THE MEDICAL BULLETIN OF
SISLI ETFAL HOSPITAL

DOI: 10.14744/SEMB.2024.37043
Med Bull Sisli Etfal Hosp 2024;58(2):189–196

Original Research

The Effects of Ketamine-Propofol and Remifentanil-Propofol Combinations on Integrated Pulmonary Index During Sedation in Gastrointestinal System Endoscopy

Zuhal Cavus, Dondu Genc Moralar, Ayfer Kaya Gok, Ali Selman Gunaydin

Department of Anaesthesiology and Reanimation, University of Health Sciences Türkiye, Gaziosmanpasa Training and Research Hospital, Istanbul, Türkiye

Abstract

Objectives: Different sedo-analgesia and monitoring methods are used during endoscopic procedures. And yet, there is no consensus on optimal sedating agents. In this study, the main aim is to compare ketamine-propofol and remifentanil propofol sedo-analgesia protocols by monitoring integrated pulmonary index (IPI).

Methods: The study population is divided into two groups: Group ketamine received 0.25 mg/kg ketamine and 0.75 mg/kg propofol at the beginning of anesthesia. 1 mcg/kg of remifentanil and 0.75 mg/kg propofol were administered to group remifentanil patients at the induction of anesthesia. Anesthesia maintenance was provided by titration of drug doses according to the Ramsey sedation scale. Measurements were taken at four different points in time: just before anesthesia was induced, five minutes after sedation was induced, ten minutes later, and five minutes after the treatment was finished.

Results: There was no significant difference in respiratory parameters such as respiratory rate, SPO2, and $EtCO_2$ measured in the T1 time period between the groups. In the T2 time period, a significant difference was found between the groups in the integrated pulmonary index (IPI), sPO2, respiratory rate, and systolic pressure parameters were found to be significantly higher in group ketamine. T3 time period results were higher in these three parameters: IPI, sPO2, and respiration rate. In the T2, T3, T4 time periods, there was a difference between the groups in the respiration count parameter and it was found to be higher in group ketamine.

Conclusion: Although it causes slight prolongation in recovery, ketamine is a safe and effective drug that can be used during endoscopic procedures.

Keywords: Capnography, endoscopy, sedation

Please cite this article as "Cavus Z, Genc Moralar D, Kaya Gok A, Gunaydin AS. The Effects of Ketamine-Propofol and Remifentanil-Propofol Combinations on Integrated Pulmonary Index During Sedation in Gastrointestinal System Endoscopy. Med Bull Sisli Etfal Hosp 2024;58(2):189–196".

Gastrointestinal endoscopy is a procedure performed for diagnostic or therapeutic purposes in gastrointestinal system diseases. The most effective method for diagnosis of gastrointestinal diseases is gastrointestinal endoscopy. Even though these procedures can be performed without sedation, as it is an invasive procedure, various sedo-analgesia-anesthesia methods are becoming widespread to provide amnesia by minimizing anxiety and pain.[1] It is known that cardiopulmonary and respiratory complications are handicaps of the use of anesthetic

Address for correspondence: Zuhal Cavus, MD. Department of Anaesthesiology and Reanimation, University of Health Sciences Türkiye, Gaziosmanpasa Training and Research Hospital, Istanbul, Türkiye
Phone: +90 532 632 31 66 **E-mail:** zuhalcavus74@gmail.com

Submitted Date: August 16, 2023 **Revised Date:** December 13, 2023 **Accepted Date:** May 03, 2024 **Available Online Date:** June 28, 2024

drugs in especially non-operating rooms.[2] Sedo-analgesia increases the safety and efficacy of endoscopic processes. Usually, complications (e.g., aspiration, oversedation, hypoventilation, vasovagal episodes, and airway obstruction) are more related to medications, and complications due to procedure (e.g. perforation, bleeding) are rare. Therefore, gastrointestinal endoscopy procedures are associated with the safety of sedation and raise concerns. These concerns make monitoring and sedation types more significant. Cardiac and respiratory minor complications are common in gastrointestinal endoscopy, especially hypoxia is an important apprehension. The incidence of hypoxia differs from 6% to 18% depending on medication and dosage. We investigated different medications' effects on the safety of endoscopic procedures by using the Integrated Pulmonary Index (IPI).

