Anesth Pain Med. 2021 December; 11(6):e121527.
doi: 10.5812/aapm.121527.

Published online 2022 January 1.
Research Article

A Comparative Study on the Effects of Ketofol, Dexmedetomidine, and Isofol in Anesthesia of Candidates for Dilatation and Curettage

Mahzad Yousefian [1,*], Ali Mohammadian Erdi [1] and Negin Haghshenas [1]

[1]Department of Anesthesiology, Alavi Hospital, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

[*]*Corresponding author*: Department of Anesthesiology, Alavi Hospital, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran. Email: dr_mahzad@yahoo.com

Received 2021 November 30; **Revised** 2021 December 12; **Accepted** 2021 December 13.

Abstract

Background: Dilatation and curettage (D & C) is one of the relatively common surgeries among women. Familiarity with the analgesics, along with their different uses and specific characteristics, can help to determine the best and most appropriate drug to control pain in the patients.
Objectives: This study aimed to compare the effects of ketofol, dexmedetomidine, and isofol in anesthesia of candidates for D & C.
Methods: In this double-blind clinical trial, 150 candidates for D & C surgeries with ASA class 1 and 2 were included. Patients were randomly divided into three groups. The first group received ketamine + propofol, the second group received dexmedetomidine, and the third group received isofol (isoflurane + propofol). Any hemodynamic changes or respiratory disorders, including apnea or hypoventilation, drop in the level of blood oxygen saturation, and the need for respiratory support, were recorded and compared.
Results: Hypoventilation was observed in 47 patients in isofol group, 18 in the dexmedetomidine group, and 42 in ketofol group. Also, 48 patients in the isofol group, eight in the dexmedetomidine group, and 33 in the ketofol group experienced apnea. Moreover, 17 patients in the dexmedetomidine group, 35 in the ketofol group, and eight in the isofol group experienced bradycardia. The rate of bradycardia was significantly higher in the dexmedetomidine group (70%) compared to the other two groups, and the rate of hypotension was significantly higher in the isofol group (P = 0.001).
Conclusions: According to the results, dexmedetomidine was associated with fewer complications during general anesthesia in D & C surgery.

Keywords: Dilatation and Curettage, Dexmedetomidine, Ketamine, Ketofol-Isofol, Propofol

1. Background

Women include half of the world's population, and certain diseases of this group of people affect the entire human population (1). Among the various treatments in this field, abortion therapy is the selected treatment in some maternity diseases such as advanced maternal heart disease, hypertensive vascular disease, invasive cervical carcinoma, fetal uterine death, and severe anatomical deformity in the fetus (2). Based on the definition of the National Center for Abortion, abortion refers to the termination of pregnancy under 20 weeks or the birth of a fetus under 500 grams, and these conditions include about 15% of pregnancies. Abortion induction is divided into two methods of mechanical and pharmacological. Medical methods include the use of drugs such as misoprostol and letrozole. Mechanical techniques include microscopic cervical dilators (3-7). Dilatation and curettage (D & C) surgery is a common procedure to determine the cause and treatment of abnormal uterine bleeding (8). The choice of anesthesia depends on the type of surgery and the patient's condition (9). The method of anesthesia for this operation can be general or regional (10). The preferred method for surgeons and patients is often general anesthesia. Due to the common bleeding in this surgery, it is crucial to maintain hemodynamics during anesthesia (11). Thus, selecting the type of drug in general anesthesia should be carefully examined, and the best drug should be selected (12).

There are several ways to control pain during anesthesia, each with different analgesic effects and side effects after anesthesia (13). In these patients, the time of waking up and leaving anesthesia, the length of stay in recovery, various side effects (such as pain, nausea, vomiting, and confusion), and general patient satisfaction are crucial because all of them are effective in faster discharge and rehabilitation of the patient or the occurrence of surgical complications such as hematoma and surgical failure (14, 15).

