Int J Physiol Pathophysiol Pharmacol 2022;14(5):289-295
www.ijppp.org /ISSN:1944-8171/IJPPP0142978

Original Article

Effect of aminophylline, ketamine and paracetamol on pain intensity after deep vitrectomy surgery

Darioush Moradi Farsani[1], Iman Nikkhoo[1], Aryan Rafiee Zadeh[2], Niloofaralsadat Nourian[3], Kamran Montazeri[1]

[1]Department of Anesthesiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran; [2]School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran; [3]School of Medicine, Islamic Azad University of Najaf Abad Branch, Isfahan, Iran

Received March 19, 2022; Accepted October 8, 2022; Epub October 15, 2022; Published October 30, 2022

Abstract: Background: Pain management after surgery is a challenging medical issue, and clinical research in this area has continued. This study aimed to compare the effect of Aminophylline, ketamine, and paracetamol on the pain intensity after deep vitrectomy and compare it with the control group. Methods: In this clinical trial, 240 patients undergoing deep vitrectomy were included in the study. The protocol of the current study was approved in the Ethics committee of Isfahan University of Medical Sciences (IR.MUI.REC.1396.3.876) and this study was registered in Iranian Registry of Clinical Trials (IRCT20210919052523N1) (https://www.irct.ir/trial/58884). The patients were randomly divided into four equal groups. Twenty minutes before surgery, in the first group, 0.15 mg/kg ketamine, in the second group 1 g acetaminophen, in the third group 3 mg/kg of aminophylline, and in the fourth group, normal saline was infused in the same manner. All drugs were diluted with 100 ccs of normal saline and infused intravenously within 15 minutes. The four groups of hemodynamic variables, pain intensity, and rescue analgesic drugs were compared. Results: There was no significant difference between the groups based on hemodynamic variables (P>0.05). The severity of pain up to 2 hours after surgery and the rescue to analgesia in the ketamine and paracetamol groups were significantly lower than that of aminophylline and placebo. Conclusion: Using ketamine or paracetamol effectively decreases pain intensity after deep vitrectomy surgery without producing significant adverse hemodynamic changes.

Keywords: Deep vitrectomy, postoperative pain, ketamine, paracetamol, aminophylline

Introduction

Acute pain during and after surgery is one of the most unpleasant side effects. It is influenced by different factors and various pharmacological and non-pharmacological approaches [1-5]. Acute pain can lead to many acute (tachycardia, myocardial ischemia, ileus and hyperglycemia) and chronic (delayed recovery and chronic pain) complications [6]. Proper postoperative pain control can lead to reduced suffering, earlier returning to normal activities, shortened period of hospitalization, reduced hospital costs and increased patient satisfaction [7]. Deep Vitrectomy is one of the painful ocular operations. Therefore, pain control has high clinical importance in these patients.

Due to the increased average age of the patients undergoing surgeries, these patients need efficient postoperative pain control as younger patients do; therefore, it seems necessary to research postoperative pain management. Opioids still play an essential role in postoperative pain control. Still, they are associated with dose-dependent side effects like respiratory depression, nausea, vomiting, urinary retention, itching, confusion, and postoperative ileus. Therefore, we need other analgesic drugs with fewer side effects [8].

Ketamine is an anesthetic drug with analgesic effects by suppressing N-Methyl-D-aspartate receptors and can be administered through intravenous, intramuscular, oral, and rectal routes [9, 10]. One study used ketamine five minutes before hysterectomy surgery and stated that it has led to decreased need for analgesic drugs after surgery [11]. In another study, using ketamine in low doses before lower extremity, tonsillectomy, and gynecologic surgeries led to less postoperative pain [12, 13].

Also, in another study, using morphine with low doses of ketamine simultaneously has led to better efficacy of morphine in postoperative pain control [14]. Ketamine can cause side effects like increased intracranial pressure, intraocular pressure, and myocardial oxygen consumption [15].

Paracetamol is a non-steroidal anti-inflammatory drug that, along with its analgesic effects, can have side effects such as tachycardia, hypertension, hepatotoxicity, and nephrotoxicity [16]. The maximum dose of paracetamol for adults is 4 grams per day and 2 grams per day for alcoholics, and the use of paracetamol for pain control has been discussed in some studies [17].