The routine use of blood pressure and pulse oximetry monitoring during endoscopy is also agreed upon in the literature. However, recommendations for sedative medications and the requirement for capnography when monitoring sedated patients are distinct.[3] The addition of capnography monitoring reduces the complications like hypoxia and hypoventilation. Hence, it is recommended that additional capnography monitoring be considered in sedation for endoscopic procedures by the U.S. and European guidelines. Using additional capnography monitoring may reduce the hypoxic events.[4,5]

The Integrated Pulmonary Index® (IPI) is an algorithm that takes account of both variables obtained by pulse oximetry, such as heart rate and arterial oxygen saturation [SpO2], and parameters measured by capnography, such as partial pressure end-tidal carbon dioxide (PetCO2) and respiratory rate. As a result, it combines the advantages of oxygenation and ventilation monitoring and may be an easy-to-use tool for maintaining a close watch on patients when they are sedated.[6] provides a score between 1 and 10, which is meant to assist the medical team in assessing the patient's respiratory state based solely on that one parameter. Numbers between 7 and 10 indicate steady characteristics, whereas numbers under 7 demand attention. The monitor alerts the endoscopic team with an audio alarm and a flashing signal around the IPI value.[7]

Different sedation protocols are defined with various medications for gastrointestinal endoscopy procedures. There is no consensus on optimal sedating agents. As the supreme drug, dose, or combination is yet to be found to provide adequate sedation during endoscopic procedures, the choice of drug, dose, or combination is important. Most of them include combinations of opioids, ketamine, benzodiazepines, and propofol to provide balanced sedation which ranges from minimal, moderate, and deep sedation.

Propofol has been used in combination with opioids for sedation in endoscopic protocols frequently. Due to its lipolytic structure, the rapid onset and recovery of this hypnotic agent are advantageous for sedation protocols.[8] Cardiovascular and respiratory depression may occur depending on the dosage. Propofol has been used as monotherapy according to the guidelines in the literature. In contrast, there are also guidelines recommending additional agents to improve the safety of moderate sedation with analgesia.

Remifentanil is an opioid that is a synthetic μ-receptor agonist like fentanyl. It has a rapid onset and provides a quick recovery. Respiratory depression is common with remifentanil. Ketamine is a dissociative anesthetic that does not cause respiratory tract depression. They both have analgesic effects and have been used for procedural sedo-analgesia.

Comparing the reliability of the remifentanil-propofol combination with the ketamine-propofol combination by using IPI in gastrointestinal endoscopy procedures is the primary aim of this study. The expectation was to provide a better respiratory situation with a ketamin-propofol combination in endoscopic procedures.

Determining respiratory complication rates and differences in sedation duration between the groups are the secondary aims of the study.

Methods

The Institutional Ethical Committee approved this prospective, observational study (protocol no: 147, 2022), which was performed by the ethical principles for human investigations as outlined by the Second Declaration of Helsinki. Our observational study was registered at clinicaltrials.gov with the protocol number (NCT05829486). Written informed consent was provided by all patients prior to inclusion in the study.

ASA class I to III risk-scored patients according to ASA (the American Society of Anesthesiologists) guidelines, patients over the age of 18 who will undergo endoscopic intervention were eligible for the study. Patients who need mechanical ventilator support or emergency endoscopic interventions, pregnant patients, a history of substance abuse and allergy to the drugs were exclusion criteria.

88 patients were assessed for eligibility. 6 of the patients needed emergency endoscopic procedures and excluded from the study according to exclusion criteria. 2 of them refused to participate. In 80 patients, there were some technical problems during the procedure, and 11 patients could not finish the procedure. A flow diagram is shown in Figure 1.

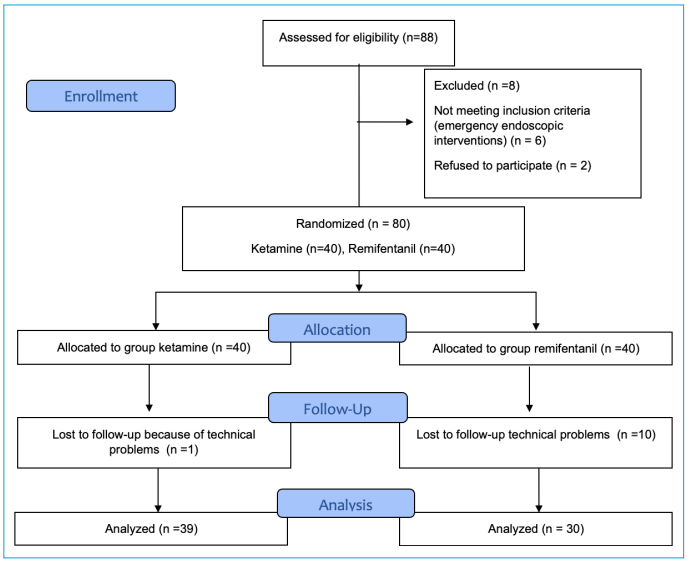

Figure 1. A flow diagram of allocated patients.

Since the endoscopic retrograde cholangiopancreatography (ERCP) procedure requires a longer and more specific anesthesia, it was excluded from the study. Gastroscopy cases were not included in the study because of their very short duration. Patients scheduled for colonoscopy or gastroscopy/colonoscopy were included in the study.

