(p) ISSN Print: 2348-6805

Assessment of Opioid-free anaesthesia for laparoscopic surgeries

Aradhana Prasad

Assistant Professor, Department of Anesthesiology, FH Medical College, Etmadpur, Agra, Uttar Pradesh, India

ABSTRACT:

Aim: Assessment of Opioid-free anaesthesia for laparoscopic surgeries. Material and methods: The study included a total of 100 patients, of which 50 patients were assigned to the opioid-sparing anaesthesia group (Group A), and the remaining 50 patients were assigned to the conventional opioid-based anaesthesia group (Group B). Convenience sampling was used, and the study enrolled 100 patients (Group B). The primary objective was to compare the pain scores in the post-operative period using the VAS for 24 hours, and the secondary objectives were to compare intra-operative haemodynamic parameters, duration of postoperative analgesia (defined as the time from completion of erector spinae plane block (ESPB) postinduction till the first analgesic requirement as indicated by VAS >5), and total analgesics consumed in the first 24 hours. Results: The VAS score for pain comparison during rest and movement was substantially greater in the conventional group at 0 h, 2 h, 4 h, 6 h, and 24 h postoperatively than in the opioid free anaesthetic group. In the group that had anaesthesia that did not include the use of opioids, around 22% of patients did not need the use of any analgesics in the post-operative phase within the first 24 hours. Both groups reported significantly different levels of total postoperative analgesic usage, however. In the conventional group, approximately 70% of patients required one dose of paracetamol (1 g), and 30% required one dose of paracetamol along with opioid (tramadol 50 mg) in view of severe pain as assessed by VAS (score > 5). In contrast, in the opioid free anaesthesia group, 64% of patients required one dose of paracetamol (1 g), and 14% required two doses of paracetamol (total 2 g) at an interval of 8 to 12 In the clinical setting, the opioid-free anaesthesia group and the conventional group had hemodynamic values that were equivalent to one another. Conclusion: When compared to the routine conventional opioid anaesthesia, the integration of ESPB into an intravenous opioid-free analgesic regimen using lignocaine and magnesium provides better postoperative pain relief with lower VAS scores, increased duration of analgesia, and reduced opioid consumption.

Key words: Block, magnesium, opioid, postoperative pain

Corresponding Author: Aradhana Prasad, Assistant Professor, Department of Anesthesiology, FH Medical College, Etmadpur, Agra, Uttar Pradesh, India

This article may be cited as: Prasad A. Assessment of Opioid-free anaesthesia for laparoscopic surgeries. J Adv Med Dent Scie Res 2016;4(6):425-430.

INTRODUCTION

Even though laparoscopic procedures are thought to be generally painless and are linked to early recovery and a shorter length of time spent in the hospital, they may nevertheless cause extreme pain, particularly in the first four hours of the immediate post-operative period. [1] This might be due to the irritation of the peritoneum that was brought on by the pressures brought on by the insufflation of carbon dioxide, the manipulation of the colon by the surgeons, or the irritation brought on by the residual or retained blood. Opioids have traditionally been the primary method of analgesia used during the perioperative period. However, they are linked with a number of major adverse effects, including respiratory depression, muscular stiffness, physical dependency, tolerance, and addiction. [2] There are around 0.7% of people who report using opioids, and India has double the worldwide rate of illegal use due to drug addiction and dependency. [3] Acute surgical pain in the immediate post-operative period is a significant risk factor for the development of chronic pain, and controlling it is a key factor in reducing the risk of chronic post-operative pain. In addition, acute surgical pain is a risk factor for the development of chronic pain. [4] Anaesthesiologists have a vital role in

identifying patients who are at risk for long-term opioid usage. As a result, they are able to reduce the amount of opioids that are administered during surgery and lessen the associated adverse effects. [5] Despite the fact that opioid-free regimens have been researched in the past, there is a dearth of published material that includes regional anaesthesia and steers clear of the use of ketamine in such regimens. [6] The purpose of this study was to provide multimodal analgesia for post-operative pain relief using drugs other than opioids. These drugs included lignocaine, magnesium, and fascial plane blocks. The reduction of the need for opioids and the associated negative effects was the primary goal of this study. The primary purpose was to evaluate the difference in post-operative pain levels between the opioid-free anaesthesia approach and the opioid-based technique using the visual analogue scale (VAS).