Familiarity with the analgesics, along with their different applications and specific characteristics, can help to determine the best and most appropriate drug for pain control in the patients (16, 17). Many efforts have been made to find newer analgesics and reduce the severity of postoperative pain to reduce the need for using opioid analgesics (18, 19). One of the most popular drugs is dexmedetomidine, which is a selective alpha-2 adrenergic agonist with high specificity and has a strong anesthetic effect (20, 21). The use of dexmedetomidine, alone or in combination with other drugs, improves hemodynamic stability by having several favorable effects, including analgesic effects, inhibition of sympathetic outputs, anti-anxiety properties, and reduction of norepinephrine levels (22, 23). Using dexmedetomidine as an adjuvant during anesthesia can reduce the incidence of early postoperative cognitive dysfunction (24).

Propofol is a drug used for fart liver clearance after injection. This drug has direct anti-nausea and vomiting effects but no analgesic effect. It is rapidly metabolized in the blood and has a half-life of about 3 - 12 hours (23, 24). Ketamine can be used as an alternative for opioids because it provides acceptable pain relief at low doses and has fewer respiratory and cardiovascular suppressive effects than opioids (25, 26). The combination of ketamine with propofol also provides an analgesic effect, and the rate of side effects is reduced due to a significant reduction in the dose of propofol (27). Ketamine is used as an anesthetic for various surgeries, acting on a variety of receptors, including nicotine and muscarinic receptors (28). Ketamine is used as an anesthetic for short-term surgery or diagnoses that do not require muscle relaxation (29, 30). This reduces the need for opioids and their complications (31) and stress response and improves recovery (32). Ketamine increases heart rate (HR) and blood pressure (BP) through sympathetic stimulation (33). It seems that the combination of ketamine and propofol can be effective in reducing complications and increasing their single-use benefits.

2. Objectives

Due to the multiplicity of candidates for D & C and considering the related complications, this study aimed to compare the effects of ketofol, dexmedetomidine, and isofol in anesthesia of patients referred for D & C to Alavi Hospital in Ardabil, Iran.

3. Methods

This double-blind, randomized clinical trial was conducted in Alavi Hospital, Department of Anesthesiology, Ardabil University of Medical Sciences, Iran, from September 2019 to September 2020. All patients (n = 150) were candidates for D & C due to missed abortion or incomplete abortion. The patients were randomly divided into three equal groups (n = 50 in each). Group A received ketofol, group B received dexmedetomidine, and group C received propofol-isoflurane (placebo).

The drugs were prepared by an anesthesia technician. After preparing the syringes, they were covered with a white label, and the injection was performed by the anesthesiologist. Next, the information was recorded by the assistant. The patient and the evaluator were unaware of the contents of the injectable drug (double-blind). In all the three groups, after the patients entered the operating room, they were first monitored, then a suitable venous route was established, and initial fluid therapy was performed (4 mL/kg normal saline). Oxygen mask was implanted for all patients. Then, midazolam (50 μg/kg), sufentanil (0.3 μg/kg), and intravenous lidocaine 2% (1 mg/kg) were injected. The first group received ketofol in the ratio of ketamine (0.5 mg/k) to propofol (1 mg/kg). The second group received dexmedetomidine at a dose of 1 μg/kg/stat for 10 minutes and then 1 g/kg/h. The third group received propofol at a dose of 1 mg/kg and then isoflurane 1%. Any hemodynamic changes and respiratory disorders, including apnea or hypoventilation, loss of blood oxygen saturation level, and need for respiratory support, were recorded in all the groups. Finally, after the operation and transfer to recovery, the recovery rate of patients in each group was recorded. All patient information was completed by an anesthesia assistant and delivered to the statistician to extract the statistics, and the variables were evaluated using statistical correlation.

The study was approved by the Ethics Committee of Ardabil University of Medical Sciences (ethics code: IR.ARUMS.REC.1398.266), and it was registered on the website of the Iran Trial Registration Center (code: IRCT20191022045203N1). Data were analyzed in SPSS software V24. *t*-test was used to examine quantitative data, and Chi-square test was used to examine qualitative data. Significance level was considered at 0.05.