IPI is a monitoring technique that uses metrics for heart rate, SPO2, and respiratory rate. SPO2, heart rate, and respiratory rates are collected with a finger probe, and it will show an instant measurement of respiratory status, whereas $EtCO_2$ is detected via nasal capnography.

A cuff was placed on the patient's arm and a sphygmomanometer was applied to take noninvasive blood pressure readings at scheduled times.

The study population is divided into two groups: Group ketamine received 0.25 mg/kg ketamine and 0.75 mg/kg propofol at the beginning of anesthesia. 1 mcg/kg of remifentanil and 0.75 mg/kg propofol were administered to group remifentanil patients at the induction of anesthesia. Anesthesia maintenance was provided by titration of drug doses according to the modified Ramsey sedation scale.

Measurements were taken at four different points in time: just before anesthesia was induced, five minutes after sedation was induced, ten minutes later, and five minutes after the treatment was finished. IPI accepts numbers from 1 to 10.

When the IPI value is 8 or more, it shows normal values; when it is between 5-7, it suggests that the patient's respiratory status needs to be carefully reviewed and treated if necessary; and when it is 4 or lower, the patient's respiratory state needs to be treated. The Ramsey sedation scale is the most widely used scale to assess the security of sedation. Both in the operating room and in settings outside of the theater, various evaluation techniques have been developed for figuring out the level of sedation. The Ramsay scale indicates a simple strategy that was outlined by Ramsey and associates in 1974. The tool displays patients in six categories, ranging from those who are awake but anxious, agitated, or restless to those who are awake but cooperative, oriented, and tranquil, as well as those who are drowsy but responsive to commands, asleep (brisk response to glabella tap or loud auditory stimulus), asleep with sluggish response to a stimulus, and finally those who have no response to noxious stimuli. The target sedation level was a Ramsay score of 3 or 4 in both groups. Below this level was considered as insufficient sedation and treated with titrated initiate propofol plus ketamine or remifentanil doses (0.25 mg/kg ketamine and 0.75 mg/kg propofol or 1 mcg/kg of remifentanil and 0.75 mg/kg propofol). The level of 5 or 6 was considered as very deep sedation, in cases of hypotension and bradycardia, fluid replacement, bolus doses of ephedrine and intravenous atropine were the treatments of choice.

When there were respiratory issues, it was essential to do practical interventions including patient stimulation, the chin lift and jaw thrust processes,[4] increasing the flow of oxygen, and[5] endotracheal intubation if needed.

IPI scores were calculated using the Capnostream 20 portable bedside monitor from Oridion Medical in Needham, Massachusetts, USA. A pulse oximeter was used to measure the peripheral oxygen saturation (SpO2) and heart rate. Data from the two groups were compared.

Awaking time, frequency of adverse reactions, Ramsay sedation scale, and anesthetic effects were also contrasted.

The Ramsay Sedation Scale is one of the most widely used sedation evaluation tools. Six categories, ranging from extreme agitation to deep coma, are used to categorize a patient's level of sedation.

Statistical Analysis

Comparison of sedation safety and efficacy of Ketamine Propofol and Remifentanil Propofol administration for patients in endoscopic interventions is the primary outcome of this study.

G Power 3.1 for the Mac OS program was used for statistical power analysis.

Analysis Averages in the G Power program made from the difference's menu. In order to reach at least 80% power, when the difference of 0.16 units between the mean IPI values of the two groups was considered clinically significant, a total of 60 patients, at least 30 from each group, were planned to be included in the study.

Statistical analyses were performed with IBM® SPSS® 26 (SPSS Inc., Chicago, IL, USA). The conformity of the variables to the normal distribution was examined using analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Descriptive analyses were given as the mean ± standard deviation for continuous data. Descriptive statistics were made by giving frequency and percentage values of categorical variables obtained from sociodemographic and clinical information. In continuous data (respiratory parameters, etc.), the t-test was used for independent groups when it showed normal distribution, and the Mann-Whitney U test was used when there was non-parametric distribution to compare binary groups (ketamine vs. remifentanil). Pearson's or Fisher's exact chi-square tests were used to compare categorical variables. A p-value below 0.05 is considered statistically significant.

Results

Comparing demographical variables between the groups, the mean age of group ketamine was found to be significantly higher than group remifentanil, and there was an average of 10 years difference (p=0.009). In terms of gender distribution among the groups, the ratio of males was high (48.7%) in group ketamine, and the female ratio was higher (76.7%) in group remifentanil (p=0.031) (Table 1).

The duration of anesthesia between the groups was examined, and duration was found to be significantly higher in group ketamine (23.0±9.7) compared to the other group (19.1±5.6) (p=0.037). The duration of the process was similar between the groups (p=0.058).

Comorbidity rates were evaluated, and they were found to be significantly higher in the remifentanil group (20.0%) Hyperlipidemia was higher in group remifentanil compared to group ketamine (p=0.005). There was no significant difference in the distribution of ASA score and smoking addiction (Table 2).

