Analg 2002; 94 (3): 577–85.
5. Alam MS, Hoque HW, Saifullah M, Ali MO. Port site and intraperitoneal infiltration of local anesthetics in the reduction of postoperative pain after laparoscopic cholecystectomy. Med Today 2009; 22: 24–28.
6. Harless M, Depp C, Collins S, Hewer I. Role of Esmolol and Perioperative Analgesia and Anesthesia: A Literature Review. AANA journal. 2015; 83 (3): 167–77.
7. Ramaswamy S, Wilson JA, Colvin L. Non-opioid-based adjuvant analgesia in perioperative care. Continuing Education in Anaesthesia, Critical Care & Pain. 2013; 13(5): 152–157.
8. Hameurlaine S, De Kock M. Should opioid free anesthesia be integrated in enhanced recovery protocols? Acta Anaesth Belg 2018; 69(2): 77–83.
9. Bakan M, Umutoglu T, Topuz U, Uysal H, Bayram M, Kadioglu H, Salihoglu Z. Opioid-free total intravenous anesthesia with propofol, dexmedetomidine and lidocaine infusions for laparoscopic cholecystectomy: a prospective, randomized, double-blinded study. Rev Bras Anestesiol 2015; 65 (3): 191–9.
10. Ryu JH, Kang MH, KS Park, Do SH. Effects of magnesium sulphate on intraoperative anaesthetic requirements and postoperative analgesia in gynaecology patients receiving total intravenous anaesthesia. Br J Anaesth 2008; 100 (3): 397–403.
11. Fu ES, Miguel R., Scharf JE. Preemptive ketamine decreases postoperative narcotic requirements in patients undergoing abdominal surgery. Anesthe Analg 1997; 84 (5): 1086–90.
12. De Oliveira GS, Almeida MD, Benzon HT, McCarthy RJ. Perioperative Single Dose Dexamethasone Systemic for Postoperative pain: A Meta-analysis of Randomized Controlled Trials. The Journal of the American Society of Anesthesiologists 2011; 115 (3): 575–88.

Резиме

ДАЛИ НЕОПИОИДНАТА ОПШТА АНЕСТЕЗИЈА Е ПОСУПЕРИОРНА ЗА ПОСТОПЕРАТИВНАТА БОЛКА НАСПРОТИ ОПИОИДНАТА ОПШТА АНЕСТЕЗИЈА КАЈ ЛАПАРОСКОПСКИТЕ ОПЕРАЦИИ НА ЖОЛЧНОТО ЌЕСЕ

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Вовед: Неопиоидната анестезија е нова анестезиолошка техника, каде што се избегнува давањето на опиоиди (фентанил) во интра- и постоперативниот период. Тоа води до намалување на несаканите ефекти на опиоидите, а со тоа и до пониски скорови на болка во периодот по операцијата.

Материјали и методи: Во оваа рандомизирана, едностранo слепа клиничка студија беа вклучени 60 пациенти, предвидени за елективни лапароскопски операции на жолчно ќесе. Од нив 30 пациенти добија општа балансирана анестезија со фентанил (опиоидна група), а другата половина пациенти доби општа балансирана анестезија со неопиоидни лекови (неопиоидна група). Кај сите 60 пациенти во постоперативниот период се следеше Визуелната аналогна скала (ВАС), скала за болка при мирување и при кашлање 1 час, 4 часа, 8 часа, 12 и 24 часа по операција. Исто така, се следеше вкупната потреба за опиоиди во постоперативниот период кај двете групи пациенти.

Резултати: Во постоперативниот период пациентите од фентанилската (опиоидна) група во сите анализирани временски точки имаа повисоки скорови на болка при мирување и при кашлање во однос на пациентите од неопиоидната група, но статистички сигнификантна разлика беше потврдена првиот час по интервенцијата и 24 часа по интервенцијата. Во неопиоидната група и при мирување и при кашлање, 24 часа по интервенцијата немаше пациенти што чувствувале болка со сила од 7, 8, 9 и 10 според ВАС скалата. Вкупната потреба за опиоиди во постоперативниот период беше значително поголема кај опиоидната група и при мирување и при кашлање, споредено со неопиоидната група.

Заклучок: Неопиоидната анестезија како дел од мултимодалната аналгезија и како нова анестезиолошка техника е сигурен метод со кој се избегнуваат несаканите ефекти предизвикани од употребата на опиоиди кај пациенти што се предвидени за елективни лапароскопски операции на жолчното ќесе.

Клучни зборови: неопиоидна анестезија, фентанил, лапароскопска холецистектомија, болка