MATERIAL AND METHODS

A tertiary care hospital served as the setting for this prospective research that did not include randomization. Informed agreement was gained from each patient after they were provided with a sheet that detailed the medicines that were administered, the fascial plane blocks that were done, and the postoperative analgesic effects of those drugs. Participants in the research ranged in age from 20 to 68 years old, and had to have a physical status of I or II as determined by the American Society of Anesthesiologists in order to have laparoscopic surgery. Participants were not allowed to take part in the study if they had a body mass index that was more than 35 kg/m2, a known allergy to local anaesthetic drugs, or hepatic and renal impairment. Both the transition to an open method and the maintenance of post-operative ventilation were taken into account as dropouts. Cholecystectomy, appendicectomy, and completely extraperitoneal inguinal hernia repair were the laparoscopic procedures that were carried out on the patient. Using power analysis and a report from an earlier research, we determined that a group size of fifty would be appropriate. [7] The study included a total of 100 patients, of which 50 patients were assigned to the opioid-sparing anaesthesia group (Group A), and the remaining 50 patients were assigned to the conventional opioid-based anaesthesia group (Group B). Convenience sampling was used, and the study enrolled 100 patients (Group B). The primary objective was to compare the pain scores in the post-operative period using the VAS for 24 hours, and the secondary objectives were to compare intraoperative haemodynamic parameters, duration of postoperative analgesia (defined as the time from completion of erector spinae plane block (ESPB) postinduction till the first analgesic requirement as indicated by VAS >5), and total analysics consumed in the first 24 hours.

Following the completion of the standard preoperative assessment, patients were brought into the operating theatre complex where their intravenous (IV) cannulas were examined to see whether or not they were allowing blood flow and whether or not they were patent. The pre-loading was performed using intravenous crystalloids at a rate of 10 mL/kg. In order to provide pre-emptive analgesia, intravenous dexamethasone 8 mg and intravenous paracetamol 15 mg/kg were administered. The following parameters were measured and recorded as part of the baseline assessment: heart rate, systolic and diastolic blood pressure; mean arterial pressure (MAP); oxygen saturation; respiratory rate; and end-tidal carbon dioxide monitoring. Anesthesia was induced intravenously with propofol at a dosage of 1 mg/kg, lignocaine at a dose of 1.5 mg/kg (bolus), and succinlycholine at a dose of 1.5 mg/kg after the patient was pre-oxygenated with 100% oxygen. After performing endotracheal intubation, cisatracurium at a dose of 0.2 mg/kg was given to the patient. The patient was kept under anaesthesia using nitrous oxide at a rate of 0.5 L/min, oxygen at a rate of 0.5 L/min, sevoflurane at a concentration of 1%, and cisatracurium was given in increasing dosages as required.

During the maintenance phase, the opioid-free anaesthesia group was given lidocaine at a rate of 1.5

mg/kg through infusion and magnesium at a rate of 2 g (bolus dosage) by a gradual intravenous injection. Both medications were administered simultaneously. After induction of anaesthesia, the patient was positioned in the lateral position for ESPB administration, which was accompanied by ultrasound guidance. The high-frequency linear probe "(sonosite-Fujifilm)" was used, and it was positioned longitudinally at the level of the T6 vertebra in a parasagittal orientation. The end of the rhomboid muscle served as the landmark for the location of the probe. [8] It was possible to see the tip of the transverse process of the relevant vertebra as well as the underlying pleura; the goal was to open up the plane between the erector spinae muscle and the transverse process. In order to make contact with the transverse process, the tip of the needle attached to the Stimuplex (B Braun) stimulator was advanced using an in-plane approach in a craniocaudal direction. In order to see the needle's location inside the erector spinae muscle, hydro dissection was performed. Following the verification, thirty millilitres of bupivacaine at a concentration of 0.25% was injected deeply into each of the muscles on both sides (total volume 60 mL).

All of the patients had their hemodynamic parameters, including their heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure, measured immediately before the induction as well as 5, 10, 15, 30, and 60 minutes following the induction. At the conclusion of the operation, the patient received an intravenous dose of 1 gramme of injectable paracetamol as a non-opioid painkiller. In the group that received traditional opioid-based anaesthesia, the induction procedure that was used was quite comparable. The intraoperative increase in blood pressure was kept stable by boluses of fentanyl at a dose of 0.5 micrograms per kilogramme. At the conclusion of the procedure, one gramme of paracetamol and four milligrammes of ondansetron were administered intravenously to each patient.