As stated in Table 2, the decreases in IPI were within the safe range. Therefore, no adverse respiratory problems accompanying these declines were observed clinically.

Table 1. Ramsey sedation scale

Ramsay Score	Response
1	Awake but anxious, agitated, or restless
2	Awake but cooperative, oriented, and tranquil
3	Drowsy but responsive to commands
4	Asleep but the brisk response to glabella tap or loud auditory stimulus
5	Asleep with sluggish response to a stimulus
6	No response to noxious stimuli

Table 2. Comparing of demographical and clinical variables among ketamine and remifentanil groups

Parameters	Ketamine (n=39)	Remifentanil (n=30)	p
Age (years)	60.0±13.4	51.4±13.1	0.009
Processing Time (minutes)	17.0±10.0	13.2±6.4	0.058
	n (%)	n (%)	p
Gender			
Male	19 (48.7)	7 (23.3)	0.031
Female	20 (51.3)	23 (76.7)	
ASA			
1	4 (10.3)	5 (16.7)	0.712
2	30 (76.9)	22 (73.3)	
3	5 (12.8)	3 (10.0)	
Smoking			
No	31 (79.5)	26 (86.7)	0.435
Yes	8 (20.5)	4 (13.3)	
DM			
No	27 (69.2)	22 (73.3)	0.710
Yes	12 (30.8)	8 (26.7)	
HT			
No	22 (56.4)	21 (70.0)	0.248
Yes	17 (43.6)	9 (30.0)	
KAH			
No	31 (79.5)	26 (86.7)	0.435
Yes	8 (20.5)	4 (13.3)	
KBY			
No	39 (100)	29 (96.7)	0.251
Yes	1 (2.6)	1 (3.3)	
SVO			
No	37 (94.9)	30 (100)	0.501
Yes	2 (5.1)	0 (0)	

Independent t-test (for continuous variables) and Pearson's or Fisher's Exact Chi-Square test (for categorical parameters) were used and p<0.05 was considered significant.

There was no significant difference in respiratory parameters such as respiratory rate, SPO2, and $EtCO_2$ measured in the baseline time period between the groups. In the T1 time period, a significant difference was found between the groups in the integrated pulmonary index (IPI) (p<0.0001), sPO2 (p<0.045), respiratory rate (p<0.0001), and systolic blood pressure parameters were found to be significantly higher in group ketamine (Fig. 2). Similarly, T2 time period results were higher in these three parameters: integrated pulmonary index (IPI) (p<0.009), sPO2 (p<0.029), and respiration rate (p<0.0001). In the T3 time period, there was a significant difference between the groups only in the respiration count parameter and it was found to be higher in group ketamine (p<0.0001) (Table 3).

While the initial dose was repeated in 26 patients in the ketamine group, the dose was repeated in 19 patients in the remifentanil group. The initial doses, titrated according to the sedation scale, were repeated at the tenth minute on average in the remifentanil group, while at a later time such as the 20th minute in the ketamine group. Additional sedative drug consumption in both groups was similar in both groups.

Between the groups, Modified Ramsay's Sedation Scale and recovery period were found to be significantly higher in group ketamine (Fig. 3).

Discussion

In this study, the reliability of the sedation procedure has been evaluated during endoscopy by using the IPI score. The use of ketamine during the procedure was found to be more reliable. While the IPI scores in the remifentanil group were 7 in two-time interval measurements (T1 and T2), that is, at a level that needs attention, in the ketamine group, they were above 8 in both measurements during the procedure, that is, in the reliable range.

When both groups were compared, although the age factor was higher in the ketamine group, respiratory complications were not found to be as high as expected. This supports the idea that ketamine use is safer in terms of respiratory stability. Comorbidity rates were similar between

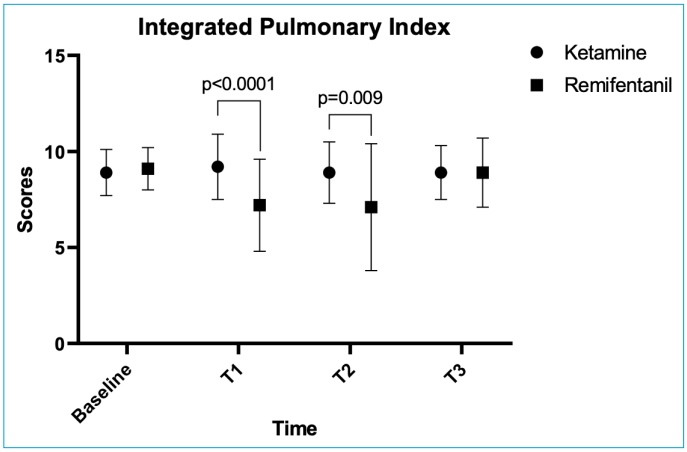

Figure 2. Comparing IPI scores between groups in different time periods. Baseline: just before sedation was induced, T1: five minutes after sedation was induced, T2: ten minutes later, T3: five minutes after the procedure was finished.

