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**Safety of applying midazolam-ketamine-propofol sedation combination under the supervision of endoscopy nurse with patient-controlled analgesia pump in colonoscopy**

Kayaaltı S *et al*. Safety of colonoscopy sedation by endoscopy nurse

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**Abstract**

***AIM***

To compare the results of midazolam-ketamine-propofol sedation performed by endoscopy nurse and anaesthetist during colonoscopy in terms of patient satisfaction and safety.

***METHODS***

American Statistical Association (ASA) I-II 60 patients who underwent colonoscopy under sedation were randomly divided into two groups [sedation under the supervision of anaesthetist (SSA) and sedation under the supervision of endoscopy nurse (SSEN)]. Both groups were initially administered 1 mg of midazolam, 50 mg of ketamine and 30-50 mg of propofol. Continuation of sedation was performed by the anaesthetist in the SSA group and the nurse with patient-controlled analgesia (PCA) pump in the SSEN group. The total propofol consumption, the duration of the procedure, recovery times, the pain [visual analogue scale (VAS)] and satisfaction score of the patients, and side effects were recorded. In addition, the patients were asked whether they remembered the procedure, and whether they would re-prefer the same method in case of re-endoscopy.

***RESULTS***

The total propofol consumption in the SSEN group was found to be significantly higher (*P*0.05) than that of the SSA group. When the groups were compared in terms of VAS score, recovery time, patient satisfaction, recall of the procedure, re-preference for the same method in case of re-endoscopy, and side effects, there were no significant differences (*P* > 0.05) between the two groups. Any long-term and requiring intervention side effects were not observed in both groups.

***CONCLUSION***

Colonoscopy sedation in ASA I-II patients can be safely performed by an endoscopy nurse using PCA pump with the incidence of side effects and patient satisfaction levels similar to sedation under anaesthetist supervision.

**Key words:** Patient-controlled analgesia pump; Colonoscopy; Nurse-administered sedation; Midazolam-ketamine-propofol combination

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**Core tip:** Sedation is frequently performed during interventional procedures such as colonoscopy. In case there are not enough anaesthetists, there are a variety of sedation protocols also applied by educated non-anaesthesia personnel. In our study, we showed that midazolam-ketamine-propofol combination can be applied under the supervision of an endoscopy nurse.

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**INTRODUCTION**

Gastrointestinal endoscopy practices have been increasing worldwide. During colonoscopy, patients do not want to be awake because of severe abdominal pain, cramps and bloating as well as embarrassment[1]. The demand for sedation in colonoscopies is increasing because of the influence of image quality in colorectal cancers and the increase in expectation of painless treatment of patients[2].

A variety of sedation techniques are used during colonoscopy. Sedoanalgesia, deep sedation under the supervision of anaesthetist (SSA), sedation under the supervision of nurse, and computer assisted sedation with target-controlled devices are among these techniques[3]. Medications used and applied techniques vary from clinic to clinic. The most commonly used agent is the midazolam. It is used alone or in combination with an opioid (meperidine, fentanyl or alfentanyl). The second most frequently used agent is propofol. Propofol may be used alone or in combination with an opioid analgesic agent or midazolam[2]. Propofol is a short-acting sedative agent without analgesic properties[4]. Therefore, when propofol is used alone, high doses are required to tolerate some invasive procedures. This can lead to life-threatening conditions such as hypotension and respiratory depression[5]. Adding opioids to the propofol reduces the incidence of side effects and also allows patients to feel less pain during the procedure. It also reduces propofol injection pain[6]. Better results are obtained when combined with propofol and ketamine which provide dissociative anaesthesia[7]. Both fentanyl and ketamine provide anaesthesia, analgesia, and anxiolysis. The delayed peak levels and prolonged duration of action of fentanyl are significant disadvantages. After intravenous administration, it reaches its peak level in 4-6 min and its duration of action ends in 20-40 min. Ketamine also has a good safety profile with the advantage of preserving spontaneous breathing and protective airway reflexes[8,9]. In our study, these features are important for sedation safety, since sedation is performed by non-anaesthesia personnel.

It is claimed that the application of propofol without anaesthetist is dangerous. Even in the United States, the Food and Drug Administration recommends that the propofol should be performed only by trained anaesthesia personnel[10,11]. However, a worldwide study has shown that no major complications occur in patients (less than 1% of 142863 patients)[12]. Patient-controlled analgesia (PCA) pump was developed for postoperative pain control. In this regard, the patient applies his own pain medication according to the need himself. The PCA pump was then used with the same logic to provide sedation rather than analgesia in several studies. There are also studies where sedation applications have been performed under the supervision of a nurse or endoscopist using these pre-programmed devices[13]. In this study, we aim to compare the application of midazolam-ketamine-propofol combination by endoscopy nurse with PCA pump and anaesthetist in terms of patient satisfaction and side effect (safety).

**MATERIALS AND METHODS**

After receiving the approval of the ethical committee of the Medical School of Erciyes University and the informed consent of the patients, the study included the American Statistical Association (ASA) I-II 60 patients who underwent the elective colonoscopy between 18 and 75 years of age. The study protocol was registered at ClinicalTrials.gov (NCT03607110, https://clinicaltrials.gov/ct2/show/NCT03607110). ASA III-IV-V patients, who have uncontrolled chronic disease (uncontrolled diabetes mellitus and hypertension), severe respiratory and cardiopulmonary insufficiency or liver, and kidney failure who did not accept the method were not included in the study. Patients with long-term analgesic, opioid, and sedative history of use, with hypersensitivity to soybean oil or eggs, and drugs used in our study, with pregnancy or pregnancy suspected or lactating, and with the use of antipsychotic or antidepressant drugs were also excluded in the examination.