Pneumoperitoneum was performed on both of the groups, and the intra-abdominal pressure was maintained between 12 and 15 mm Hg throughout the procedure. End-tidal carbon dioxide levels were maintained at less than 35 mmHg throughout the experiment. In the past, each and every laparoscopic procedure required the creation of four ports, the largest of which was 10 millimetres and was located at the level of the xiphoid process, while the lowest port was situated at the level of the umbilicus (T6-T10). All patients were evaluated in the post anaesthesia care unit after extubation for their levels of discomfort, vital signs, and any adverse effects that may have occurred. Follow up scores and monitoring were done at 0, 2, 4, 6, 12, and 24 hours postoperatively. Rescue non opioid analgesic paracetamol 1 g was given if VAS score was >5, and opioid analgesic in the form of injection tramadol 50 mg was given to those who complained of persistent severe pain [VAS 8–10] limiting movement. The data collecting proforma was used to keep track of both the amount of overall analgesic use as well as the amount of time that had passed from the first request for analgesic medication.

DATA ANALYSIS

The analysis of the data was carried out using SPSS Version 25.0. The categorical variables were represented as frequency, while the numerical variables were expressed as mean standard deviation. Descriptive statistics were produced for all of the variables, and they were used to describe the data. The Mann–Whitney test was used in order to make the comparison between the two groups' VAS scores. In order to compare repeated measurements, the **Table 1: VAS score comparison at rest**

Friedman test was carried out. In all of the statistical tests, a p value of less than 0.05 was deemed significant, and the confidence range that was employed was 95%.

RESULTS

This research included a total of 100 different patients. They all finished the trial, and their data was included in the subsequent analysis. The VAS score for pain comparison during rest and movement was substantially greater in the conventional group at 0 h, 2 h, 4 h, 6 h, and 24 h postoperatively than in the opioid free anaesthetic group. These findings are shown in Tables 1 and 2.

IC	e 1. VAS score comparison at rest				
	Parameter	Opioid-free anaesthesia (Median)	Conventional group (Median	P value	
	VAS 0 hour	2.5	4.5	0.001	
	VAS 2	2.5	4.5	0.001	
	VAS 4	2.5	4.5	0.001	
	VAS 6	2.5	4.5	0.001	
	VAS 12	1.5	2.5	0.21	
	VAS 24	0	1.5	0.63	

Table 2: VAS score comparison during movement

Parameter	Opioid-free anaesthesia (Median)	Conventional group (Median	P value
VAS 0 hour	3.5	5.5	0.001
VAS 2	3.5	5.5	0.001
VAS 4	3.5	5.5	0.001
VAS 6	2.5	3.5	0.001
VAS 12	2.5	2.5	0.21
VAS 24	2.5	2.5	0.63

The overall duration of analgesia was somewhat different for each of the groups taken into consideration here. In the group that received opioid-free anaesthesia, the duration of analgesia obtained was 14.90 ± 5.73 h, which is substantially longer than

the duration of analgesia attained in the conventional group (7.81 ± 1.20) h. [Table 3] reveals that there was no discernible difference in the total time required for surgery between the two groups

 Table 3: Duration of analgesia and surgery using descriptive statistics

Parameter	Opioid-free anaesthesia (Median)	Conventional group (Median
Age (years)	44.97±9.51	43.36±11.56
Duration of surgery (h)	1.71±0.25	1.53±0.43
Duration of analgesia (h)	14.90±5.73	7.81±1.20

Table 4: Consumption of analgesics using frequency

Parameter	Opioid-free anaesthesia <i>n</i> (%)	Conventional group <i>n</i> (%)
No dose of analgesics	11 (22)	-
1 dose of paracetamol	32 (64)	35 (70)
2 doses of paracetamol	7 (14)	-
1 dose of paracetamol	-	15 (30)
+ tramadol		

In the group that had anaesthesia that did not include the use of opioids, around 22% of patients did not need the use of any analgesics in the post-operative phase within the first 24 hours. Both groups reported significantly different levels of total postoperative analgesic usage, however. In the conventional group, approximately 70% of patients required one dose of paracetamol (1 g), and 30% required one dose of paracetamol along with opioid (tramadol 50 mg) in view of severe pain as assessed by VAS (score > 5). In contrast, in the opioid free anaesthesia group, 64% If of patients required one dose of paracetamol (1 g), and 14% required two doses of paracetamol (total 2 g) at an interval of 8 to 12 In the clinical setting, the opioid-free anaesthesia group and the conventional group had hemodynamic values that were equivalent to one another. Both groups did not show any statistically significant differences in heart rate (0.73 [Table 5: Comparison of intraoperative haemodynamics

bpm; 95% CI [3.89 to 5.71], P = 0.42) and diastolic blood pressure (0.065 mmHg; 95% CI [0.27 to 9.01], P = 0.07); however, the conventional group did show a statistically significant decrease in systolic blood pressure (0.01 mm Hg; 95% CI [1.39 to 10.99], P =0.0 However, the difference was not big enough to be clinically relevant. Also, the difference in mean arterial pressure (MAP) (P = 0.02) was statistically significant when compared between the two groups [Table 5].

