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

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Abstract

Introduction: Tolerance 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, O₂ 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, O₂ 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. 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.

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.
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. 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.

Lidocaine is used as a pretreatment at the site of propofol injection; however, it was reported that lidocaine alone could not reduce pain. 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. 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 IRT20200921048789N2 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, O2 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. \((P\text{-value} = 0.121)\). Also, there was no significant difference between the three groups when comparing the recovery time \((P\text{-value} = 0.138)\).

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.

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 |

| 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 | 0.016 |
| No   | 26 | 30 | 33 | 89 | 99 |
| Total | 33 | 33 | 33 | 99 |
| Apnea | Yes | 9 | 3 | 1 | 13 | 0.009 |
| No   | 24 | 30 | 32 | 86 | 99 |
| Total | 33 | 33 | 33 | 99 |
| Need for jaw thrust during the procedure | Yes | 4 | 2 | 0 | 6 | 0.121 |
| No   | 29 | 31 | 33 | 93 | 99 |
| Total | 33 | 33 | 33 | 99 |
| Recovery Time | <15 | 30 | 33 | 29 | 92 | 0.138 |
| >15 | 3 | 0 | 4 | 7 |
| Total | 33 | 33 | 33 | 99 |
| P. Satisfaction | Yes | 26 | 31 | 33 | 90 | 0.008 |
| No   | 7 | 2 | 0 | 9 |
| Total | 33 | 33 | 33 | 99 |
| \(O_2\) Saturation | <95 | 14 | 13 | 5 | 32 | 0.034 |
| >95 | 19 | 20 | 28 | 67 | 99 |
| Total | 33 | 33 | 33 | 99 |
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.\textsuperscript{[14,20,21]}

The study by Nevesa et al.\textsuperscript{[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.,\textsuperscript{[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.\textsuperscript{[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.\textsuperscript{[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.\textsuperscript{[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 \textit{O}_2 \text{ 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.\textsuperscript{[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](image-url)
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.

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**Conflicts of interest**

There are no conflicts of interest.

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