Original Article

Evaluation of anesthesia quality with three methods: "propofol + fentanyl" vs. "propofol + fentanyl + lidocaine" vs. "propofol + fentanyl + lidocaine + ketamine" in patients referred to the scoping ward

Sepehr Edalatkhah, Ebrahim Hazrati, Mahmoodreza Hashemi, Alireza Golaghaei, Behroz Kheradmand, Mohamadreza Rafiei

Research Center of Surgery and Trauma, AJA University of Medical Sciences, Tehran, Iran

Abstract

Introduction: Toleration of the complexity and pain of interventions such as endoscopy and colonoscopy is highly difficult for patients. Considering the disagreement on the method of injection of propofol, this study was performed to evaluate the quality of anesthesia using the three methods of propofol + fentanyl, propofol + fentanyl + lidocaine, and propofol + fentanyl + lidocaine + ketamine. **Methods:** This one-way blind clinical trial study included 99 patients who were admitted in three groups by block randomization method. In a group of patients that were sedated with propofol + fentanyl + lidocaine + ketamine, the dose of all drugs is reduced by half the amount of the other groups. Variables included age, sex, frequency of cough, apnea, need for jaw thrust maneuver, O_2 saturation, duration of recovery, and procedural satisfaction. Data were analyzed using SPSS version 20.0. *P* value of < 0.05 was considered to be significant. **Results:** The three groups were similar in terms of demographic characteristics. The effects of the three sedation protocols on the variables showed that patient's apnea, cough, O_2 saturation, and also proceduralist satisfaction in the group of the patient that sedated with four drugs was significantly higher ($P < 0.05$) than other groups. But there was no significant difference between the three groups when comparing the recovery time and need for jaw thrust during the procedure. **Conclusion:** The findings of the present study showed that the use of combination of "propofol + fentanyl + lidocaine + ketamine" with lower doses, significantly results in higher quality sedation compared with higher doses of "propofol + fentanyl + lidocaine" or "propofol + fentanyl" for scoping procedures.

Keywords: Fentanyl, ketamine, lidocaine, propofol, sedation

Introduction

Invasive procedures such as endoscopy and colonoscopy have been widely used for the diagnosis and treatment of diseases and have been very effective in advancing the goals of specialists.[1] However, the complexity of this method, pain, and intolerance of patients during these interventions, has led anesthesiologists to try to provide a variety of methods to sedate patients, increase their satisfaction, and improve the quality and accuracy of specialists.[2]

Also, with the increasing number of infectious diseases and their risks, preventive and protective measures are the first line of defense against infectious diseases. Therefore, the use of methods that minimize invasive interventions is at the top of the goals of the world's health systems.[3]

Address for correspondence: Dr. Mohamadreza Rafiei, Research Center of Surgery and Trauma, AJA University of Medical Sciences, Tehran, Iran.
E-mail: mo_rafiei@armyums.ac.ir.

Received: 12-07-2021 **Revised:** 25-10-2021
Accepted: 13-12-2021 **Published:** 16-02-2022

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_1387_21

How to cite this article: Edalatkhah S, Hazrati E, Hashemi M, Golaghaei A, Kheradmand B, Rafiei M. Evaluation of anesthesia quality with three methods: "propofol + fentanyl" vs. "propofol + fentanyl + lidocaine" vs. "propofol + fentanyl + lidocaine + ketamine" in patients referred to the scoping ward. J Family Med Prim Care 2022;11:672-6.

Propofol is increasingly utilized for deep sedation during esophagogastroduodenoscopy (EGD) because of its rapid onset of action, relatively rapid recovery time, and improved satisfaction among endoscopists.[3] But propofol-induced anesthesia is associated with side effects such as severe injection pain, hypotension, fear and anxiety, ischemia or myocardial infarction, and thrombophlebitis in patients. However, the use of other medications, such as ketamine, lidocaine, and fentanyl, in combination with propofol can reduce the side effects and pain of propofol injection, and increase the patients' satisfaction.[4-6]

Lidocaine is used as a pretreatment at the site of propofol injection;[7] however, it was reported that lidocaine alone could not reduce pain.[8,9] In some studies, fentanyl and butorphanol injection were used to reduce pain, and in some studies, midazolam, which has antianxiety, sedative, anticonvulsant, and muscle relaxant effects, was used to relieve pain.[10-12] Due to the contrasting results obtained from different studies and also the importance of using propofol in invasive procedures, it is necessary to investigate the use of different compounds in combination with propofol.