	Opioid-free anaesthesia	Conventional group	P value
SBP (mmHg)	118.33±9.89	111.97±9.44	0.02
DBP (mmHg)	80.83±8.75	76.48±9.25	0.07
HR (bpm)	74.47±8.00	73.61±10.43	0.61
MAP (mmHg)	93.53±8.10	88.22±7.76	0.02

DISCUSSION

In this particular research, the VAS ratings that were recorded postoperatively in the group that did not receive opioids were lower. This may be ascribed to the use of fascial plane blocks, which are a standard component of the care that we provide for laparoscopic procedures, as well as our opioid-sparing regimen, which consisted of lignocaine and magnesium. Both of these factors were present. In a randomised controlled trial (RCT) on 40 patients to evaluate the efficacy of ESPB on cholecystectomy, where both the groups received IV patient-controlled analgesia containing morphine, it was found that pain scores were 0 at 12 and 24 h compared to pain scores (0-1) at 12 and 24 h of the control group, and the difference was statistically significant. The RCT was conducted to evaluate the efficacy of ESPB on [8]

Additionally, in the present investigation, the bigger difference in duration of analgesia (7 hours) across both groups is attributed to the ESPB and the amount that was utilised (60 mL), which emphasises its usefulness in post-operative pain treatment. This was shown to be the case when comparing the two groups. Also, in order to achieve the desired results, ESPB was combined with systemic non-opioid analgesics like lignocaine and magnesium infusions. Ketamine was avoided due to the negative effects and impact it had on recovery, including emergence reactions, hallucinations, dissociative states, apnoea, and vivid dreams. Because of this, our work is both fascinating and unique in comparison to other research that has been done on opioid-free analgesia.

In the group that received opioid-free anaesthesia, total analgesic consumption was lower, and none of the patients required opioid as rescue analgesia. On the other hand, in the group that received conventional opioids, 10 patients required tramadol 50 mg as a secondary analgesic due to paracetamol because they

had a higher VAS score, which limited their movement. This demonstrates to us that using a multimodal analgesic strategy will do away with the need for the use of opioids during the perioperative phase.

For the treatment of persistent thoracic neuropathic pain, Forero et al.[9] recently presented an approach called ESPB. After being injected into the EPSB, the local anaesthetic travels via the thoracolumbar fascia, where it acts on the ventral and dorsal rami of the spinal nerve to provide visceral and somatic analgesia. [10] Continuous extracorporeal membrane oxygenation (ESPB) generated a considerable reduction in the amount of morphine that was consumed after open heart operations, as well as speedy patient mobilisation and a reduction in discomfort. [11] Several experts have voiced their view that this method, which is risk-free and simple to carry out, might be a component of the multimodal analgesia for the programmes that are designed to facilitate "improved recovery after surgery." [11]