4. Results

The results showed that the rate of hypoventilation was significantly higher in the isofol group (94%) compared to other two groups (P = 0.001). The apnea rate was compared among the three groups. According to the results, 48 patients (96%) in the isofol group, eight (16%) in the dexmedetomidine group, and 33 (66%) in the ketofol group had apnea. The apnea rate was significantly higher in the isofol group (86%) compared to the other two groups (P = 0.001) (Table 1).

Table 1. Rate of Apnea in the Three Groups

Group	Yes; No. (%)	P-Value
Isofol	48 (86)	
Dexmedetomidine	8 (16)	0.001
Ketofol	33 (66)	

Regarding the duration of apnea, the patients with apnea were divided into two groups: under 60 seconds and above 60 seconds. The duration of apnea over 60 seconds was significantly higher in the isofol group (70%) compared to the other groups (Table 2).

Table 2. Duration of Apnea in the Three Groups

Duration of Apnea	< 60; No. (%)	> 60; No. (%)	P-Value
Isofol	15 (30)	35 (70)	
Dexmedetomidine	46 (92)	4 (8)	0.001
Ketofol	21 (42)	29 (58)	

Bradycardia was observed in 17 (34%) patients in the isofol group, 35 (70%) in the dexmedetomidine group, and eight (16%) in the ketofol group. Moreover, the rate of bradycardia was significantly higher in the dexmedetomidine group (70%) compared to other groups (P = 0.001) (Table 3).

Table 3. The Rate of Bradycardia in the Three Groups

Bradycardia	Yes; No. (%)	P-Value
Isofol	17 (34)	
Dexmedetomidine	35 (70)	0.001
Ketofol	8 (16)	

Hypotension was observed in 31 (62%) patients in the isofol group, 11 (22%) in the dexmedetomidine group, and 10 (20%) in the ketofol group. According to Table 4, the rate of hypotension was significantly higher in the isofol group (62%) compared to the other groups (P = 0.001) (Table 4).

Table 4. The Rate of Hypotension in the Three Groups

Hypotension	Yes; No. (%)	P-Value
Isofol	31 (62)	
Dexmedetomidine	11 (22)	0.001
Ketofol	10 (20)	

Regarding the need for drug replication for appropriate depth of anesthesia, 15 (30%) patients in the isofol group, 22 (44%) in the dexmedetomidine group, and 20 (40%) in the ketofol group needed a re-injection of the drug. The need for drug replication in the dexmedetomidine group was higher than other two groups (44%), but the difference among the three groups was not statistically significant (Table 5).

Table 5. The Need for Drug Replication for Appropriate Anesthesia Depth

Group	Yes; No. (%)	P-Value
Isofol	15 (30)	
Dexmedetomidine	22 (44)	0.03
Ketofol	20 (40)	

Regarding the state of late awakening, patients in the dexmedetomidine group remained awake significantly higher (38%) than the other two groups (P = 0.001). In case of patients that were not awake at the end of the operation, the longest time (10 - 20 minutes) was related to the isofol group with 70%, which was significantly longer than the other groups (P = 0.024).

5. Discussion

In this study, we attempted to find the safest method for anesthesia of candidates for D & C. In another study, Rahimzadeh et al. (34) compared the effects of dexmedetomidine and remifentanil on the rate of discharge from recovery in patients undergoing posterior spinal fusion surgery. In the mentioned study, 40 patients were randomly divided into two groups of remifentanil (R) and dexmedetomidine (D), and the rate of hypoventilation was lower in the dexmedetomidine group. Although this difference was not significant, the general rate of hypoventilation was lower compared to the dexmedetomidine group. This difference might be attributed to different sample sizes in the studies.