Before the procedure, the group in which the patients would be included was randomly determined by the endoscopy nurse. The patients were given a proper diet before the procedure and the intestinal cleansing was -implemented. After 8 h of fasting, the peripheral vascular route was opened with a 20G cannula and 8 mL kg/h crystalloid solution was performed. Prior to sedation, all patients were monitored for heart rate, mean arterial pressure, and peripheral oxygen saturation (SpO2) measurements. All patients were given 5 lt/min oxygen with nasal cannula. Colonoscopy; was performed by two experienced endoscopists who were trained in the same center on the same dates.

During the procedure, the monitored data and the cardiopulmonary side effects were recorded once in a minute for the first 5-min period and once in every 5 min in the next period. In the SSA group, the anaesthetist was at the bedside of the patient. A total of two nurses, one was trained for sedation and the other of whom would assist the endoscopist during the colonoscopy, were presented in the supervision of endoscopy nurse (SSEN) group. The nurse trained for sedation was informed about possible side effects such as desaturation (< 90%), hypotension (systolic < 90 mm-Hg), and bradycardia (< 50) during the procedure and was also trained to perform the necessary interventions (such as jaw-thrust and head tilt chin lift manoeuvres or using oropharyngeal airway in case of desaturation or atropine administration in case of bradycardia or 250 cc of fluid loading in case of hypotension). If hypotension is continued, 5-10 mg IV ephedrine will be administered. In cases where peripheral oxygen saturation don’t increase or continue to decline (below 85) the anaesthetist will intervene. In the case of long-term desaturation, the materials required for emergency airway management (bag mask ventilation, intubation, *etc.*) will be available in the endoscopy room to provide respiratory support. The anaesthetist was not at the bedside of the patient in the group SSA. However, the anaesthetist was ready in the endoscopy unit for intervention in emergency situations such as intubation and cardiopulmonary resuscitation.

Sedation protocol: Both groups were initially administered 1 mg of midazolam, 50 mg of ketamine, and 30-50 mg of propofol (30 mg in patients over 65 years old and 50 mg in patients under 65 years old). Afterwards, the propofol required for the SSA group was determined and administered by the anaesthetist to provide adequate sedation and patient comfort. For SSEN group, the continuation of sedation was performed by endoscopy nurse using PCA pump (Accumate 1100; Woo Young Medical, Seoul, Korea). Each time the endoscopy nurse pressed the PCA pump according to the patient’s clinical response or tolerance, the patient was administered propofol 10-20 mg (10 mg in patients over 65 years old, 20 mg in patients under 65 years) with a delay of about 10-20 s. At the end of the procedure, the total drug consumption, the duration of the procedure, and the patients’ eye opening/recovery times were recorded.

Patient Satisfaction: Patients were monitored until the Aldrete Recovery Score (ARS) was ≥ 9. Patients with the ARS ≥ 9 were transferred to another eligible unit. In order to evaluate patient satisfaction, the patients were asked of questions about the procedure in this unit. A visual analogue scale (VAS) was used to evaluate the pain after the procedure. Patients were asked to rate their pain on a scale of 0-10. Zero (0) would mean “no pain” and ten (10) would mean “worst imaginable pain”.

Patients were also questioned about whether they remembered the operation and side effects. Side effects such as hypotension, bradycardia and desaturation, which require serious and rapid intervention, and frequently encountered side effects such as nausea, vomiting, and headache, which may adversely affect patient satisfaction, included in the patient follow-up form as main substances. Apart from these side effects, endoscopy nurse was especially informed about complications related to ketamine such as emergence reactions, hypertension, tachycardia, visual hallucinations, vivid dreams, tonic-clonic movements, diplopia, and nystagmus. However, in the patient follow-up form, these side effects were not mentioned separately, were included under the title of other side effects. In addition, patient satisfaction was determined by satisfaction score of 4 (1 very good, 2 good, 3 not bad, 4 bad). Two days after the procedure, the patients were asked whether they would re-prefer for the same method in case of re-endoscopy and their answers were recorded. Patients were questioned for possible delayed side effects when they were contacted 2 d after the colonoscopy to determine method preference.

***Statistical method***

Mean SD, median lowest, highest, frequency, and ratio values were used in the descriptive statistics of the data. The distribution of the variables was measured by the Kolmogorov Smirnov test. Mann-Whitney *U* test was utilized in the analysis of quantitative independent data. Chi-square test was -employed to analyse qualitative independent data, and Fischer test was used when chi-square test conditions were not met. In all analyses, the *P*-value < 0.05 was considered as statistically significant. SPSS 22.0 program was used in the analyses.

**RESULTS**

There was no significant difference (*P* > 0.05) between SSA group and SSEN group in terms of demographic data such as age, gender distribution, and ASA distribution. Patients’ demographic data is given in Table 1.

The total propofol used in the SSEN group was found to be significantly higher (*P* < 0.05) than the SSA group. Reaching the cecum and total procedure time in the SSEN group were found to be significantly higher (*P* < 0.05) than in the SSA group (Table 2).