Aminophylline is a component of xanthine compounds that can bronchodilation and interact with xanthine-containing compounds such as coffee. Some studies have pointed to the analgesic effects of aminophylline [18]. Complications of aminophylline include tachycardia, restlessness, nausea and vomiting and mild respiratory and cardiac output suppression. Different studies have indicated various analgesic properties for these drugs and stated that each has specific complications [17, 18].

Due to the side effects of conventional analgesic drugs such as opioids, there is a marked necessity for other analgesic drugs with fewer side effects. Since we found no proper comparison between the three mentioned analgesics, especially in ocular operations, we decided to design this research.

Materials and methods

Study design

This study was a double-blind randomized clinical trial (physician and patient are unaware of the type of medication used) in Feiz university hospital, Isfahan, Iran 2016-2017. This study has the approval of the protocol of the study in the Ethical committee (IR.MUI.REC.1396.3.876) and registration of study in the Iranian Registry of Clinical Trials (IRCT20210919052523N1).

Inclusion and exclusion criteria

The inclusion criteria were age between 40-80 years, American society of anesthesiologists (ASA) physical status I or II, candidates of deep vitrectomy, no pregnancy, no history of smoking, drugs and alcohol abuse, no history of any liver diseases and cardiac arrhythmia, no history of ischemic heart diseases and heart valve diseases, hypertension and sinus tachycardia, weight less than 100 kg, no reports of chronic pain lasting more than six months, no history of allergy to drugs, aminophylline or non-steroidal anti-inflammatory drugs (NSAIDs), no obvious preoperative anxiety and no history of taking anti-anxiety drugs and signing the written informed consent to participate in this study. Exclusion criteria were the patient's cardiac arrest or any complications that required an alteration in anesthesia methods, an increase in heart rate above 80 beats per minute, and if they declared that they did not consent to continue participation in the study.

Groupings and interventions

After taking written consent from patients and making the fundamental adjustments, patients were randomly divided into four groups in the operating room: group 1, ketamine recipients (group k), group 2, acetaminophen recipients (group P), group 3 (aminophylline recipients) and group 4 (placebo).

General anesthesia was used in all patients by injecting Thiopental sodium 5 mg/kg, fentanyl 2 mg/kg, and Atracurium 0.5 mg/kg intravenously; if necessary, a quarter of this dose was repeated when needed. Anesthesia was maintained in both groups using isoflurane 1.2% and the combination of oxygen and N_2O 50% each. All patients received a 5 ml/kg intravenous infusion of Ringer lactate solution before induction of anesthesia to prevent hypotension. Then, in coordination with the surgeon approximately 20 minutes before surgery ended, about 0.15 mg/kg of ketamine was injected intravenously in the first group, in the second group, patients received 1 g acetaminophen intravenous infusion, and in the third group, patients were given 3 mg/kg of aminophylline intravenous infusion within 15 minutes. N/S diluted all to a volume of 100 ccs, and the patients in the fourth group received 100 ml of sterile normal saline in the same manner.

Additional procedures

If systolic blood pressure drops above 20% of baseline before induction of anesthesia or heart rate is below 40 beats per minute, it was

initially treated by intravenous fluid administration. If no responses were detected, patients were given ephedrine or atropine, respectively. Reducing anesthetics was considered in case of hypotension that did not respond to a fluid replacement or bradycardia treatment. In both groups, we discontinued isoflurane at the end of the surgery, and when the eye dressing was complete, we discontinued N_2O. The lungs were ventilated with 100% oxygen at 4 L/min until the patient's spontaneous ventilation began. Neuromuscular block was reversed by neostigmine at a dose of 0.04 mg/kg and atropine 0.02 mg/kg and the patient was awakened and the endotracheal tube was removed.

After surgery, patients were transferred to the recovery room and ophthalmology department afterward. In addition, to make the study double-blinded, two individuals were used for the operation as the anesthesiologist prescribed the medication, and another person, unaware of the type of the prescribed medication, was in charge of collecting data.