Also, in our study, 48 (86%) patients in the isofol group, eight (16%) in the dexmedetomidine group, and 33 (66%) in the ketofol group experienced apnea. The rate of apnea was significantly higher in the isofol group (86%). In a similar study, Yousefian et al. (35) compared ketofol and sodium thiopental in general anesthesia of the patients who were candidates for D & C in Alavi Hospital in Ardabil in 2016. They found that respiratory depression was lower in dexmedetomidine group, and the lowest rate of apnea was observed in the dexmedetomidine group. Dexmedetomidine gained advantages of effective sedation with minimal respiratory depression, decreased intraocular pressure, and reduced pain during the local anesthetic injection (33). In another study, it was found that combining dexmedetomidine with clonidine is effective in lowering intraoperative bleeding (36). Some studies suggest that the use of dexmedetomidine, a selective α-2 antagonist, reduces the incidence of cognitive impairment and delirium in mechanically ventilated patients (37).

In another study, it was found that a combination of ketamine and propofol called ketofol could reduce the risk of coughing due to drug injections (38, 39). Regarding the need for drug repetition for appropriate depth of anesthesia, 15 (30%) patients in the isofol group, 22 (44%) in the dexmedetomidine group, and 20 (40%) in the ketofol group needed re-injection. The need for drug replication in the dexmedetomidine group (44%) was higher than the other groups, but the difference was not statistically significant (P = 0.033). In the study conducted by Rahimzadeh et al., the dose of anesthetic after surgery was lower in the dexmedetomidine group, but this difference was not significant (P = 0.033) (34). Dose replication is not associated with the type of drug.

Garg et al. (40) examined the low dose of ketamine and dexmedetomidine infusion to control pain after spinal surgery in 66 patients who were candidates for spinal surgery. Patients were divided into three equal groups (n = 22 in each). The first group received ketamine at dose of 0.25 mg/kg and then 0.25 mg/kg/ h. The second group received dexmedetomidine bolus at a dose of 0.5 μg/kg and then 0.3 μg/kg/h by infusion. The third group received midazolam (10 μg/kg as a bolus and 10 μg/kg/h as an infusion). The third group received only midazolam exactly as the previous two groups. Patients were monitored for 48 hours. The analgesic time was 860 minutes for the ketamine group, 580 minutes for the dexmedetomidine group, and 265 minutes for the control group. There was a significant increase in analgesia time in both ketamine and dexmedetomidine groups compared to the control group. In comparing ketamine and dexmedetomidine groups, a significantly longer analgesia time was observed in the ketamine group. No apnea and hemodynamic instability were observed in any of the patients. The study recommended ketamine as a more effective drug (35).

Unlike the study conducted by Garg et al. (40), our study showed no significant difference in this regard. This difference might be attributed to the dose of drug and the type of surgery used in the two studies. Regarding the mean duration of discharge from recovery in the three groups, the mean time was 33.2 minutes in the isofol group, 31.6 minutes in the dexmedetomidine group, and 35.4 minutes in the ketofol group. According to the results, the mean time of discharge from recovery was almost the same for all the three groups, and our study did not show any difference. However, in a study conducted by Abdellatif et al. (41), children weighing more than 10 kg were included and randomly divided into three groups of dexmedetomidine-propofol (DP), dexmedetomidine-ketamine (DK), and dexmedetomidine (D). A significant difference was found between DP group and other groups in terms of recovery time. In this study, the researchers recommended the use of DP.

5.1. Conclusions

According to our results, the hypoventilation and apnea rates, as well as the duration of apnea, were significantly lower in the dexmedetomidine group. Moreover, the rate of bradycardia was significantly higher in the dexmedetomidine group, and the rate of hypotension was significantly higher in the isofol group. In addition, no significant difference was observed among the groups in terms of need for drug repetition and recovery time. Accordingly, we recommend using dexmedetomidine for anesthesia due to its lower risks.

Footnotes

Authors' Contribution: Study concept and design and analysis and interpretation of data, A. M.; Drafting of the manuscript and critical revision of the manuscript for important intellectual content, N. H.

Clinical Trial Registration Code: IRCT20191022045203N1.

Conflict of Interests: The authors have no conflicts of interest to disclose.