Therefore, this study aimed to evaluate the quality of anesthesia with the three methods of "propofol + fentanyl," "propofol + fentanyl + lidocaine," and "propofol + fentanyl + lidocaine + ketamine" in patients referred to the gastroenterology ward.

Methods and Materials

This one-way blind clinical trial study was carried out in the Department of Anesthesiology at 501 AJA hospital of the AJA University of medical sciences. The study was approved on 02/16/2021 in the Institutional Ethics Committee of AJA university of medical sciences with the ID IR.AJAUMS.REC.1399.239 and was registered on 03/12/2021 with the code IRCT20200921048789N2 in the Clinical Trial Registration Center of Iran. The study was planned for 99 patients who were referred to the scoping ward for diagnostic purposes. The clinical trial was registered before patient enrollment and patient consent was written.

Inclusion and exclusion criteria

Inclusion criteria include all patients aged 18 to 70 years who were referred to 501 AJA Hospital for scoping since the approval of the plan and sign the informed written consent form to participate in the research plan. Patient under 18 or over 70 years of age or the American Society of Anesthesiologists (ASA) physical status classification 4 or 5, History of uncontrolled blood pressure, chronic obstructive pulmonary disease (COPD), psychotic or neurological disorders, seizures, use of drugs affecting the central nervous system, and pregnancy were excluded from the study.

Patients and data collection

The sample size in this study was 99 patients who were admitted to the study by block randomization method. For this purpose, the letter A was used to place patients in the group that was sedated with "propofol + fentanyl," the letter B was used in the group with "propofol + fentanyl + lidocaine," and the letter C is used in the group with "propofol + fentanyl + lidocaine + ketamine." The size of all blocks was equal and in this three-group experiment, we used six blocks (including two people in group A, two people in group B, and two people in group C) that were obtained using random sequence generation software. Also, to hide the random sequence on the participants, opaque-sealed envelopes with random sequences (SNOSE) were used, and each sequence was recorded on a card, and the cards were placed in the envelopes, respectively. Based on the order of entry of eligible participants in the research, the envelopes were opened in order and the assigned group of the participant was determined.

The sedation was provided by a qualified and certified nurse anesthetist. In group A, patients were sedated with propofol-lipuro: initial dose 1 mg/kg and repeat dose 0.5 mg/kg every 3–5 min and fentanyl (Rotex Medica): 0.5 μg/kg single dose. In group B, patients were sedated with propofol-lipuro: initial dose 1 mg/kg and repeat dose 0.5 mg/kg every 3–5 min and fentanyl (Rotex Medica): 0.5 μg/kg single dose and lidocaine (Pasteur): 1.5 mg/kg single dose and in group C, patients were sedated with propofol (lipuro): initial dose 0.5 mg/kg and repeat dose 0.25 mg/kg every 3–5 min and fentanyl (Rotex Medica): 0.25 μg/kg single dose and lidocaine (Pasteur): 0.75 mg/kg single dose and ketamine (Rotex Medica) 0.5 mg/kg single dose. (In group C, where four drugs are used for sedation, the dose of all drugs is reduced by half the amount of the other groups.)

A questionnaire was administered to gather information on the quality of sedation represented by variables such as age, sex, frequency of cough, apnea, need for jaw thrust maneuver, O_2 saturation, duration of recovery, and procedural satisfaction.

During the endoscopic procedure, blood pressure, pulse rate, and oxygen saturation were monitored. Once the procedure was complete, patients were transferred to the recovery room where a dedicated nurse continued to monitor the patient's vital signs and other desired variables. Procedural satisfaction was measured by asking proceduralists to rate their satisfaction of sedation quality and procedure from excellent to poor. Recovery time was taken as the time it took the patient to leave the recovery room and was measured in minutes. Frequency of cough, apnea, and need for jaw thrust maneuver were also measured during and after the procedure and recorded in a questionnaire.

Statistical analysis

Data were analyzed using Statistical Package for Social Science (SPSS) for Windows (version 20.0) The Chi-square test was used to test for any associations between demographic variables, whereas the one-way ANOVA test was used to compare the continuous variables. Statistical significance was assessed at the 5% level. (P-value of < 0.05 was considered to be significant.)

Results

The baseline characteristics of 99 patients in this study are shown in Table 1. The three groups were similar in terms of demographic characteristics. There was no significant difference in age and gender ($P > 0.05$) between groups in terms of demographics [Table 1].

The effects of the three sedation protocols on the variables were evaluated. Patient's apnea ($P = 0.009$), cough ($P = 0.016$), O_2 saturation ($P = 0.034$), and also proceduralist satisfaction ($P = 0.008$) in the group of patients sedated with propofol + fentanyl + lidocaine + ketamine were found to be significantly higher ($P < 0.05$) than other groups.