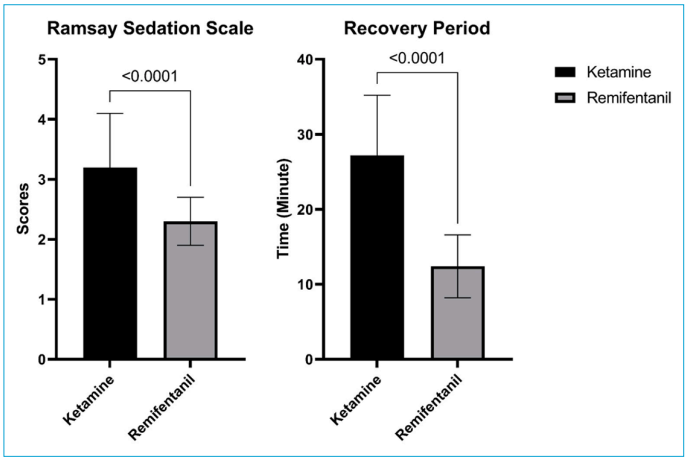

Figure 3. Comparing RSS score and recovery period among groups.

Table 3. Comparing parameters among ketamine and remifentanil groups

Parameters	Ketamine (n=39) Mean±SD	Remifentanil (n=30) Mean±SD	p
Integrated Pulmonary Index			
Baseline	8.9±1.2	9.1±1.1	0.617
T1	9.2±1.7	7.2±2.4	<0.0001
T2	8.9±1.6	7.1±3.3	0.009
T3	8.9±1.4	8.9±1.8	0.899
sPO2 (%)			
Baseline	98.4±1.4	98.8±1.2	0.229
T1	98.5±1.9	97.1±3.4	0.045
T2	98.5±2.1	97.1±2.9	0.029
T3	98.5±2.2	97.8±2.2	0.248
Pulse			
Baseline	84.6±17.7	86.2±16.7	0.698
T1	81.0±15.3	80.5±18.9	0.899
T2	76.6±14.5	81.4±17.1	0.214
T3	77.1±12.6	80.0±17.8	0.441
Respiration Count			
Baseline	20.4±5.5	20.4±3.4	0.972
T1	18.3±5.9	11.2±5.8	<0.0001
T2	22.1±11.8	11.0±6.2	<0.0001
T3	20.2±4.3	15.6±5.2	<0.0001
EtCO2 (mmHg)			
Baseline	33.3±4.5	33.3±3.7	0.992
T1	34.9±5.9	35.8±10.6	0.670
T2	33.2±5.2	34.2±12.3	0.664
T3	32.5±5.2	35.2±7.9	0.113
Systolic Blood Pressure			
Baseline	137.6±17.5	142.7±17.4	0.228
T1	143.0±22.7	123.4±16.7	<0.0001
T2	135.8±18.8	122.7±22.4	0.010
T3	132.5±19.2	127.6±22.0	0.330
Diastolic Blood Pressure			
Baseline	80.8±13.5	83.4±15.6	0.463
T1	82.9±17.4	75.8±12.7	0.062
T2	79.5±12.9	76.9±11.2	0.380
T3	76.3±14.2	74.6±11.8	0.599

Independent t test and Mann-Whitney U test used, p<0.05 considered significant.

the groups. ASA score and smoking addiction statistical distributions were also similar between the groups.

Even though respiratory complications seemed to be reduced in the group ketamine, sedation scores were significantly better in the group remifentanil. The reduction in IPI scores occurred significantly in the time intervals following just after the induction. Recovery time was significantly better in the remifentanil group. The mean age ratio was significantly higher in group ketamine and the predominance of male gender was noticeable in this group.

Hypoxemia during esophagogastroduodenoscopy was described by Rimmer et al.[9] in 1989; they attributed hypoxemia to the medication, and either the mechanical effect of the endoscope or a reflex stimulated by it. Still, the most feared complication during endoscopic procedures is hypoxemia, which is thought to be due to the use of different drugs and doses. Therefore, in this study, we compared possible respiratory complications with 2 different drugs using IPI.

Champreeda et al.[10] aimed to determine the incidence of postoperative respiratory differences among patients undergoing major surgery, in the first-night ward care after surgery. They concluded that apnea is more apparent by using a noninvasive capnography monitor, but these events are not related to pulmonary complications. Similarly in this study, it was found that apnea detection is more practical using a monitor like IPI. Respiratory complications were appointed with IPI because of $EtCO_2$ content. Since decreases in IPI scores occur in the early minutes following anesthesia induction, it is considered that hypoxia during the procedure is drug-related in the foreground. Decreases were in the group remifentanil and scores were around 7 (the respiratory status of the patient should be carefully examined and intervened if necessary). By close monitoring and early interventions, IPI was not dropped below 7.