When patients were asked about their satisfaction, 1 patient in the SSEN group and 5 patients in the SSA group expressed their satisfaction as “not bad”, the rest of patients expressed their satisfaction with “good” or “very good”. In each groups, 3 patients said that they remembered the procedure. All patients in both groups except 2 patients in the SSA group stated that they would re-prefer the same method for the second time. However, when the groups were compared in terms of patient satisfaction, recall of the procedure, and re-preferring the same method in case of re-endoscopy, there was no significant difference (*P* > 0.05) between the two groups (Table 2).

Patients’ pain was evaluated by VAS score after the procedure. The highest recorded VAS value is 4. In each groups, only one patient had a VAS score of 4. The mean value of the VAS score is 1 in each group. Recovery times are also similar between the two groups. There was no statistically significant difference (*P* > 0.05) between the two groups in terms of VAS score and recovery time.

Two groups were also compared in terms of hemodynamic parameters recorded during the procedure. Pulse values taken at the baseline, 1st minute, 2nd minute, 3rd minute, 4th minute, 5th minute, 8th minute, and afterwards did not differ significantly between the two groups (*P* > 0.05). While the systolic and diastolic pressure values of the SSA and SSEN groups did not differ significantly (*P* > 0.05) at the baseline, 1st minute, 2nd minute, 3rd minute, and 4th minute, Systolic and diastolic pressure values were found to be significantly lower (*P* < 0.05) in the SSEN group than in the SSA group in the 5th minute, 8th minute, and afterwards. SPO2 values for the baseline and 1st minute in the SSEN group were found to be significantly higher (*P* < 0.05) than in the SSA group, There was no significant (*P* > 0.05) difference in SPO2 values for 2nd minute, 3rd minute, 4th minute, 8th minutes and afterwards between the two groups (Table 3).

The groups were also compared in terms of the side effects that might occur during the procedure. In each groups, hypotension and headache occurred in 2 patients. Bradycardia was observed in only 1 patient in the SSEN group. When the groups were compared in terms of desaturation, 4 patients in the SSEN group and 1 patient in the SSA group had desaturation. Nausea and vomiting were not seen in either group. However, there was no statistically significant difference (*P* > 0.05) between the two groups (Table 4).

**DISCUSSION**

In the majority of developed countries, various sedation applications are made for endoscopic procedures in low-risk patients. When we examine the agents used for analgesia and sedation in endoscopic procedures over time; meperidine was first used as an analgesic, followed by extensive use of the meperidine diazepam combination. This combination, which is often preferred, is accepted as a traditional sedation method. Later, midazolam was preferred in endoscopy sedation with shorter duration of action and higher efficacy than diazepam. A few years after midazolam, propofol, an ultra-short acting hypnotic agent, started to be used[2].

Propofol sedation is becoming more popular day by day due to its features such as pain relief during endoscopy and the ability to have a quick recovery time[3]. However, it is controversial whether the propofol should be applied by anaesthesia personnel or educated non-anaesthesia personnel. In European and American guidelines, it is stated that sedation applied by non-anaesthesia personnel should be applied only in low-risk patients and that sedation personnel should be qualified to rescue patients from any level of sedation including general anaesthesia[14]. However, in various studies it has been shown that sedation performed by non-anaesthesia personnel can be safely performed as long as it is performed by educated personnel[15-18]. Walker *et al*[19] showed that sedation performed by non-anaesthesia personnel in colonoscopy can be applied more easily and with lower risk than esophagogastroduodenoscopy. In a study/review by Rex *et al*[16], records of sedation applications performed by non-anaesthesia personnel from various centers around the world have been reviewed and evaluated. In this review/study involving 646080 patients, only 11 cases of emergency endotracheal intubation and 4 deaths were reported.

In guidelines for propofol administration of non-anaesthesia personnel, it has been stated that ASA III and over patient procedures, long complex procedures, and difficult airway conditions require an anaesthetic personnel[14,20]. In our study, ASA I-II patients were included in the study. There are a variety of studies on sedation applications without anaesthesia personnel in patients undergoing the colonoscopy. Patient-controlled sedation (PCS) studies were conducted in which the patient determined his/her own sedation level with PCA pump[13,21]. In this method, the patients press the button when they feel uncomfortable. A certain period of time passes until they are sedated. In these studies, it is mentioned that patients suffer from pain, although not severe. Feeling pain and time to get sedated may cause patients to opt out the method. For this reason, sedation practices under the SSEN are increasing rapidly in recent years. It has been shown in several studies that sedation and colonoscopy practices under the SSEN are safe and effective[19,22,23]. In a study comparing PCS with SSEN, it has been shown that many patients prefer SSEN instead of PCS because of the anxiety they feel[24]. We also preferred SSEN instead of PCS in our study. We applied propofol with the PCA pump in order to reduce the human-caused mistakes. The PCA pump allows us to easily dispense the right dose of medicine repeatedly without requiring our attention.

In the study by Poon *et al*[25], it was found that SSEN with PCA pump was effective and safe in healthy individuals who would undergo colonoscopy. In another study by Liu *et al*[26], while a group was administered propofol-alfentanil by method of SSEN with PCA pump, opioid-benzodiazepine was administered to the other group by the anaesthetist. As a result of the study, there was no significant difference between groups in terms of side effects, pain scores, and the willingness to repeat the colonoscopy with the same sedation method. In the SSEN group, it was stated that only deeper sedation was obtained. Since two sets of sedation protocols were applied, it was thought that this situation was caused by the difference in drug combinations used rather than SSEN method.