Data collection

After the patients were transferred to recovery (postanesthesia care unit), the pain intensity was measured based on the Visual Analogue Scale (VAS). According to this criteria, the patient's pain is scored from 0 (no pain) to 10 (highest pain). The measured hemodynamic variables included mean arterial pressure (MAP), heart rate (HR), and respiratory rate (RR). The definition of mean arterial pressure (MAP) is the average arterial pressure throughout one cardiac cycle, systole, and diastole. These data were measured on arrival to recovery and then at 15 and 30 minutes, 2, 4, 8, and 24 after entry to the recovery unit. Intravenous pethidine was injected at a dose of 0.5 mg/kg if the pain intensity was more than three based on VAS criteria. The recovery time was also recorded. Total analgesic consumption was recorded at the end of 24 hours according to VAS criteria. Recovery time was also registered.

Statistical analysis

According to the sample size formula, 1-α and 1-β are confidence levels and test power, which have been considered 0.95 and 0.80, respectively, and z1-α/2 and z1-β were calculated at 1.96 and 0.84, respectively, according to the standard distribution table. ES is Cohen's effect size, considered 0.5 in the present study. Thus, the sample size was 60 patients in each group. The collected data were entered into the computer and analyzed by SPSS 24 software. To analyze the data, descriptive statistics, including frequency tables and central and dispersion indices, were used to describe the essential characteristics of the subjects. Data were analyzed using repeated measures ANOVA and Friedman tests to compare the changes in the variables during the intervention, and one-way ANOVA, Kruskal-Wallis, Chi-square, and Fisher exact tests were used to compare the four groups. The significance level was considered 0.05 in all tests.

Results

Study population

In this study, 240 patients were randomly divided into four groups, including ketamine (31 males and 29 females), acetaminophen (35 males and 25 females), aminophylline (34 males and 26 females) and placebo (41 males and 19 females) (**Figure 1**). There was no significant difference between these groups based on age and sex (P>0.05). There was also no significant difference between the groups based on recovery time (P = 0.11) (**Table 1**).

Comparison of hemodynamics

There was no significant difference between these four groups based on mean arterial pressure (MAP), heart rate, and respiratory rate at times 0, 15, and 30 min, 2, 4, 8, and 24 hours postoperatively (P>0.05) (**Table 2**).

Pain assessments

There was a significant difference between the groups according to the intensity of pain at 0, 15, and 30 minutes and 2 hours after surgery (P<0.001) based on the POST HOC test. At all-time points, there was a significant difference between ketamine with aminophylline and placebo (P<0.001). There was also a considerable difference between acetaminophen with aminophylline and placebo (P<0.001). But there was no significant difference between ket-