A meta-analysis was conducted in 2014 to evaluate the clinical consequences of intraoperative doses of opioid. It found that high doses of opioids during surgery cause higher acute postoperative pain, which in turn leads to an increase in the consumption of postoperative analgesics as well as long-term analgesic use.[12] A few clinical trials have emphasised the ability of opioids to expand the region of secondary hyperalgesia surrounding the surgical site. This potential of opioids has been brought to light. This is connected with two phenomena that are interrelated termed tolerance and opioid induced hyperalgesia, which are most often encountered with remifentanyl infusions. Both of these conditions are associated with remifentanyl. [13] Lidocaine is a prototypical amino-amide that functions as a weak base and a local anaesthetic with a brief duration of action. At larger doses, people have reported experiencing adverse effects include disorientation, agitation, a metallic taste, perioral numbness, dizziness, slurred speech, diplopia, tinnitus, muscle spasms, and seizures. The use of intravenous lignocaine during surgery has been shown to reduce perioperative complications such as pain, nausea, narcotic intake, inflammation, and the need for early bowel function following surgery. [14] Lignocaine has been shown to have analgesic effects at concentrations lower than 5 micrograms per millilitre. In addition to that, it contains qualities that make it an anti-hyperalgesic and an anticonvulsant.[15] The need of inhalational medications, muscle relaxants, and post-operative ileus may all be decreased with intraoperative lidocaine infusion. In the present research, it was found that repeated dosages of muscle relaxants were not necessary at any point throughout the surgical procedure. This resulted in a significant improvement in terms of cost-effectiveness. Continuous infusion of lidocaine did not reveal a significant difference in pain levels at 24 hours compared to the placebo group, according to a Cochrane review study that included 68 RCTs as part of its research. [16] In addition, the effects of intravenous lignocaine on the necessity for anaesthetics and the intraoperative haemodynamics of surgical procedures have been investigated in a great deal of clinical research. A randomised controlled trial with two levels of blinding found no significant differences in mean arterial pressure (MAP) and heart rate before induction, during surgery, or in the recovery phase. However, the study found that the mean end-tidal concentration of sevoflurane was 48% lower in the lignocaine group. [17] In the present trial, hemodynamic parameters were nearly steady in 82% of the patients in both groups. Diltiazem 5 mg was administered as required to those patients who had intraoperative elevations in blood pressure.

In addition, magnesium, which acts as an antagonist at N-methyl-aspartate receptors, produces analgesic effects by controlling the amount of calcium that can enter cells. It eliminates hypersensitivity in post-injury conditions and stops central sensitization from occurring as a result. [18] There has been research done and published on the effect that magnesium plays in lowering the amount of anaesthetic needed and bringing about controlled hypotension. [19]

The present investigation found that intraoperative usage of magnesium sulphate (MgSO4) was linked with improved intraoperative haemodynamics as well as improved post-operative analgesia without any noticeable negative effects. The results of a metaanalysis of four randomised controlled trials on the analgesic effect of magnesium after laparoscopic cholecystectomy showed a significant decrease in pain scores at an early stage (at 2 and 8 h), as well as a reduction in the amount of analgesic medication consumed post-operatively. [20] Additionally, the injection of MgSO4 intravenously during surgery was shown in a meta-analysis of 11 randomised controlled trials to have the potential to minimise unpleasant effects such as vomiting, nausea, shivering, and the need for post-operative analgesics. [21]

There have been a number of studies that have been published regarding the many different protocols for opioid-free anaesthesia. The use of propofol, dexmedetomidine, and lignocaine infusions for laparoscopic cholecystectomy was shown in a randomised controlled trial to be associated with lower pain scores, reduced consumption of rescue analgesics, and was also described as an alternative to the use of opioids, particularly for patients who were at a high risk for post-operative nausea and vomiting. [6] None of the patients in the present research suffered substantial adverse effects of opioids in the post-operative period. These adverse effects include nausea, vomiting, respiratory depression, and ileus. The after-surgery discomfort experienced by one-third of the patients, which was ascribed to the effects of residual carbon dioxide and occurred in the right shoulder tip, occurred in the recovery room.

This research is not without its share of caveats and restrictions. Due to the absence of randomization in this research, there is the potential for bias. A higher VAS score inhibits movement and coughing, which in turn delays ambulation and recuperation. As a result, the cut-off for pain management was set at a VAS of more than 5, since this value was determined to be optimal. As a consequence, the findings of many other research may not be comparable.

CONCLUSION

When compared to the routine conventional opioid anaesthesia, the integration of ESPB into an intravenous opioid-free analgesic regimen using lignocaine and magnesium provides better postoperative pain relief with lower VAS scores, increased duration of analgesia, and reduced opioid consumption. These benefits can be attributed to the combination of these three factors. Opioid-free anaesthesia is an option that might be considered for some individuals who are unable to tolerate the negative effects that are associated with opioid use.

REFERENCES

- 1. Ekstein P, Szold A, Sagie B, Werbin N, Klausner JM, Weinbroum AA. Laparoscopic surgery may be associated with severe pain and high analgesia requirements in the immediate postoperative period. Ann Surg 2006;243:41-6.
- 2. Oderda GM, Evans RS, Lloyd J, et al. Cost of opioidrelated adverse drug events in surgical patients. J Pain Symptom Manage 2003; 25(3): 276-83.
- 3. Chia Y-Y, Liu K, Wang JJ, Kuo MC, Ho ST. Intraoperative high dose fentanyl induces postoperative fentanyl tolerance. Can J Anaesth 1999; 46(9): 872-7.
- Ziemann-Gimmel P, Goldfarb AA, Koppman J, Marema RT. Opioidfree total intravenous anaesthesia reduces postoperative nausea and vomiting in bariatric surgery beyond triple prophylaxis. Br J Anaesth 2014; 112(5): 906-11.