In a randomized prospective tri-center study, Riphaus et al.[11] could not document the advantage of IPI assessment during deep sedation with midazolam and propofol for endoscopic procedures. However, they claim that monitorization with IPI reduces apnea episodes compared to standard monitorization. They thought that interventions were done immediately under the monitorization of IPI.

Depending on the literature, noninvasive IPI monitors seem to be beneficial in ambulatory anesthesia. Our results and clinical observations were also encouraging for the widespread use of IPI, like the literature.[12,13]

We did not find it necessary to use BIS in our patients whom we followed with the Sedation Scale, as we remained within the safe sedation range, did not suppress breathing and circulation, and applied conscious sedation.

Although there are many studies on the safety and effectiveness of IPI, the number of studies comparing the sedation protocol using IPI is limited.

An anesthetic usually used for outdoor anesthesia is propofol.[14-16]

Close patient monitoring is advised to prevent oversedation, especially when coupled with other medications like opioids, due to their limited therapeutic window.[17] This is especially true for ASA II-III patients who typically undergo endoscopic procedures and may have co-morbidities related to the heart, lungs, or metabolism.

Propofol was found to have similar risks of hypoxia (OR, 0.82; 95% CI, 0.63-1.07), and hypotension (OR, 0.92; 95% CI, 0.64-1.32); for non-advanced procedures, propofol was slightly less likely to result in complications (OR, 0.61; 95% CI, 0.38-0.99), according to a recent meta-analysis of 27 studies, many of which were randomized controlled trials.[18]

We used propofol in both groups because it is an effective and safe hypnotic frequently used in sedation procedures all over the world. When two medications are taken together, their effects may be amplified, and drug consumption may be decreased. The coadministration of ketamine and remifentanil with propofol in this study led to higher Ramsey sedation scale and a lower need for extra medicine (supplement and rescue study drug required).

According to Fabbri et al.[19] due to its safe and practical profile, subanesthetic dosages of ketamine along with a widely used infusion regimen of low-dose remifentanil and continuous propofol infusion should be employed in ERCP procedures. The combination has positive clinical effects. In fact, it avoids heavy sedation, maintains enough analgesia when under conscious sedation, and causes less post-procedural nausea and vomiting with shorter recovery durations. Ketamine must therefore be viewed as more than just a "rescue drug" and as a highly recommended drug for use in situations outside of the operating room. They mentioned failure to accurately measuring of breathing depth when using propofol is one of the major issues with the sedation approach as a limitation. Capnography is considered as a helpful tool in the evaluation of patients undergoing sedation and analgesia as to their ventilator conditions.

Although we did not use the drugs as a continuous infusion in our study, we preferred more cautious monitoring with IPI. Although both ketamine and remifentanil were found to be quite safe in their study, in this study we also detected less obvious changes that occurred with remifentanil early,intervened and prevented possible respiratory problems. Despite the fact that there were no major adverse effects during the experiment, the earlier warning

that capnography could provide may have practical applications since it may give doctors a longer window to act and stop additional respiratory deterioration.

Weiniger et al.[20] in their study highlight the limitations of respiratory variables used as early warning monitoring for apneas. When administering remifentanil to laboring women, $EtCO_2$ may be a better respiratory monitor than pulse oximetry because it was the variable that detected apnea the earliest. It is the only study determining respiratory complications of remifentanil by using IPI. Only 15% of apneas were picked up by pulse oximetry, the most popular method for detecting respiratory depression during childbirth. The majority of apnea occurrences were detected by alert trigger levels for $EtCO_2$ (15 mm Hg), RR (8 bpm), and IPI (4); however, the positive predictive rate was low for these variables, leading to many false warnings.

Remifentanil was found to be more effective in respiratory complications in this study likewise. Although our IPI results were not as low as in their study, we also found low values in IPI in the remifentanil group. In the ketamine group, IPI scores were even higher than baseline in T1, T2, and T3 timelines. There were not any respiratory complications in the ketamine group. The Ramsey sedation scale has shown better results in the ketamine group but recovery time was shorter compared to the ketamine group.