In a sedation protocol, the total amount of drug used is reduced due to the synergistic effect of drugs on each other formed by adding adjuvant drugs in addition to propofol[6]. Total doses of propofol used in previous studies ranged from 124 to 188 mg[19,25-28]. Lower levels of propofol were used in studies where propofol was used in combination with other medicines[25,26], when compared studies where propofol alone used[19,27,28]. In our study, the consumption of propofol decreased as expected by the addition of ketamine, which provides analgesia and dissociative anaesthesia, and midazolam, which has amnesic and sedative properties, to the sedation protocol. The total amount of propofol used in both groups was significantly lower than the previous studies in which the SSEN method was applied. (The consumption of propofol in the SSEN group and SSA group was 83.0 ± 57.1, 59.7 ± 17.5 respectively). In our study, propofol consumption was significantly higher in the SSEN group. The reason for this significant difference in propofol consumption was thought to be the longer duration of the operations in the SSEN group. The duration of the procedure is significantly higher in the SSEN group than in the SSA group. When interviewed with the endoscopist, it was stated that two sedation methods did not affect the difficulty of operation. Therefore, this difference may be due to the small number of patients or the fact that the procedure was performed by two different endoscopists.

Cardiovascular and respiratory depression can be observed during sedation. Our most important goal in colonoscopy sedation is to ensure the safety of patients as well as comfort. For this reason, we aimed to have less cardiovascular and respiratory side effects by using lower doses of propofol with a combined sedation protocol. There is no analgesic activity of propofol. However, it has a synergistic effect when used with analgesic agents[29]. In a study by Hsu *et al*[30], one group of patients who underwent gastrointestinal endoscopy were performed sedation with propofol alone and the other group with propofol-midazolam-fentanyl combination. As a result, it was stated that propofol alone group had higher total propofol consumption and incidence of hypotension; the recovery time of this group was also longer. Some clinicians avoid propofol administration without anaesthetist because of the absence of propofol antidote in a possible cardiopulmonary complication. However, the short duration of the propofol balances this negative feature. In our study, no serious long-term side effects were observed in any of the patients. All of the cardiopulmonary side effects that occurred were ended shortly (less than 30 s) without the need for intervention. Of course, a much safer SSEN application can be achieved by the fact that the patient is closely followed up with monitored and sedation practitioners is trained in cardiopulmonary resuscitation. Only low-risk patients with ASA I-II were included in our study, but Heuss *et al*[31] showed that propofol can be safely applied in gastrointestinal endoscopy even in high-risk patients. They stated that these patients should be more closely monitored in terms of desaturation and propofol use in these patients would be appropriate at doses of 10%-20% lower than in ASA I-II patients.

Complications such as emergence reactions, hypertension, tachycardia, visual hallucinations, vivid dreams, tonic-clonic movements, diplopia, nystagmus, increased intracranial pressure, and increased intraocular pressure are among the complications associated with ketamine[32]. Even 24 h after application, side effects such as severe confusion, hallucinations, unusual thoughts, or extreme fear can be seen[33]. In our study, nausea, vomiting, and agitation that were the possible side effects due to ketamine added to the sedation protocol were not observed in any of the patients in both groups[34]. The use of ketamine in combination with low doses of propofol and midazolam may have reduced the incidence of side effects. Guit *et al*[35] showed that ketamine-related side effects are reduced, when ketamine is combined with propofol.

In our study, several questions were asked to patients in order to determine patient satisfaction, which is one of our primary goals. There was no significant difference between the groups in terms of patient satisfaction score and re-preference for the same sedation method in case of re-endoscopy. All of the patients in the SSEN group and 93.3% of the patients in the SSA group stated that they would re-prefer the same sedation method in case of re-endoscopy. Poon et al. reported that 92% of patients would re-prefer the same sedation method in a new endoscopy procedure[25]. The result of our study is similar to the results of this study. One of the questions asked to evaluate patient satisfaction is whether the patient remembered the operation. There was no significant difference between the groups in terms of recall of the procedure. Adequate sedation and pain control provides a comfortable and successful colonoscopy. When the pain status of the patients was questioned in our study, 96.6% of the patients in the SSEN group and 86.6% of the patients in the SSA group were found to have a VAS below 1. Liu *et al*[26] also compared the two sedation methods under the supervision of an anaesthetist/nurse using PCA pump. In their study, there was no significant difference between the groups in terms of patient satisfaction and VAS values.

In conclusion,this study demonstrated that the combination of midazolam-ketamine-propofol could be performed under the supervision of both anaesthetist and endoscopy nurse with a PCA device in colonoscopy sedation of low-risk (ASA I-II) patients with similar side effects. There is a need for further studies with ASA III-IV patients and also with more patients.

A small sample size ASA I-II patients with low cardiovascular risk were included in the study. The expected incidence of adverse events is less than 0.01%, and studies with a small sample size may reduce this rate.