Data Reproducibility: The data presented in this study are openly available in one of the repositories or will be available on request from the corresponding author by this journal representative at any time during submission or after publication. Otherwise, all consequences of possible withdrawal or future retraction will be with the corresponding author.

Ethical Approval: The study was approved by the Ethics Committee of Ardabil University of Medical Sciences (ethics code: IR.ARUMS.REC.1398.266).

Funding/Support: No external funding source was used for this study.

Informed Consent: It was not declared by the authors.

References

1. Imani F, Rahimzadeh P, Faiz HR, Nowruzina S, Shakeri A, Ghahremani M. Comparison of the Post-Caesarean Analgesic Effect of Adding Dexmedetomidine to Paracetamol and Ketorolac: A Randomized Clinical Trial. *Anesth Pain Med*. 2018;**8**(5). e85311. doi: 10.5812/aapm.85311. [PubMed: 30538943]. [PubMed Central: PMC6252045].

2. El-Hamid AMA, Yassin HM. Effect of intranasal dexmedetomidine on emergence agitation after sevoflurane anesthesia in children undergoing tonsillectomy and/or adenoidectomy. *Saudi J Anaesth*. 2017;**11**(2):137–43. doi: 10.4103/1658-354X.203020. [PubMed: 28442950]. [PubMed Central: PMC5389230].
3. Tas A, Mistanoglu V, Darcin S, Kececioglu M. Tramadol versus fentanyl during propofol-based deep sedation for uterine dilatation and curettage: a prospective study. *J Obstet Gynaecol Res*. 2014;**40**(3):749–53. doi: 10.1111/jog.12259. [PubMed: 24320560].
4. Sahin L, Sahin M, Aktas O, Kilic E, Mandollu E. Comparison of propofol/ketamine versus propofol/alfentanil for dilatation and curettage. *Clin Exp Obstet Gynecol*. 2012;**39**(1):72–5. [PubMed: 22675960].
5. Ugur B, Ogurlu M, Yilmaz S, Kivrak V. Determining the optimal fentanyl dose for dilation and curettage procedures. *Clin Exp Obstet Gynecol*. 2012;**39**(4):509–11. [PubMed: 23444755].
6. Mo Y, Qiu S. Effects of dexmedetomidine in reducing post-cesarean adverse reactions. *Exp Ther Med*. 2017;**14**(3):2036–9. doi: 10.3892/etm.2017.4759. [PubMed: 28962122]. [PubMed Central: PMC5609173].
7. Cao L, Qian Z, Huang L. Comparison of Curettage and Hysteroscopy Plus Curettage After Uterine Arterial Embolization in the Treatment of Cesarean Scar Pregnancy. *ResearchSquare*. 2020;**6**(2):158–64. doi: 10.21203/rs.3.rs-39244/v1.
8. Butwick AJ, Ramachandran B, Hegde P, Riley ET, El-Sayed YY, Nelson LM. Risk Factors for Severe Postpartum Hemorrhage After Cesarean Delivery: Case-Control Studies. *Anesth Analg*. 2017;**125**(2):523–32. doi: 10.1213/ANE.0000000000001962. [PubMed: 28277324]. [PubMed Central: PMC5522356].
9. Akhondzadeh R, Ghomeishi A, Soltani F, Khoshooei A. The Effect of Different Doses of Isoflurane on Hemodynamic Changes and Bleeding in Patients Undergoing Endoscopic Sinus Surgery under General Anesthesia. *Anesth Pain Med*. 2019;**9**(1). e57864. doi: 10.5812/aapm.57864. [PubMed: 30881904]. [PubMed Central: PMC6413045].