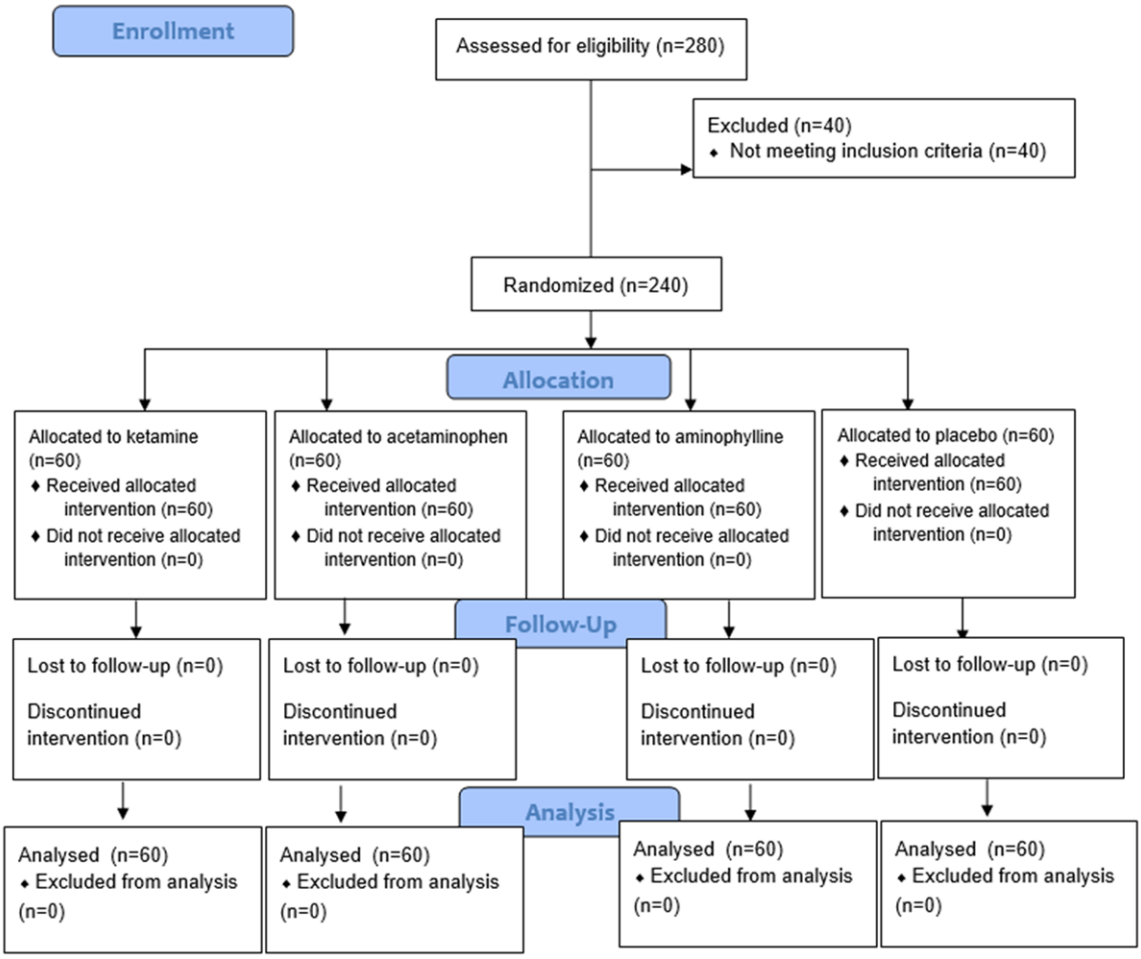

Figure 1. Consort diagram of enrollment and exclusion of patients from study.

Table 1. Demographic variables studied in groups

Variable		Ketamine group	Acetaminophen group	Aminophylline group	Placebo group	*P*-value
Age [24]		58.12 ± 11.08	59.41 ± 9.99	59.30 ± 10.68	59.44 ± 9.59	0.88*
Sex	Man	31 (51.7%)	35 (58.3%)	34 (56.7%)	41 (68.3%)	0.30**
	Female	29 (48.3%)	25 (41.7%)	26 (43.3%)	19 (31.7%)	
Duration of recovery (minute)		34.14 ± 4.95	35.84 ± 6.87	33.82 ± 7.03	36.22 ± 6.65	0.11*

*One way ANOVA, **Chi Square.

amine and acetaminophen as well as aminophylline and placebo (P>0.05). Therefore, pain intensity in ketamine and acetaminophen groups was significantly lower than in aminophylline and placebo until 2 hours after surgery. On the other hand, there was a significant difference between the groups according to the need for analgesics (P<0.001) so that the need for analgesics was lower in the ketamine, acetaminophen, aminophylline, and placebo groups, respectively (**Table 3**). No significant drug-induced side effects or other complications were seen in the study groups.

Discussion

According to the results of this study, ketamine and acetaminophen are more effective drugs for controlling postoperative pain and the need for analgesics than aminophylline and placebo