**Article Highlights**

***Research background***

Sedation is performed in many centers during the colonoscopy procedure. However, since there are a limited number of anesthesiologists, there are centers where colonoscopy is performed without sedation. In the literature, there are several studies in which colonoscopy sedation is performed without anesthesia personnel. In this study, we aim to evaluate the patient satisfaction and the side effects of colonoscopy sedation performed by endoscopy nurse with patient-controlled analgesia (PCA) pump.

***Research motivation***

In studies where colonoscopy sedation was performed under the supervision of a nurse, propofol is often used alone or in combination with agents such as fentanyl, meperidine or midazolam. Ketamine, which protects spontaneous breathing and protective airway reflexes by providing dissociative anesthesia, was not used in colonoscopy in adult patients. In our study, we wanted to determine the advantages and disadvantages of ketamine in combination with propofol and midazolam without anesthesia personnel in colonoscopy.

***Research objectives***

It is aimed to perform ketamine-midazolam-propofol sedation with minimum side effects and to obtain the best patient satisfaction under the supervision of a nurse in low risk patients in colonoscopy. Individual dose errors were tried to be minimized by using PCA pump.

***Research methods***

60 American Statistical Association (ASA) I-II patients who underwent colonoscopy were included in the study. Patients were randomly divided into two groups [sedation under the supervision of anaesthetist (SSA) and sedation under the supervision of endoscopy nurse (SSEN)]. Both groups were initially administered 1 mg of midazolam, 50 mg of ketamine, and 30-50 mg of propofol. Then the required dose of propofol in SSA group was determined and administered by anesthesiologist. In SSEN group, the continuation of sedation was carried out by the nurse with PCA pump. Data such as patient satisfaction, incidence of side effects, total drug consumption, and duration of procedure were recorded and differences among the groups were evaluated.

***Research results***

There were no statistically significant differences (*P* ˃ 0.05) between the two groups in terms of patient satisfaction, the rate of re-preference for the same method in case of re-endoscopy, and the side effects. The total propofol consumption in the SSEN group was significantly higher (*P* < 0.05), whereas the systolic and diastolic pressure values were found to be significantly lower (*P* < 0.05) at 5 min, and after 8 min. Reaching the cecum and total procedure time were significantly longer (*P* < 0.05) in the SSEN group. No significant prolonged side effects were observed in both groups.

***Research conclusions***

In ASA I-II patients, sedation under the supervision of nurses with PCA pump in colonoscopy has similar side effects and patient satisfaction levels as sedation under SSA.

***Research perspectives***

There is a need for further studies with ASA III-IV patients and also with more patients.

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**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**: 232-240 [PMID: 26841268 DOI: 10.1055/s-0042-100613]

2 **Ferreira AO**, Cravo M. Sedation in gastrointestinal endoscopy: Where are we at in 2014? *World J Gastrointest Endosc* 2015; **7**: 102-109 [PMID: 25685266 DOI: 10.4253/wjge.v7.i2.102]

3 **Lin OS**. Sedation for routine gastrointestinal endoscopic procedures: a review on efficacy, safety, efficiency, cost and satisfaction. *Intest Res* 2017; **15**: 456-466 [PMID: 29142513 DOI: 10.5217/ir.2017.15.4.456]

4 **Faulx AL**, Vela S, Das A, Cooper G, Sivak MV, Isenberg G, Chak A. The changing landscape of practice patterns regarding unsedated endoscopy and propofol use: a national Web survey. *Gastrointest Endosc* 2005; **62**: 9-15 [PMID: 15990813 DOI: 10.1016/S0016-5107(05)00518-3]

5 **Türk HŞ**, Aydoğmuş M, Ünsal O, Köksal HM, Açik ME, Oba S. Sedation-analgesia in elective colonoscopy: propofol-fentanyl versus propofol-alfentanil. *Braz J Anesthesiol* 2013; **63**: 352-357 [PMID: 23931250 DOI: 10.1016/j.bjan.2012.07.006]

6 **Joo HS**, Perks WJ, Kataoka MT, Errett L, Pace K, Honey RJ. A comparison of patient-controlled sedation using either remifentanil or remifentanil-propofol for shock wave lithotripsy. *Anesth Analg* 2001; **93**: 1227-1232 [PMID: 11682403 DOI: 10.1097/00000539-200111000-00037]

7 **Alletag MJ**, Auerbach MA, Baum CR. Ketamine, propofol, and ketofol use for pediatric sedation. *Pediatr Emerg Care* 2012; **28**: 1391-5; quiz 1396-8 [PMID: 23222112 DOI: 10.1097/PEC.0b013e318276fde2]

8 **Green SM**, Krauss B. Clinical practice guideline for emergency department ketamine dissociative sedation in children. *Ann Emerg Med* 2004; **44**: 460-471 [PMID: 15520705 DOI: 10.1016/S0196064404006365]

9 **Strayer RJ**, Nelson LS. Adverse events associated with ketamine for procedural sedation in adults. *Am J Emerg Med* 2008; **26**: 985-1028 [PMID: 19091264 DOI: 10.1016/j.ajem.2007.12.005]

10 **Rex DK**. Effect of the Centers for Medicare &amp; Medicaid Services policy about deep sedation on use of propofol. *Ann Intern Med* 2011; **154**: 622-626 [PMID: 21536938 DOI: 10.7326/0003-4819-154-9-201105030-00007]