According to Table 2, the need for jaw thrust during the procedure was not significantly different between the three groups. (P-value = 0.121). Also, there was no significant difference between the three groups when comparing the recovery time (P-value = 0.138).

According to data, we do not have any report of the need to jaw thrust maneuver during the procedure in Group 3. This is also true of the recovery time.

In the group of patients who were sedated with propofol + fentanyl + lidocaine + ketamine, not a single case of procedural dissatisfaction and cough of patients was recorded. Moreover, the number of patients who developed apnea during the procedure was only one. However, in the second group, three cases and in the first group, nine cases of apnea were reported in patients.

Discussion

Scoping procedures such as endoscopy and colonoscopy are often performed for diagnosis, treatment, and prevention of a variety of symptoms and diseases of the gastrointestinal tract.[13-15] Several anesthetic techniques are intended to increase tolerance and satisfaction with the procedure and reduce the risks of complications.[6,16,17]

Due to the side effects of various anesthetic drugs, there is no perfect drug at present, so we will need to find the perfect combination to achieve the perfect sedation. Several factors are important in determining whether a sedative-analgesic combination is clinically acceptable. These include hemodynamic stability, effectiveness of the sedative-analgesic, the time required for the procedure to start, and recovery times.[18,19] For

Table 1: Patients' demographic data

Groups Variable	1 (propofol + fentanyl) Means±SD *n* (%)	2 (propofol + fentanyl + lidocaine) Means±SD *n* (%)	3 (propofol + fentanyl + lidocaine + ketamine) Means±SD *n* (%)	Total	Sig.
Age	44.9±16.2	38.9±15.4	42.4±16.8		0.326
Sex					
Female	17 (51.5%)	18 (54.5%)	16 (48.5%)	51	
Male	16 (48.5%)	15 (45.5%)	17 (51.5%)	48	0.763
Total	33	33	33	99	

One-way ANOVA test./Chi-square test

Table 2: Comparison of cough, apnea, need for jaw thrust during the procedure, recovery time, proceduralist satisfaction, and O_2 saturation of patients in three groups

Groups	Variable	1 (propofol + fentanyl)	2 (propofol + fentanyl + lidocaine)	3 (propofol + fentanyl + lidocaine + ketamine)	Total	Sig.
Cough	Yes	7	3	0	10	
	No	26	30	33	89	0.016
	Total	33	33	33	99	
Apnea	Yes	9	3	1	13	
	No	24	30	32	86	0.009
	Total	33	33	33	99	
Need for jaw thrust during the procedure	Yes	4	2	0	6	
	No	29	31	33	93	0.121
	Total	33	33	33	99	
Recovery Time	<15	30	33	29	92	
	>15	3	0	4	7	0.138
	Total	33	33	33	99	
P. Satisfaction	Yes	26	31	33	90	
	No	7	2	0	9	0.008
	Total	33	33	33	99	
O_2 Saturation	<95	14	13	5	32	
	>95	19	20	28	67	0.034
	Total	33	33	33	99	

One-way ANOVA test

example, reduction in propofol consumption is an important technical aspect because the drug has no specific antidotes or antagonists, which can be considered a limiting factor for its use.[14,20,21]

The study by Nevesa *et al.*[21] showed that the combination of midazolam, fentanyl, and propofol for colonoscopy sedation reduces propofol consumption and provides greater patient satisfaction. In a study by Mazanicov *et al.*,[22] in 80 patients presenting for elective ERCP who received propofol + remifentanil, level of sedation was markedly lighter and propofol consumption significantly smaller than in the propofol infusion group The study of Amini A, *et al.*[23] showed that low-dose of fentanyl, propofol, midazolam, ketamine and lidocaine combination was more successful in induction of deep sedation compared with a regular dose of propofol and fentanyl combination. The study by Correia *et al.*[24] showed that Sedation with propofol plus fentanyl was more efficacious with a shorter recovery time compared with midazolam plus fentanyl. The study by Yan *et al.*[25] showed that ketamine + propofol had a lower frequency of adverse respiratory events in patients undergoing procedural sedation and analgesia (PSA) in the emergency department compared with propofol alone.