Table 2. Hemodynamic variables studied in the postoperative groups

Variable		Ketamine group	Acetaminophen group	Aminophylline group	Placebo group	*P*-value*
Mean arterial pressure (MAP) (mmhg)	0	87.53 ± 12.80	89.01 ± 17.01	82.24 ± 14.34	85.58 ± 10.60	0.10
	15 m	85.84 ± 12.56	90.14 ± 11.95	86.02 ± 15.58	85.01 ± 11.06	0.21
	30 m	82.39 ± 11.77	87.32 ± 8.83	82.75 ± 14.86	82.98 ± 12.69	0.18
	2 h	83.69 ± 9.34	83.73 ± 12.57	83.45 ± 14.37	87.89 ± 14.13	0.20
	4 h	84.23 ± 10.65	79.97 ± 10.93	85.03 ± 13.61	85.66 ± 12.86	0.12
	8 h	80.22 ± 9.71	80.51 ± 9.24	80.20 ± 8.20	78.13 ± 5.75	0.41
	24 h	79.75 ± 7.96	78.94 ± 9.90	78.88 ± 8.97	76.82 ± 8.43	0.36
heart rate (beat per minute)	0	79.71 ± 15.52	78.21 ± 11.24	79.53 ± 9.35	83.51 ± 15.78	0.15
	15 m	77.46 ± 12.91	77.24 ± 10.76	76.98 ± 9.74	82.24 ± 15.62	0.08
	30 m	74.03 ± 11.37	76.27 ± 11.04	73.87 ± 8.96	77.98 ± 11.93	0.13
	2 h	73.21 ± 13.36	76.64 ± 11.29	74.29 ± 9.61	78.03 ± 16.45	0.18
	4 h	74.10 ± 10.87	75.55 ± 9.17	74.03 ± 6.71	77.20 ± 9.73	0.20
	8 h	78.85 ± 4.72	76.81 ± 9.84	79.53 ± 10.30	78.70 ± 12.41	0.48
	24 h	75.78 ± 8.90	74.06 ± 9.27	77.16 ± 11.56	77.61 ± 6.43	0.15
Respiratory rate	0	21.46 ± 8.76	21.61 ± 4.79	23.13 ± 4.61	23.01 ± 3.31	0.23
	15 m	18.81 ± 2.09	19.87 ± 2.52	19.43 ± 2.30	19.49 ± 2.34	0.10
	30 m	18.36 ± 2.89	19.01 ± 2.71	19.28 ± 1.23	19.10 ± 1.63	0.13
	2 h	19.23 ± 1.60	18.60 ± 3.34	19.95 ± 2.78	19.59 ± 1.74	0.07
	4 h	19.83 ± 0.90	19.12 ± 2.89	20.71 ± 2.95	19.62 ± 2.42	0.09
	8 h	19.21 ± 2.01	18.61 ± 2.87	19.63 ± 2.36	19.50 ± 2.33	0.10
	24 h	17.27 ± 3.17	17.47 ± 2.45	17.74 ± 2.39	17.37 ± 3.33	0.83

*One-way ANOVA.

Table 3. Postoperative pain and need for analgesic in groups

Variable		Ketamine group	Acetaminophen group	Aminophylline group	Placebo group	*P*-value
Pain intensity	0	5.63 ± 1.09	5.98 ± 1.13	7.21 ± 1.06	7.45 ± 1.33	<0.001*
	15 m	4.68 ± 1.07	4.98 ± 1.13	6.05 ± 1.06	6.45 ± 1.33	<0.001*
	30 m	3.91 ± 1.13	4.60 ± 1.21	4.50 ± 1.15	6.01 ± 1.24	<0.001*
	2 h	3.03 ± 1.19	3.03 ± 0.99	3.60 ± 1.13	4.93 ± 1.29	<0.001*
	4 h	1.68 ± 0.84	1.32 ± 1.17	1.74 ± 0.77	1.49 ± 1.15	0.11*
	8 h	0.77 ± 0.82	0.50 ± 0.80	0.60 ± 0.73	0.67 ± 0.83	0.31*
	24 h	0.24 ± 0.43	0.17 ± 0.42	0.16 ± 0.37	0.22 ± 0.45	0.71*
Need for analgesic medication (nr-%)		11 (18.3%)	15 (25%)	41 (68.3%)	48 (80%)	<0.001**
satisfaction	Satisfied	36 (60%)	41 (68.3%)	25 (41.7%)	9 (15%)	<0.001**
	Relatively satisfied	22 (36.7%)	17 (28.3%)	33 (55%)	34 (56.7%)	
	Relatively unsatisfied	2 (3.3%)	2 (3.3%)	2 (3.3%)	17 (28.3%)	

*One-way ANOVA, **Chi Square.

in patients undergoing deep vitrectomy. These two drugs also cause slight changes in hemodynamic variables and do not cause severe side effects.

As discussed earlier, postoperative pain control is a major clinical issue in patients undergoing surgical procedures. In a study by Faiz and colleagues, they found that injecting acetaminophen had more efficacy than ketamine in reducing pain after a hysterectomy [19]. The results of this study were inconsistent with our findings because ketamine and acetaminophen were similarly effective in reducing pain and the need for analgesics in our research.