11 **Aisenberg J**, Cohen LB, Piorkowski JD Jr. Propofol use under the direction of trained gastroenterologists: an analysis of the medicolegal implications. *Am J Gastroenterol* 2007; **102**: 707-713 [PMID: 17397402 DOI: 10.1111/j.1572-0241.2006.00955.x]

12 **Lienhart A,** Carli P, Marty J, Pourriat J. Digestive endoscopies: who does what? Proceedings of the Annales francaises d'anesthesie et de reanimation 2002: 343-346

13 **Crepeau T**, Poincloux L, Bonny C, Lighetto S, Jaffeux P, Artigue F, Walleckx P, Bazin JE, Dapoigny M, Bommelaer G. Significance of patient-controlled sedation during colonoscopy. Results from a prospective randomized controlled study. *Gastroenterol Clin Biol* 2005; **29**: 1090-1096 [PMID: 16505753 DOI: 10.1016/S0399-8320(05)82172-4]

14 **American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists.**. Practice guidelines for sedation and analgesia by non-anesthesiologists. *Anesthesiology* 2002; **96**: 1004-1017 [PMID: 11964611 DOI: 10.1097/00000542-200204000-00031]

15 **Sieg A**; bng-Study-Group, Beck S, Scholl SG, Heil FJ, Gotthardt DN, Stremmel W, Rex DK, Friedrich K. Safety analysis of endoscopist-directed propofol sedation: a prospective, national multicenter study of 24 441 patients in German outpatient practices. *J Gastroenterol Hepatol* 2014; **29**: 517-523 [PMID: 24716213 DOI: 10.1111/jgh.12458]

16 **Rex DK**, Deenadayalu VP, Eid E, Imperiale TF, Walker JA, Sandhu K, Clarke AC, Hillman LC, Horiuchi A, Cohen LB, Heuss LT, Peter S, Beglinger C, Sinnott JA, Welton T, Rofail M, Subei I, Sleven R, Jordan P, Goff J, Gerstenberger PD, Munnings H, Tagle M, Sipe BW, Wehrmann T, Di Palma JA, Occhipinti KE, Barbi E, Riphaus A, Amann ST, Tohda G, McClellan T, Thueson C, Morse J, Meah N. Endoscopist-directed administration of propofol: a worldwide safety experience. *Gastroenterology* 2009; **137**: 1229-37; quiz 1518-9 [PMID: 19549528 DOI: 10.1053/j.gastro.2009.06.042]

17 **Rex DK**, Heuss LT, Walker JA, Qi R. Trained registered nurses/endoscopy teams can administer propofol safely for endoscopy. *Gastroenterology* 2005; **129**: 1384-1391 [PMID: 16285939 DOI: 10.1053/j.gastro.2005.08.014]

18 **Sathananthan D**, Young E, Nind G, George B, Ashby A, Drummond S, Redel K, Green N, Singh R. Assessing the safety of physician-directed nurse-administered propofol sedation in low-risk patients undergoing endoscopy and colonoscopy. *Endosc Int Open* 2017; **5**: E110-E115 [PMID: 28210707 DOI: 10.1055/s-0042-121667]

19 **Walker JA**, McIntyre RD, Schleinitz PF, Jacobson KN, Haulk AA, Adesman P, Tolleson S, Parent R, Donnelly R, Rex DK. Nurse-administered propofol sedation without anesthesia specialists in 9152 endoscopic cases in an ambulatory surgery center. *Am J Gastroenterol* 2003; **98**: 1744-1750 [PMID: 12907328 DOI: 10.1111/j.1572-0241.2003.07605.x]

20 **Dumonceau JM**, Riphaus A, Beilenhoff U, Vilmann P, Hornslet P, Aparicio JR, Dinis-Ribeiro M, Giostra E, Ortmann M, Knape JT, Ladas S, Paspatis G, Ponsioen CY, Racz I, Wehrmann T, Walder B. European curriculum for sedation training in gastrointestinal endoscopy: position statement of the European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA). *Endoscopy* 2013; **45**: 496-504 [PMID: 23702777 DOI: 10.1055/s-0033-1344142]

21 **Sultan SS**. Patient-controlled sedation with propofol/remifentanil versus propofol/alfentanil for patients undergoing outpatient colonoscopy, a randomized, controlled double-blind study. *Saudi J Anaesth* 2014; **8**: S36-S40 [PMID: 25538518 DOI: 10.4103/1658-354X.144068]

22 **Sieg A**. Propofol sedation in outpatient colonoscopy by trained practice nurses supervised by the gastroenterologist: a prospective evaluation of over 3000 cases. *Z Gastroenterol* 2007; **45**: 697-701 [PMID: 17701858 DOI: 10.1055/s-2007-963349]

23 **Tohda G**, Higashi S, Wakahara S, Morikawa M, Sakumoto H, Kane T. Propofol sedation during endoscopic procedures: safe and effective administration by registered nurses supervised by endoscopists. *Endoscopy* 2006; **38**: 360-367 [PMID: 16680635 DOI: 10.1055/s-2005-921192]

24 **Heuss LT**, Drewe J, Schnieper P, Tapparelli CB, Pflimlin E, Beglinger C. Patient-controlled versus nurse-administered sedation with propofol during colonoscopy. A prospective randomized trial. *Am J Gastroenterol* 2004; **99**: 511-518 [PMID: 15056094 DOI: 10.1111/j.1572-0241.2004.04088.x]