Ketamine, a phencyclidine analog, binds to the phencyclidine recognition site in the NMDA receptor ion-channel complex to serve as a non-competitive inhibitor of the N-methyl-Daspartate (NMDA) receptor in the central nervous system. Both in experimental pain and postoperative pain, ketamine analgesic dosages seem to be mediated by this non-opioid phencyclidine receptor pathway. Norketamine, the main metabolite of ketamine, has also been shown in laboratory tests to have antinociceptive qualities and to selectively inhibit NMDA receptor function at the spinal and supraspinal levels. According to reports, using ketamine has a synergistic pharmacodynamic impact that lowers the need for opioids. Furthermore, ketamine can be used in procedures where it is essential to protect airway reflexes due to its high safety margins.[21-23] In adult and pediatric patients with inadequate sedation undergoing endoscopic procedures or for operations in the emergency room, ketamine was only used as an additional drug to achieve successful and safe sedation.[24-26]

We recommend the routine use of bolus dosages of ketamine in our prospective randomized research. In order to produce conscious sedation and profound analgesia, which are highly desirable for all endoscopic operations carried out outside of the operating room, it can be combined with low dosages of propofol infusion. This method has been proven to be both safe and successful. Adequate sedation level was achieved with ketamine and propofol combinations, except for a slight increase in oral secretions and minimal prolongation in sedation time.

Limitations

To find out the association between ketamine and other drugs, a significant number of patients are required. The study comprised 69 patients; nevertheless, a larger sample size might have revealed differences between the groups. Although Sia et al.[27] imposed a limit of 15 seconds for desaturation in their model with the administration of oxygen at a rate of 4 L/min, apnea in pregnant women was tolerated for periods of minutes in models using preoxygenation. In our study, adequate preoxygenation could not be performed due to elevated patient circulation.

Also, the positive predictive values to identify apnea for the individual physiological variables could change if an apnea definition was used for 15 or 60 seconds and any such alert limits and thresholds would change the results.

Conclusion

Although there was a moderate prolongation in the recovery period in the ketamine group, the Ramsey sedation scale was significantly higher. Measurements using IPI have shown that ketamine causes fewer respiratory complications than opioids. The use of ketamine in endoscopic procedures provides sufficient, convenient, and safe sedation and analgesia.

Disclosures

Ethics Committee Approval: The Institutional Ethical Committee of Gaziosmanpaşa Training and Research Hospital approved this prospective, observational study with a protocol no:147, 2022.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Financial support (Funder's name): The author(s) received no financial support for the research, authorship, and/or publication of this article.

Authorship Contributions: Concept – Z.C.; Design – Z.C., D.G.M.; Supervision – D.G.M.; Fundings – A.K.G.; Materials – A.K.G., A.S.G.; Data collection &/or processing – Z.C., A.S.G.; Analysis and/or interpretation – D.G.M.; Literature search – Z.C.; Writing – Z.C.; Critical review - D.G.M.

Use of AI for Writing Assistance: None declared.