In our study, which was conducted for the first time in Iran to achieve an appropriate combination by comparing the combined use of four medications, including propofol, fentanyl, lidocaine, and ketamine, it was found that the combination of propofol, fentanyl, lidocaine, and ketamine, was more suitable in terms of sedating the patients and shortening the recovery period, in comparison with other studied combinations. In other words, following the injection of propofol + fentanyl + lidocaine + ketamine at a lower dose, side effects such as cough, apnea, need for jaw drifts during surgery, recovery time, and O_2 saturation decreased significantly and patient satisfaction increased, in comparison with the other two groups in the study. These results are consistent with the results of the study by Amini *et al.*[23] A higher sedation score seems to be directly related to shorter recovery time because the sedation score in the propofol + fentanyl + lidocaine + ketamine group was higher than the other two groups and consequently the recovery time was shorter.

During the study, no case was removed from any group after the intervention [Figure 1] and all three groups were equal in terms of the size of the study population until the end of the research (33 people). The mean age was the same in all three groups [according to Table 1] and all three groups were equal in terms of the number of men and women, which increases the validity of the results of this study.

Conclusion

The findings of the present study showed that the use of combination of "propofol + fentanyl + lidocaine + ketamine" with lower doses, significantly results in higher quality sedation compared with higher doses of "propofol + fentanyl + lidocaine" or "propofol + fentanyl" for scoping procedures. The use of multidrug combinations for sedation allows the use of lower doses of drugs and thus reduces side effects and increases procedural satisfaction.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient (s) has/have