25 **Poon CM**, Leung TL, Wong CW, Chan YL, Leung TC, Leong HT. Safety of nurse-administered propofol sedation using PCA pump for outpatient colonoscopy in Chinese patients: a pilot study. *Asian J Surg* 2007; **30**: 239-243 [PMID: 17962125 DOI: 10.1016/S1015-9584(08)60032-9]

26 **Liu SY**, Poon CM, Leung TL, Wong CW, Chan YL, Leung TC, Leong HT. Nurse-administered propofol-alfentanil sedation using a patient-controlled analgesia pump compared with opioid-benzodiazepine sedation for outpatient colonoscopy. *Endoscopy* 2009; **41**: 522-528 [PMID: 19440955 DOI: 10.1055/s-0029-1214711]

27 **Sipe BW**, Rex DK, Latinovich D, Overley C, Kinser K, Bratcher L, Kareken D. Propofol versus midazolam/meperidine for outpatient colonoscopy: administration by nurses supervised by endoscopists. *Gastrointest Endosc* 2002; **55**: 815-825 [PMID: 12024134 DOI: 10.1067/mge.2002.124636]

28 **Külling D**, Rothenbühler R, Inauen W. Safety of nonanesthetist sedation with propofol for outpatient colonoscopy and esophagogastroduodenoscopy. *Endoscopy* 2003; **35**: 679-682 [PMID: 12929064 DOI: 10.1055/s-2003-41518]

29 **Horn E**, Nesbit SA. Pharmacology and pharmacokinetics of sedatives and analgesics. *Gastrointest Endosc Clin N Am* 2004; **14**: 247-268 [PMID: 15121142 DOI: 10.1016/j.giec.2004.01.001]

30 **Hsu CD**, Huang JM, Chuang YP, Wei HY, Su YC, Wu JY, Wang WM, Hsu HT, Huang HF, Lu IC, Lu DV. Propofol target-controlled infusion for sedated gastrointestinal endoscopy: A comparison of propofol alone versus propofol-fentanyl-midazolam. *Kaohsiung J Med Sci* 2015; **31**: 580-584 [PMID: 26678938 DOI: 10.1016/j.kjms.2015.09.004]

31 **Heuss LT**, Schnieper P, Drewe J, Pflimlin E, Beglinger C. Safety of propofol for conscious sedation during endoscopic procedures in high-risk patients-a prospective, controlled study. *Am J Gastroenterol* 2003; **98**: 1751-1757 [PMID: 12907329 DOI: 10.1111/j.1572-0241.2003.07596.x]

32 ketamine (Rx) [cited 8 Nov 2018]. Available from: https://reference.medscape.com/drug/ketalar-ketamine-343099#4

33 Ketamine Hydrochloride (Ketamine HCl) side effects drug center [cited 8 Nov 2018]. Available from: https://www.rxlist.com/ketamine-hydrochloride-side-effects-drug-center.htm

34 **Shah A**, Mosdossy G, McLeod S, Lehnhardt K, Peddle M, Rieder M. A blinded, randomized controlled trial to evaluate ketamine/propofol versus ketamine alone for procedural sedation in children. *Ann Emerg Med* 2011; **57**: 425-33.e2 [PMID: 20947210 DOI: 10.1016/j.annemergmed.2010.08.032]

35 **Guit JB**, Koning HM, Coster ML, Niemeijer RP, Mackie DP. Ketamine as analgesic for total intravenous anaesthesia with propofol. *Anaesthesia* 1991; **46**: 24-27 [PMID: 1996747 DOI: 10.1111/j.1365-2044.1991.tb09308.x]

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**Table 1 Patients’ demographic data *n* (%)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | | **Endoscopist** | | **Anaesthetist** | | ***P*** |
| **mean ± SD** | **Median** | **mean ± SD** | **Median** |
| Age | | 53.6 ± 15.5 | 57.5 | 59.9 ± 11.8 | 62.0 | 0.1131 |
| Sex | Female | 18 (60.0) |  | 17 (56.7) |  | 0.7932 |
| Male | 12 (40.0) |  | 13 (43.3) |  |
| ASA | I | 18 (60.0) |  | 11 (36.7) |  | 0.0712 |
| II | 12 (40.0) |  | 19 (63.3) |  |

1Mann-Whitney *U* test; 2Chi-square test. ASA: American Statistical Association.

**Table 2 Information of propofol consumption, durations (reaching the cecum, operation, and recovery), patient satisfaction, operation re-preference, and recall of the procedure *n* (%)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | **Endoscopist** | | **Anaesthetist** | | ***P*** |
|  | **mean ± SD** | **Median** | **mean ± SD** | **Median** |  |
| Propofol consumption dose | | 83.0 ± 57.1 | 70.0 | 59.7 ± 17.5 | 50.0 | **0.0141** |
| Reaching the cecum (min) | | 5.8 ± 4.9 | 5.5 | 4.9 ± 2.2 | 4.0 | 0.0041 |
| Total operation (min) | | 13.7 ± 7.2 | 13.0 | 9.5 ± 3.6 | 8.5 | 0.0221 |
| Eye opening/Recovery (min) | | 1.6 ± 1.2 | 1.0 | 2.0 ± 0.8 | 2.0 | 1.0001 |
| VAS | | 0.5 ± 0.8 | 0.0 | 0.5 ± 0.9 | 0.0 | 0.8031 |
| Patient Satisfaction | I | 19 (63.3) |  | 12 (40.0) |  | 0.0982 |
| II | 10 (33.3) |  | 13 (43.3) |  |
| III | 1 (3.3) |  | 5 (16.7) |  |
| Operation re-preference? | | 30 (100.0) |  | 28 (93.3) |  | 0.4922 |
| Recall of the procedure | (-) | 27 (90.0) |  | 27 (90.0) |  | 1.0002 |
| (+) | 3 (10.0) |  | 3 (10.0) |  |
| 1Mann-Whitney *U* test; 2Chi-square test. VAS: Visual analogue scale. | | | | | | |