10. Krishnamohan A, Siriwardana V, Skowno JJ. Using a pulse oximeter to determine clinical depth of anesthesia-investigation of the utility of the perfusion index. *Paediatr Anaesth*. 2016;**26**(11):1106–11. doi: 10.1111/pan.13000. [PubMed: 27569026].
11. Mostafa MF, Hamed E, Amin AH, Herdan R. Dexmedetomidine versus clonidine adjuvants to levobupivacaine for ultrasound-guided transversus abdominis plane block in paediatric laparoscopic orchiopexy: Randomized, double-blind study. *Eur J Pain*. 2021;**25**(2):497–507. doi: 10.1002/ejp.1689. [PubMed: 33128801].
12. Imani F, Zaman B, De Negri P. Postoperative Pain Management: Role of Dexmedetomidine as an Adjuvant. *Anesth Pain Med*. 2020;**10**(6). e112176. doi: 10.5812/aapm.112176. [PubMed: 34150582]. [PubMed Central: PMC8207883].
13. Malik KM, Imani F, Beckerly R, Chovatiya R. Risk of Opioid Use Disorder from Exposure to Opioids in the Perioperative Period: A Systematic Review. *Anesth Pain Med*. 2020;**10**(1). e101339. doi: 10.5812/aapm.101339. [PubMed: 32337175]. [PubMed Central: PMC7158240].
14. Vishnu Vardhan A, Vishnu Mahesh Babu B, Sai Naveena Lakshmi B. Effect of Dexamethasone with Bupivacaine on Duration of Supra Clavicular Block Compared to Bupivacaine with Normal Saline: A Prospective, Randomized and Double Blind Study. *J Evol Med Dent Sci*. 2014;**3**(28):7861–9. doi: 10.14260/jemds/2014/2984.
15. Hadipourzadeh F, Mousavi S, Heydarpur A, Sadeghi A, Ferasat-Kish R. Evaluation of the Adding Paracetamol to Dexmedetomidine in Pain Management After Adult Cardiac Surgery. *Anesth Pain Med*. 2021;**11**(3). e110274. doi: 10.5812/aapm.110274. [PubMed: 34540629]. [PubMed Central: PMC8438704].
16. Banga PK, Singh DK, Dadu S, Singh M. A comparative evaluation of the effect of intravenous dexmedetomidine and clonidine on intraocular pressure after suxamethonium and intubation. *Saudi J Anaesth*. 2015;**9**(2):179–83. doi: 10.4103/1658-354X.152878. [PubMed: 25829907]. [PubMed Central: PMC4374224].
17. Shoukry A, Abd el Kawy AS. Efficacy and Safety of Magnesium versus Dexmedetomidine as Additives to Local Anesthetic Mixture Using Single Injection Percutaneous Peribulbar Anesthesia in Vitreoretinal Surgeries. *Open Anesthesiol J*. 2018;**12**(1):94–100. doi: 10.2174/2589645801812010094.
18. Toledano RD, de Velde M. Epidural anesthesia and analgesia. In: Hadzic A, editor. *Hadzic's Textbook of Regional Anesthesia and Acute Pain Management*. 2nd ed. New York, USA: McGraw Hill; 2017.
19. Rupniewska-Ladyko A, Malec-Milewska M. A High Dose of Fentanyl May Accelerate the Onset of Acute Postoperative Pain. *Anesth Pain Med*. 2019;**9**(5). e94498. doi: 10.5812/aapm.94498. [PubMed: 31903331]. [PubMed Central: PMC6935250].
20. Li Y, Gong L, Wu X, Gao H, Zheng H, Lan W. Randomized controlled trial of hysteroscopy or ultrasonography versus no guidance during D&C after uterine artery chemoembolization for cesarean scar pregnancy. *Int J Gynaecol Obstet*. 2016;**135**(2):158–62. doi: 10.1016/j.ijgo.2016.04.019. [PubMed: 27634054].