Aminophylline, which is clinically used as a bronchodilator, stops the anti-adenosine ac-

tion, so it can be used to shorten recovery time after general anesthesia. A few studies have recently indicated that aminophylline can have analgesic effects similar to analgesic drugs and has no side effects [20]. On the other hand, some studies have shown that aminophylline has no impact on pain relief [21]. In our study, aminophylline also had no analgesic effects like ketamine and acetaminophen. Some studies have also suggested that using aminophylline can be associated with shortened recovery duration, hypotension, and decreased heart rate [22]. These data are in line with the findings of our study. In this survey, we showed that ketamine and acetaminophen are two efficient drugs with few complications that can be appropriately used for postoperative pain control and the need for analgesics in patients undergoing deep vitrectomy.

In a study by Sadrolsadat and colleagues, it was concluded that injecting acetaminophen prophylactically was a safe and effective way for postoperative pain control and the need for analgesics in patients undergoing deep vitrectomy [23]. In another study comparing the effects of ketamine-paracetamol combination with paracetamol alone, it was concluded that the pain intensity in the first group was significantly lower compared to the second group. Notably, the results of this study have high clinical importance, and physicians should pay attention to the analgesic properties of the studied agents in this study.

By comparing our data with previous studies, it was indicated that ketamine and acetaminophen are more effective drugs for controlling postoperative pain. These data could have high clinical importance and we recommend that anesthesiologists and surgeons should pay more attention to effectiveness of these agents.

Limitations of our study included small sample size, inability to evaluate the efficacy of these drugs during surgery, lack of consideration of other factors influencing these drugs, and similar studies in this field. It should be mentioned that the data related to this survey were restricted and we did not evaluate multiple indicators. This could be accounted as a limitation of our study. It is recommended that further studies should be conducted on this issue.

Conclusion

Therefore, according to the results of our study and other studies, ketamine and acetaminophen are two efficient drugs with few complications that can be appropriately used for postoperative pain control and the need for analgesics in patients undergoing deep vitrectomy. Aminophylline use may also be effective in reducing pain in these patients, but in our study, it did not have much effect on pain relief. Therefore, we hope more similar studies will be done in this field.

Disclosure of conflict of interest

None.

Address correspondence to: Darioush Moradi Farsani, Department of Anesthesiology, School of Medicine, Isfahan University of Medical Sciences, Hezar Jarib St., Isfahan, Iran. Tel: +98 913 305 0830; Fax: +983136688597; E-mail: dmoradi@med.mui.ac.ir

References

[1] Nie JJ, Sun S and Huang SQ. Effect of oxycodone patient-controlled intravenous analgesia after cesarean section: a randomized controlled study. J Pain Res 2017; 10: 2649-2655.

[2] Rahimi Varposhti M, Moradi Farsani D, Ghadimi K and Asadi M. Reduction of oculocardiac reflex with Tetracaine eye drop in strabismus surgery. Strabismus 2019; 27: 1-5.

[3] Haddad S, Ghadimi K, Abrishamkar R and Asl NSM. Comparing laparoscopy and laparotomy procedures in the radical hysterectomy surgery for endometrial cancer: a basic review. Am J Transl Res 2021; 13: 2456.

[4] Farsani DM, Ghadimi K, Abrishamkar R, Montazeri K and Peyman A. Evaluating sedative effects of dexmedetomidine and morphine in the patients with opioid use disorder undergoing cataract surgery. Am J Clin Exp Immunol 2021; 10: 30.

[5] Dehghani M, Fadaei B, Rastegar S, Zarezadeh A, Ghadimi K, Nikkhah R and Eslami S. Modified camitz versus BRAND procedures for the treatment of severe carpal tunnel syndrome: a comparative trial study. Arch Bone Jt Surg 2020; 8: 420.

[6] Aljabi Y, El-Shawarby A, Cawley DT and Aherne T. Effect of epidural methylprednisolone on post-operative pain and length of hospital stay in patients undergoing lumbar microdiscectomy. Surgeon 2015; 13: 245-9.