**Table 3 Hemodynamic changes during the procedure**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | | **Endoscopist** | | **Anaesthetist** | | ***P*1** |
| **mean ± SD** | **Median** | **mean ± SD** | **Median** |
| Pulse (beats per minute) | Baseline | 82.8 ± 13.3 | 82.5 | 84.2 ± 11.7 | 85.5 | 0.673 |
| 1st min | 81.4 ± 13.3 | 79.0 | 85.7 ± 14.6 | 84.0 | 0.251 |
| 2nd min | 80.9 ± 13.8 | 79.0 | 83.5 ± 17.9 | 81.0 | 0.*716* |
| 3rd min | 80.8 ± 13.5 | 79.0 | 80.7 ± 19.2 | 79.5 | 0.704 |
| 4th min | 81.0 ± 15.3 | 80.0 | 80.1 ± 18.5 | 77.5 | 0.665 |
| 5th min | 81.9 ± 14.6 | 81.0 | 80.5 ± 18.8 | 78.0 | 0.414 |
| ≥ 8th min | 81.1 ± 14.7 | 78.5 | 77.5 ± 14.4 | 75.0 | 0.336 |
| Systolic blood pressure (mm Hg) | Baseline | 131.0 ± 20.5 | 131.5 | 136.1 ± 22.3 | 135.0 | 0.412 |
| 1st min | 126.2 ± 17.6 | 121.0 | 129.9 ± 19.4 | 132.5 | 0.579 |
| 2nd min | 124.2 ± 13.6 | 125.0 | 125.7 ± 29.5 | 121.5 | 0.519 |
| 3rd min | 123.4 ± 13.9 | 122.0 | 126.5 ± 27.9 | 123.0 | 0.952 |
| 4th min | 126.5 ± 15.9 | 125.0 | 131.8 ± 30.3 | 129.5 | 0.448 |
| 5th min | 123.8 ± 13.4 | 122.0 | 139.3 ± 28.7 | 141.0 | 0.014 |
| ≥8th min | 124.1 ± 17.2 | 120.5 | 142.3 ± 26.7 | 141.0 | 0.003 |
| Diastolic blood pressure (mm Hg) | Baseline | 73.2 ± 12.3 | 70.5 | 73.4 ± 13.4 | 74.0 | 0.871 |
| 1st min | 70.6 ± 10.2 | 69.5 | 74.7 ± 14.0 | 74.0 | 0.183 |
| 2nd min | 71.1 ± 11.1 | 71.0 | 72.9 ± 18.3 | 69.0 | 0.988 |
| 3rd min | 71.2 ± 11.1 | 70.0 | 76.3 ± 18.2 | 75.5 | 0.359 |
| 4th min | 72.8 ± 11.1 | 72.0 | 78.7 ± 17.9 | 80.5 | 0.175 |
| 5th min | 69.2 ± 11.5 | 69.5 | 81.9 ± 17.2 | 82.0 | 0.002 |
| ≥8th min | 73.2 ± 11.8 | 70.5 | 83.4 ± 16.8 | 82.0 | 0.005 |
| SPO₂ | Baseline | 96.7 ± 1.9 | 97.0 | 94.4 ± 2.7 | 94.0 | 0.000 |
| 1st min | 96.0 ± 2.8 | 97.0 | 94.7 ± 2.4 | 95.0 | 0.014 |
| 2nd min | 96.5 ± 3.5 | 97.0 | 95.3 ± 2.2 | 95.5 | 0.071 |
| 3rd min | 96.2 ± 2.8 | 97.0 | 95.9 ± 2.0 | 95.5 | 0.307 |
| 4th min | 96.4 ± 2.3 | 97.0 | 96.3 ± 1.9 | 96.0 | 0.502 |
| 5th min | 95.1 ± 5.3 | 97.0 | 96.1 ± 1.7 | 96.0 | 0.685 |
| ≥8th min | 96.1 ± 2.3 | 97.0 | 96.0 ± 1.4 | 96.0 | 0.422 |

1Mann-Whitney *U* test.

**Table 4 Side effects experienced by patients during the procedure *n* (%)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | | **Endoscopist** | **Anaesthetist** | ***P*1** |
| Cardio pulmonary | Hypotension | 2 (6.7) | 2 (6.7) | 1.000 |
| Bradycardia | 1 (3.3) | 0 (0.0) | 1.000 |
| Desaturation | 4 (13.3) | 1 (3.3) | 0.161 |
| Other side effects | Nausea and Vomiting | 0 (0.0) | 0 (0.0) | 1.000 |
| Headache | 2 (6.7) | 2 (6.7) | 1.000 |

1Chi-square test.