21. Oriby ME, Elrashidy A. Comparative Effects of Total Intravenous Anesthesia with Propofol and Remifentanil Versus Inhalational Sevoflurane with Dexmedetomidine on Emergence Delirium in Children Undergoing Strabismus Surgery. *Anesth Pain Med*. 2021;**11**(1). e109048. doi: 10.5812/aapm.109048. [PubMed: 34221936]. [PubMed Central: PMC8236675].
22. Janatmakan F, Nassajian N, Jarirahmadi S, Tabatabaee K, Zafari M. Comparison of the Effect of Dexmedetomidine and Remifentanil on Pain Control After Spinal Surgery: A Double-Blind, Randomized Clinical Trial. *Anesth Pain Med*. 2021;**11**(2). e111533. doi: 10.5812/aapm.111533. [PubMed: 34336614]. [PubMed Central: PMC8314072].
23. Asri S, Hosseinzadeh H, Eydi M, Marahem M, Dehghani A, Soleimanpour H. Effect of Dexmedetomidine Combined with Inhalation of Isoflurane on Oxygenation Following One-Lung Ventilation in Thoracic Surgery. *Anesth Pain Med*. 2020;**10**(1). e95287. doi: 10.5812/aapm.95287. [PubMed: 32309196]. [PubMed Central: PMC7145426].
24. Bahr MH, Rashwan DAE, Kasem SA. The Effect of Dexmedetomidine and Esmolol on Early Postoperative Cognitive Dysfunction After Middle Ear Surgery Under Hypotensive Technique: A Comparative, Randomized, Double-blind Study. *Anesth Pain Med*. 2021;**11**(1). e107659. doi: 10.5812/aapm.107659. [PubMed: 34221933]. [PubMed Central: PMC8236574].
25. Shah DM, Arora M, Trikha A, Prasad G, Sunder R, Kotwal P, et al. Comparison of dexamethasone and clonidine as an adjuvant to 1.5% lignocaine with adrenaline in infraclavicular brachial plexus block for upper limb surgeries. *J Anaesthesiol Clin Pharmacol*. 2015;**31**(3):354–9. doi: 10.4103/0970-9185.161672. [PubMed: 26330715]. [PubMed Central: PMC4541183].
26. El Mourad MB, Elghamry MR, Mansour RF, Afandy ME. Comparison of Intravenous Dexmedetomidine-Propofol Versus Ketofol for Sedation During Awake Fiberoptic Intubation: A Prospective, Randomized Study. *Anesth Pain Med*. 2019;**9**(1). e86442. doi: 10.5812/aapm.86442. [PubMed: 30881913]. [PubMed Central: PMC6412910].
27. Florio P, Puzzutiello R, Filippeschi M, D'Onofrio P, Mereu L, Morelli R, et al. Low-dose spinal anesthesia with hyperbaric bupivacaine with intrathecal fentanyl for operative hysteroscopy: a case series study. *J Minim Invasive Gynecol*. 2012;**19**(1):107–12. doi: 10.1016/j.jmig.2011.08.728. [PubMed: 22070928].
28. Sabertanha A, Shakhsemampour B, Ekrami M, Allahyari E. Comparison of Infusion of Propofol and Ketamine-Propofol Mixture (Ketofol) as Anesthetic Maintenance Agents on Blood Pressure of Patients Undergoing Orthopedic Leg Surgeries. *Anesth Pain Med*. 2019;**9**(6). e96998. doi: 10.5812/aapm.96998. [PubMed: 32280617]. [PubMed Central: PMC7118446].
29. Mohammad Khalil A, Makram Botros J, Boules ML, Gaber Ragab S. Reliable and Rapid Smooth Extubation After "Ketamine-Propfol Mixture" for Induction of General Anesthesia in Laparoscopic Drilling of