References

1. Wallace MB, Kinnan S. To register and report is good for the science of endoscopy. Endoscopy 2023;55:42–3. [CrossRef]

2. Hepner DL, Siddiqui UD. Endoscopy and Sedation. Am J Gastroenterol 2022;117:33–8. [CrossRef]
3. Dossa F, Megetto O, Yakubu M, Zhang DDQ, Baxter NN. Sedation practices for routine gastrointestinal endoscopy: a systematic review of recommendations. BMC Gastroenterol 2021;21:22. [CrossRef]
4. Storm AC, Fishman DS, Buxbaum JL, Coelho-Prabhu N, Al-Haddad MA, Amateau SK, et al; ASGE Standards of Practice Committee. American Society for Gastrointestinal Endoscopy guideline on informed consent for GI endoscopic procedures. Gastrointest Endosc 2022;95:207–215. [CrossRef]
5. Dumonceau JM, Riphaus A, Schreiber F, Vilmann P, Beilenhoff U, Aparicio JR, et al. Non-anesthesiologist administration of propofol for gastrointestinal endoscopy: European Society of Gastrointestinal Endoscopy, European Society of Gastroenterology and Endoscopy Nurses and Associates Guideline--Updated June 2015. Endoscopy 2015;47:1175–89. [CrossRef]
6. Ronen M, Weissbrod R, Overdyk FJ, Ajizian S. Smart respiratory monitoring: clinical development and validation of the IPI™ (Integrated Pulmonary Index) algorithm. J Clin Monit Comput 2017;31:435–42. [CrossRef]
7. Berkenstadt H, Ben-Menachem E, Herman A, Dach R. An evaluation of the Integrated Pulmonary Index (IPI) for the detection of respiratory events in sedated patients undergoing colonoscopy. J Clin Monit Comput 2012;26:177–81. [CrossRef]
8. Zhou S, Zhu Z, Dai W, Qi S, Tian W, Zhang Y, et al. National survey on sedation for gastrointestinal endoscopy in 2758 Chinese hospitals. Br J Anaesth 2021;127:56–64. [CrossRef]
9. Rimmer KP, Graham K, Whitelaw WA, Field SK. Mechanisms of hypoxemia during panendoscopy. J Clin Gastroenterol 1989;11:17–22. [CrossRef]
10. Champreeda V, Hu R, Chan B, Tomasek O, Lin YH, Weinberg L, et al. Nocturnal respiratory abnormalities among ward-level postoperative patients as detected by the Capnostream 20p monitor: a blinded observational study. PLoS One 2023;18:e0280436.
11. Riphaus A, Wehrmann T, Kronshage T, Geist C, Pox CP, Heringlake S, et al. Clinical value of the Integrated Pulmonary Index® during sedation for interventional upper GI-endoscopy: a randomized, prospective tri-center study. Dig Liver Dis 2017;49:45–9. [CrossRef]
12. Wang Y, Liu F, Zhang Y, Yang X, Wu J. The effect of capnography on the incidence of hypoxia during sedation for EGD and colonoscopy in mildly obese patients: a randomized, controlled study. BMC Anesthesiol 2023;23:188. [CrossRef]
13. Beitz A, Riphaus A, Meining A, Kronshage T, Geist C, Wagenpfeil S, et al. Capnographic monitoring reduces the incidence of arterial oxygen desaturation and hypoxemia during propofol sedation for colonoscopy: a randomized, controlled study (ColoCap Study). Am J Gastroenterol 2012;107:1205–12. [CrossRef]
14. Wehrmann T, Grotkamp J, Stergiou N, Riphaus A, Kluge A, Lembcke B, et al. Electroencephalogram monitoring facilitates sedation with propofol for routine ERCP: a randomized, controlled trial. Gastrointest Endosc 2002;56:817–24. [CrossRef]
15. Seifert H, Schmitt TH, Gultekin 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. [CrossRef]
16. VanNatta ME, Rex DK. Propofol alone titrated to deep sedation versus propofol in combination with opioids and/or benzodiazepines and titrated to moderate sedation for colonoscopy. Am J Gastroenterol 2006;101:2209–17. [CrossRef]
17. Rudner R, Jalowiecki P, Kawecki P, Gonciarz M, Mularczyk A, Petelenz M. Conscious analgesia/sedation with remifentanil and propofol versus total intravenous anesthesia with fentanyl, midazolam, and propofol for outpatient colonoscopy. Gastrointest Endosc 2003;57:657–63. [CrossRef]
18. Wadhwa V, Issa D, Garg S, Lopez R, Sanaka MR, Vargo JJ. Similar risk of cardiopulmonary adverse events between propofol and traditional anesthesia for gastrointestinal endoscopy: a systematic review and meta-analysis. Clin Gastroenterol Hepatol 2017;15:194–206. [CrossRef]
19. Fabbri LP, Nucera M, Marsili M, Al Malyan M, Becchi C. Ketamine, propofol and low dose remifentanil versus propofol and remifentanil for ERCP outside the operating room: is ketamine not only a "rescue drug"? Med Sci Monit 2012;18:CR575–80. [CrossRef]
20. Weiniger CF, Carvalho B, Stocki D, Einav S. Analysis of physiological respiratory variable alarm alerts among laboring women receiving remifentanil. Anesth Analg 2017;124:1211–8. [CrossRef]
21. Church L, lodge D. N-methyl-D-aspartate antagonism is central to the actions of ketamine and other phencyclidine receptor lignds. In: Domino EF, editor. Status of Ketamine in Anesthesiology. Ann Arbor: NPP Books; 1990. pp. 501–19.
22. Oye I, Paulsen O, Maurste A. Effects of ketamine on sensory perception: evidence for a role of NMDA receptors. J Pharmacol Exp Ther 1992;260:1209–60.
23. Menigaux C, Fletcher D, Dupont X, Guignard B, Guirimand F, Chauvin M. The benefits of intraoperative small-dose Ketamine on postoperative pain after anterior cruciate ligament repair. Anesth Analg 2000;90:129–35. [CrossRef]
24. van Beek EJ, Leroy PL. Safe and effective procedural sedation for gastro-intestinal endoscopy in children: a systematic review. J Pediatr Gastroenterol Nutr 2012;54:171–85. [CrossRef]
25. Chiaretti A, Ruggiero A, Barbi E, Pierri F, Maurizi P, Fantacci C, et al. Comparison of propofol versus propofol-ketamine combination in pediatric oncologic procedures performed by non-anesthesiologists. Pediatr Blood Cancer 2011;57:1163–7. [CrossRef]
26. Nejati A, Moharari RS, Ashraf H, Labaf A, Golshani K. Ketamine/propofol versus midazolam/fentanyl for procedural sedation and analgesia in the emergency department: a randomized, prospective, double-blind trial. Acad Emerg Med 2011;18:800–6. [CrossRef]
27. Sia AT, Sng BL, Leo S. Novel vital signs-controlled, patient-assisted intravenous analgesia using remifentanil for labour and delivery. Int J Obstet Anesth 2014;23:196–8. [CrossRef]