- 5. White, P.F. The role of non-opioid analgesic techniques in the management of pain after ambulatory surgery. *Anesth. Analg.* **2002**, *94*, 577–585.
- Warren-Stomberg, M.; Brattwall, M.; Jakobsson, J.G. Non-opioid analgesics for pain management following ambulatory surgery: A review. *Minerva Anestesiol.* 2013, 79, 1077–1087.
- McMahon, S.B.; Koltzenburg, M.; Tracey, I.; Turk, D. (Eds.) *Wall and Melzack's Textbook of Pain*, 6th ed.; Elsevier Health Sciences: New York, NY, USA, 2013.
- Stoelting, R.; Flood, P.; Rathmell, J.; Shafer, S. (Eds.) *Stoelting's Handbook of Pharmacology & Physiology in Anaesthetic Practice*, 3rd ed.; Wolters Kluwer: Philadelphia, PA, USA, 2015.
- 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: Α prospective, randomized. double-blinded study. Braz. L Anesthesiol. 2015, 65, 191-199.
- Ziemann-Gimmel, P.; Goldfarb, A.A.; Koppman, J.; Marema, R.T. Opioid-free total intravenous anaesthesia reduces postoperative nausea and vomiting in bariatric surgery beyond triple prophylaxis. *Br. J. Anaesth.* 2014, *112*, 906–911.
- Stark, P.A.; Myles, P.S.; Burke, J.A. Development and psychometric evaluation of a postoperative quality of recovery score: The QoR-15. Anesthesiology 2013, 118, 1332–1340.
- Macintyre, P.E.; Huxtable, C.A.; Flint, S.L.P.; Dobbin, M.D.H. Costs and Consequences: A Review of Discharge Opioid Prescribing for ongoing Management of Acute Pain. *Anaesth. Intensive Care* 2014, 42, 558–574.
- Guignard, B.; Bossard, A.E.; Coste, C.; Sessler, D.I.; Lebrault, C.; Alfonsi, P.; Fletcher, D.; Chauvin, M. Acute opioid tolerance: Intraoperative remifentanil

increases postoperative pain and morphine requirement. *Anesthesiology* **2000**, *93*, 409–417.

- Vakkuri A, Yli-Hankala A, Talja P, *et al.* Timefrequency balanced spectral entropy as a measure of anesthetic drug effect in central nervous system during sevoflurane, propofol, and thiopental anesthesia. Acta Anaesthesiol Scand 2004; 48(2): 145-53.
- 15. Dirks J, Fabricius P, Petersen KL, Rowbotham MC, Dahl JB. The effect of systemic lidocaine on pain and secondary hyperalgesia associated with the heat/capsaicin sensitization model in healthy volunteers. Anesth Analg 2000;91:967–72.
- Gulec CMSN, Yeksan AN, Oba S. Comparison of decurarization using sugammadex and neostigmin after rocuronium during desflutan anesthesia 2015; 48-53.
- Saadawy IM, Kaki AM, Abd El Latif AA, Abd-Elmaksoud AM, Tolba OM. Lidocaine vs. magnesium: Effect on analgesia after a laparoscopic cholecystectomy. Acta Anaesthesiol Scand 2010;54:549-56.
- Parks WC, Wilson CL, López-Boado YS. Matrix metalloproteinases as modulators of inflammation and innate immunity. *Nat Rev Immunol*. 2004;4(8):617– 629
- 19. Hwang W, Lee J, Park J, Joo J. Dexmedetomidine versus remifentanil in postoperative pain control after spinal surgery: a randomized controlled study. *BMC Anesthesiol.* 2015;15(1):21.
- Myles PS, Weitkamp B, Jones K, Melick J, Hensen S. Validity and reliability of a postoperative quality of recovery score: the QoR-40. Br J Anaesth. 2000;84(1):11–15.
- 21. Shu RC, Zhang LL, Wang CY, et al. Spinal peroxynitrite contributes to remifentanil-induced postoperative hyperalgesia via enhancement of divalent metal transporter 1 without iron-responsive element-mediated iron accumulation in rats. *Anesthesiology*. 2015;122(4):908–920.