[7] Rahimi M, Farsani DM, Naghibi K and Alikiaii B. Preemptive morphine suppository for postoperative pain relief after laparoscopic cholecystectomy. Adv Biomed Res 2016; 5: 57.
[8] Galea S, Merchant RM and Lurie N. The mental health consequences of COVID-19 and physical distancing: the need for prevention and early intervention. JAMA Intern Med 2020; 180: 817-8.
[9] Lee J, Park HP, Jeong MH, Son JD and Kim HC. Efficacy of ketamine for postoperative pain following robotic thyroidectomy: a prospective randomised study. Int J Med Res 2018; 46: 1109-20.
[10] Park PJ, Makhni MC, Cerpa M, Lehman RA and Lenke LG. The role of perioperative ketamine in postoperative pain control following spinal surgery. J Spine Surg 2020; 6: 591-597.
[11] Steinberg AC, Schimpf MO, White AB, Mathews C, Ellington DR, Jeppson P, Crisp C, Aschkenazi SO, Mamik MM, Balk EM and Murphy M. Preemptive analgesia for postoperative hysterectomy pain control: systematic review and clinical practice guidelines. Am J Obstet Gynecol 2017; 217: 303-13.
[12] Carley ME, Chaparro LE, Choinière M, Kehlet H, Moore RA, Van Den Kerkhof E and Gilron I. Pharmacotherapy for the prevention of chronic pain after surgery in adults: an updated systematic review and meta-analysis. Anesthesiology 2021; 135: 304-25.
[13] Tolska HK, Hamunen K, Takala A and Kontinen V. Systematic review of analgesics and dexamethasone for post-tonsillectomy pain in adults. Br J Anaesth 2019; 123: e397-e411.
[14] Kuroda Y, Nonaka M, Kamikubo Y, Ogawa H, Murayama T, Kurebayashi N, Sakairi H, Miyano K, Komatsu A, Dodo T and Nakano-Ito K. Inhibition of endothelin A receptor by a novel, selective receptor antagonist enhances morphine-induced analgesia: possible functional interaction of dimerized endothelin A and μ-opioid receptors. Biomed Pharmacother 2021; 141: 111800.
[15] Yildiz M, Kozanhan B, Iyisoy MS, Canıtez A, Aksoy N and Eryigit A. The effect of erector spinae plane block on postoperative analgesia and respiratory function in patients undergoing laparoscopic cholecystectomy: a double-blind randomized controlled trial. J Clin Anesth 2021; 74: 110403.
[16] Roberts E, Nunes VD, Buckner S, Latchem S, Constanti M, Miller P, Doherty M, Zhang W, Birrell F and Porcheret M. Paracetamol: not as safe as we thought? A systematic literature review of observational studies. Ann Rheum Dis 2016; 75: 552-559.
[17] Kimiaei Asadi H, Nikooseresht M, Noori L and Behnoud F. The effect of administration of ketamine and paracetamol versus paracetamol singly on postoperative pain, nausea and vomiting after pediatric adenotonsillectomy. Anesth Pain Med 2016; 6: e31210.
[18] Yang CJ, Chen T, Ni X, Yu WY and Wang W. Effect of pre-administration with aminophylline on the occurrence of post-dural puncture headache in women undergoing caesarean section by combined spinal-epidural anaesthesia. J Int Med Res 2019; 47: 420-6.
[19] Wick EC, Grant MC and Wu CL. Postoperative multimodal analgesia pain management with nonopioid analgesics and techniques: a review. JAMA Surg 2017; 152: 691-7.
[20] Kasim SA, Bahr MH, Abdelkader M and Rashwan DA. The effect of preoperative aminophylline on the recovery profile after major pelvic-abdominal surgeries: a randomized controlled double-blinded study. BMC Anesthesiol 2021; 21: 1-8.
[21] Basurto Ona X, Uriona Tuma SM, Martínez García L, Solà I and Bonfill Cosp X. Drug therapy for preventing post-dural puncture headache. Cochrane Database Syst Rev 2013; 2013: CD001792.
[22] Mohammed MI, El-Hamamsy MM, Botros JM and Yassen HM. Effect of aminophylline on atracurium induced neuromuscular block. Egypt J Hosp Med 2018; 71: 3254-60.
[23] Sadrolsadat SH, Yousefshahi F, Ostadalipour A, Mohammadi FZ and Makarem J. Effect of intravenous acetaminophen on postoperative pain in vitrectomy: a randomized, double-blind, clinical trial. Anesth Pain Med 2017; 7: e13639.
[24] Knepper C, Ellemunter H, Eder J, Niedermayr K, Haerter B, Hofer P, Scholl-Bürgi S, Müller T and Heinz-Erian P. Low sodium status in cystic fibrosis-as assessed by calculating fractional Na+ excretion - is associated with decreased growth parameters. J Cyst Fibros 2016; 15: 400-5.