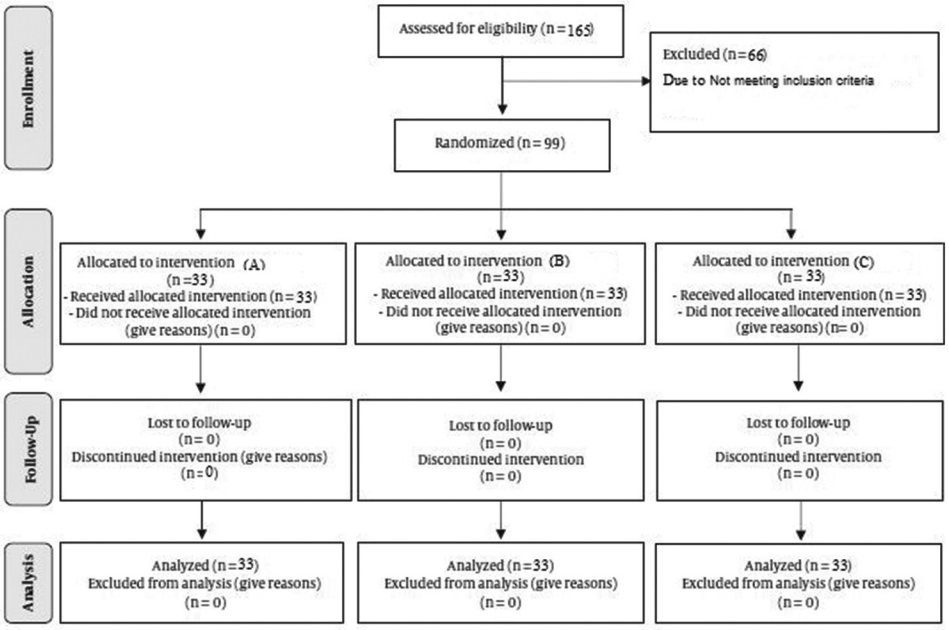

Figure 1: Overview of the study

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Ghanouni A, Plumb A, Hewitson P, Nickerson C, Rees CJ, von Wagner C. Patients' experience of colonoscopy in the english bowel cancer screening programme. Endoscopy 2016;48:232-40.
2. Cohen LB, Wecsler JS, Gaetano JN, Benson AA, Miller KM, Durkalski V, *et al.* Endoscopic sedation in the United States: Results from a nationwide survey. Ame J Gastroenterol 2006;101:967-74.
3. Radaelli F, Meucci G, Sgroi G, Minoli G. Technical performance of colonoscopy: The key role of sedation/analgesia and other quality indicators. Am J Gastroenterol 2008;103:1122-30.
4. Seip B, Bretthauer M, Dahler S, Friestad J, Huppertz-Hauss G, Høie O, *et al.* Patient satisfaction with on-demand sedation for outpatient colonoscopy. Endoscopy 2010;42:639-46.
5. Seifert H, Schmitt TH, Gültekin T, Caspary WF, Wehrmann T. Sedation with propofol plus midazolam versus propofol alone for interventional endoscopic procedures: A prospective, randomized study. Aliment Pharmacol Ther 2000;14:1207-14.
6. Goulson DT, Fragneto RY. Anesthesia for gastrointestinal endoscopic procedures. Anesthesiol Clin 2009;27:71-85.
7. Disma N, Astuto M, Rizzo G, Rosano G, Naso P, Aprile G, *et al.* Propofol sedation with fentanyl or midazolam during oesophagogastroduodenoscopy in children. Eur J Anaesthesiol 2005;22:848-52.
8. Cohen SP, Bhatia A, Buvanendran A, Schwenk ES, Wasan AD, Hurley RW, *et al.* Consensus guidelines on the use of intravenous ketamine infusions for chronic pain from the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists. Reg Anesth Pain Med 2018;43:521-46.
9. Hana Z, Abdulla S, Alam A, Ma D. Ketamine: Old drug but new use for neuropathic pain. Transl Perioper Pain Med 2018;5:1-13. doi: 10.31480/2330-4871/062.
10. Dezfouli SMM, Khosravi S. Systematic review of the effective factors in pain management in children. Pak J Med Health Sci 2020;14:1236-43.
11. Mahmoudinezhad Dezfouli SM, Khosravi S. Impact of meningitis on cognitive skills and development in children. Indian J Forensic Med Toxicol 2021;15:2674-8.
12. Forster C, Vanhaudenhuyse A, Gast P, Louis E, Hick G, Brichant JF, Joris J. Intravenous infusion of lidocaine significantly reduces propofol dose for colonoscopy: A randomised placebo-controlled study. Br J Anaesth 2018;121:1059-64.
13. Padmanabhan U, Leslie K, Eer AS, Maruff P, Silbert BS. Early cognitive impairment after sedation for colonoscopy: The effect of adding midazolam and/or fentanyl to propofol. Anesth Analg 2009;109:1448-55.
14. Ahmadi A, Polyak S, Draganov PV. Colorectal cancer surveillance in inflammatory bowel disease: The search continues. World J Gastroenterol 2009;15:61-6.
15. Lin OS. Sedation for routine gastrointestinal endoscopic procedures: A review on efficacy, safety, efficiency, cost and satisfaction. Intest Res 2017;15:456-66.
16. Jalowiecki P, Rudner R, Gonciarz M, Kawecki P, Petelenz M, Dziurdzik P. Sole use of dexmedetomidine has limited utility for conscious sedation during outpatient colonoscopy. Anesthesiology 2005;103:269-73.
17. Cappell MS. Reducing the incidence and mortality of colon cancer: Mass screening and colonoscopic polypectomy. Gastroenterol Clin North Am 2008;37:129-60, vii-viii.
18. Michaud L. Sedation for diagnostic upper gastrointestinal endoscopy: A survey of the francophone pediatric hepatology, gastroenterology, and nutrition group. Endoscopy 2005;37:167-70.
19. EL-Rab NAG, Abd El-Rahem MG, Mohamed MK. A comparative study between propofol–ketamine and propofol–fentanyl for sedation during pediatric diagnostic upper gastrointestinal endoscopy. J Curr Med Res Pract 2019;4:344.
20. Qadeer MA, Vargo JJ, Khandwala F, Lopez R, Zuccaro G. Propofol versus traditional sedative agents for gastrointestinal endoscopy: A meta-analysis. Clin Gastroenterol Hepatol 2005;3:1049-56.
21. Neves JF, Araújo MM, Araújo Fde P, Ferreira CM, Duarte FB, Pace FH, *et al.* [Colonoscopy sedation: Clinical trial comparing propofol and fentanyl with or without midazolam]. Rev Bras Anestesiol 2016;66:231-6.
22. Mazanikov M, Udd M, Kylänpää L, Lindström O, Aho P, Halttunen J, *et al.* Patient-controlled sedation with propofol and remifentanil for ERCP: A randomized, controlled study. Gastrointest Endosc 2011;73:260-6.
23. Amini A, Arhami Dolatabadi A, Kariman H, Hatamabadi H, Memary E, Salimi S, *et al.* Low-dose fentanyl, propofol, midazolam, ketamine and lidocaine combination vs. regular dose propofol and fentanyl combination for deep sedation induction; a randomized clinical trial. Emergency (Tehran, Iran) 2018;6:e57.
24. Correia LM, Bonilha DQ, Gomes GF, Brito JR, Nakao FS, Lenz L, *et al.* Sedation during upper GI endoscopy in cirrhotic outpatients: A randomized, controlled trial comparing propofol and fentanyl with midazolam and fentanyl. Gastrointest Endosc 2011;73:45-51., e1.
25. Yan JW, McLeod SL, Iansavitchene A. Ketamine-propofol versus propofol alone for procedural sedation in the emergency department: A systematic review and meta-analysis. Acad Emerg Med 2015;22:1003-13.