Polycystic Ovary: A Randomized, Double-blind, Comparative Study. *Anesth Pain Med*. 2021;**11**(2). e113919. doi: 10.5812/aapm.113919. [PubMed: 34336631]. [PubMed Central: PMC8314091].

30. Kucuk M, Ugur B, Ogurlu M. Comparing the administration of fentanyl 1 microg kg(-)(1) and fentanyl 0.5 microg kg(-)(1) in dilation and curettage procedures. *Gynecol Endocrinol*. 2012;**28**(9):736–9. doi: 10.3109/09513590.2011.652248. [PubMed: 22316334].
31. Sayed ADM, Mohamed AS. Intrauterine lignocaine versus paracervical block for pain relief during cervical dilatation and endometrial curettage. *Sci J Al-Azhar Med Fac Girls*. 2017;**1**(1):7–13. doi: 10.4103/sjamf.sjamf_8_17.
32. Akhondzadeh R, Olapour A, Rashidi M, Elyasinia F. Comparison of Sedation with Dexmedetomidine Alfentanil Versus Ketamine-Alfentanil in Patients Undergoing Closed Reduction of Nasal Fractures. *Anesth Pain Med*. 2020;**10**(4). e102946. doi: 10.5812/aapm.102946. [PubMed: 33134144]. [PubMed Central: PMC7539046].
33. Bettocchi S, Ceci O, Vicino M, Marello F, Impedovo L, Selvaggi L. Diagnostic inadequacy of dilatation and curettage. *Fertil Steril*. 2001;**75**(4):803–5. doi: 10.1016/s0015-0282(00)01792-1. [PubMed: 11287038].
34. Rahimzadeh P, Faiz SH, Alimian M, Mohammadian Erdi A. Remifentanil versus dexmedtomidine for posterior spinal fusion surgery. *Med J Islam Repub Iran*. 2015;**29**:215. [PubMed: 26478873]. [PubMed Central: PMC4606949].
35. Yousefian M, Farzipour S, Noroozi V, Salmanfar T. A Comparative Study of Ketofol and Thiopental Sodium in Patients undergoing Dilation and Curettage by General Anesthesia. *Rev Latinoam Hipertens*. 2018;**13**(6).
36. Rasmussen LS, Johnson T, Kuipers HM, Kristensen D, Siersma VD, Vila P, et al. Does anaesthesia cause postoperative cognitive dysfunction? A randomised study of regional versus general anaesthesia in 438 elderly patients. *Acta Anaesthesiol Scand*. 2003;**47**(3):260–6. doi: 10.1034/j.1399-6576.2003.00057.x. [PubMed: 12648190].
37. Kumar CM, Chua AWY, Imani F, Sehat-Kashani S. Practical Considerations for Dexmedetomidine Sedation in Adult Cataract Surgery Under Local/Regional Anesthesia: A Narrative Review. *Anesth Pain Med*. 2021;**11**(4). e118271. doi: 10.5812/aapm.118271. [PubMed: 34692445]. [PubMed Central: PMC8520679].
38. Janatmakan F, Nesioonpour S, Javaherforoosh Zadeh F, Teimouri A, Vaziri M. Comparing the Effect of Clonidine and Dexmedetomidine on Intraoperative Bleeding in Spine Surgery. *Anesth Pain Med*. 2019;**9**(1). e83967. doi: 10.5812/aapm.83967. [PubMed: 30881906]. [PubMed Central: PMC6408748].
39. Soltani F, Tabatabaei S, Jannatmakan F, Nasajian N, Amiri F, Darkhor R, et al. Comparison of the Effects of Haloperidol and Dexmedetomidine on Delirium and Agitation in Patients with a Traumatic Brain Injury Admitted to the Intensive Care Unit. *Anesth Pain Med*. 2021;**11**(3). e113802. doi: 10.5812/aapm.113802. [PubMed: 34540634]. [PubMed Central: PMC8438711].
40. Garg N, Panda NB, Gandhi KA, Bhagat H, Batra YK, Grover VK, et al. Comparison of Small Dose Ketamine and Dexmedetomidine Infusion for Postoperative Analgesia in Spine Surgery–A Prospective Randomized Double-blind Placebo Controlled Study. *J Neurosurg Anesthesiol*. 2016;**28**(1):27–31. doi: 10.1097/ANA.0000000000000193. [PubMed: 26018671].
41. Abdellatif MK, Ibrahim TH. Dexmedetomidine/propofol versus dexmedetomidine/ketamine versus dexmedetomidine as a sole agent for pediatric sedation during MRI. *Ain Shams J Anesthesiol*. 2019;**11**(1):1–6.