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The Effects of Propofol and Ketofol on Hemodynamics, End-Tidal Carbon Dioxide, Integrated Pulmonary Index and Recovery in Patients Undergoing Endoscopy and Colonoscopy

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Abstract

BACKGROUND/AIMS: In this study, we aimed to compare the effects of propofol and ketofol on hemodynamics, end-tidal carbon dioxide ($EtCO_2$), integrated pulmonary index (IPI), peripheral oxygen saturation (SpO_2) and sedation quality during endoscopy and colonoscopy performed under anesthesia.

MATERIALS AND METHODS: One hundred patients aged 18-79 years with American Society of Anesthesiology class I-III were randomly divided into two groups: the propofol group (1%) and the ketofol mixture group (group P and group K, respectively). Sedation was achieved with 0.15 mL/kg doses of both drugs, followed by additional 0.05 mL/kg doses based on the patients' Ramsey Sedation Scores. Before the procedure, the basal values of heart rate (HR), $EtCO_2$, IPI, and SpO_2 were obtained, as well as instantaneous trend data. systolic blood pressure, diastolic blood pressure, and mean blood pressure values were recorded prior to the procedure (baseline values), at the 1st, 5th, 10th, 15th, 25th, 30th minutes, and at the conclusion of the procedure. The duration of anesthesia and the procedure, the amount of propofol administered, the rate of spontaneous eye opening, and recovery parameters were also recorded.

RESULTS: The mean blood pressure values at the 1st, 5th, 10th, 15th, 20th minutes, at the end of the intervention, and at the 5th minute after the procedure were found to be higher in group K compared to group P. HR, SpO_2, $EtCO_2$ and IPI values were higher in group K than in group P. Time to spontaneous eye opening was significantly lower in group K compared to group P. In addition, the recovery period during which the modified Aldrete score was >9 did not differ between groups. Additional doses and total propofol consumed during the procedure were significantly lower in group K than in group P.

CONCLUSION: Ketofol appears superior to propofol in endoscopic procedures due to its superior hemodynamic and respiratory stability, without affecting recovery time. Incorporating non-invasive $EtCO_2$ and IPI measurements into standard respiratory monitoring equipment improves monitoring quality and facilitates its execution.

Keywords: Colonoscopy, endoscopy, ketamine, propofol, pulmonary, sedation

INTRODUCTION

One of the most common non-operating room anesthesia applications involves endoscopic procedures of the gastrointestinal system (GIS). Short-acting anesthetic medications without side effects should be preferred, as these procedures are performed daily.[1,2] Propofol is one of the most frequently administered intravenous anesthetics currently available. It is utilized extensively both inside and outside

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the operating room. It is superior to other anesthetic agents such as thiopental, benzodiazepines, and opioids due to its rapid recovery, minimal residual effects on the central nervous system, and antiemetic properties. In recent years, it has been favored for use as the sole anesthetic agent during endoscopic procedures.[3] When propofol is used as the sole anesthetic agent, high doses may be necessary in order to achieve the level and quality of sedation necessary for this procedure. However, high doses of propofol may increase the likelihood of anesthesia-related adverse effects. Therefore, various drugs, such as ketamine, lidocaine, and dexmedetomidine, are used in order to reduce the required dose of propofol.[4,5]

Ketamine, on the other hand differs from other anesthetic agents because it does not have a depressant effect on the cardiovascular and respiratory systems, and yet it has analgesic properties.[6] When propofol and ketamine are combined, the deficiencies in the efficacy of propofol are compensated for by the sympathomimetic and analgesic effects of ketamine, and the side effects of ketamine, such as nausea, vomiting, and psychomimetic effects, are mitigated by the antiemetic and potent hypnotic effects of propofol. Previous research has demonstrated that the combination of ketamine and propofol in the same syringe (ketofol) leads to more stable hemodynamics and reduces the likelihood of side effects.[7]

Ensuring patient safety during anesthesia applications outside of the operating room remains an important concern, and there is a need for new monitoring methods which will contribute to standard monitoring during such procedures. The integrated pulmonary index (IPI) is a numerical value which combines four important parameters measured by noninvasive end-tidal carbon dioxide ($EtCO_2$) monitoring in order to provide a straightforward indication of the patient's ventilation status. $EtCO_2$, respiratory rate, oxygen saturation (SpO_2), and heart rate (HR) are these integrated parameters.[8] Consequently, IPI combines the advantages of ventilation monitoring and oxygenation monitoring and may be used as a simple and portable device for monitoring patients during sedation, as it may enable the earlier detection of problems in comparison to conventional monitoring. Additional ventilation status monitoring with capnography decreases the incidence of respiratory depression and hypoxemia.[9,10]

The primary aim of this study was to compare the effects of propofol and ketofol on hemodynamics during endoscopy and colonoscopy under anesthesia. The secondary objective was to compare their effects on respiratory parameters using the new monitoring techniques of $EtCO_2$ and IPI. In addition, the quantity and quality of sedation were also recorded. Our hypothesis is that ketofol will produce superior hemodynamic, respiratory, and sedative outcomes compared to propofol alone.

MATERIALS AND METHODS

Study Design

This double-blind, randomized, prospective study was conducted in the Anesthesiology and Reanimation and Gastroenterology Clinics of the University of Health Sciences Türkiye, Samsun Training and Research Hospital (approval number: 2019/4/32, date: 01.01.2020-01.07.2020), after approval by the Local Ethics Committee (Clinical Research Ethics Committee of University of Health Sciences Türkiye, Samsun Training and Research Hospital) and the Medicines and Medical Devices Agency (19-AKD-123). This study adhered to the Declaration of Helsinki and written informed consent was obtained from each participant.

Study Population

After obtaining informed consent, one hundred American Society of Anesthesiology (ASA) I, II, and III patients aged 18 to 70 who underwent elective upper GIS endoscopy and colonoscopy were included in this study. The following patients were excluded: those who did not consent to inclusion in this study, patients with a history of allergy to any medications used in this study, those with uncontrolled hypertension, severe renal, hepatic, cardiovascular, and respiratory system disease, those patients with a history of epilepsy, those with intracranial space-occupying lesions, patients who were pregnant, patients with severe neuropsychiatric disorders, and those with a body mass index >30.

Setting

The closed envelope method was used to randomly assign patients into two groups consisting of 50 patients each: group P (propofol) and group K (ketofol). The same gastroenterologist performed all endoscopy and colonoscopy procedures, and the same anesthesiologist administered sedoanalgesia to all patients. Our study was designed to be double-blinded and accordingly the patient, the anesthetist, and the gastroenterologist were unaware of which anesthetic medication would be administered.

Preparation of Ketofol and Propofol

100 mg of ketamine (2 mL of 50 mg/mL Ketalar; Pfizer, Zentiva, Türkiye) and 200 mg of propofol (10 mL of 2% propofol Lipuro; Fresenius Kabi GmbH, Austria) were withdrawn into a 20 mL syringe to complete the total volume to 20 mL. Thus, a mixture of 10 mg/mL propofol + 5 mg/mL ketamine was obtained (mixture with 2:1 ratio).

The preparation of propofol; 10 mg/mL propofol was prepared by withdrawing 1% propofol-Lipuro (10 mL of 2% propofol Lipuro; Fresenius Kabi GmbH, Austria) from the ampoule into a 20 mL syringe.

Preparation Before Endoscopy

Patients fasted for 8 hours before the procedure. Their demographic information such as their age, gender, body weight, and height were recorded upon admission. Oxygen (2-4 L/min) was administered via nasal cannula. After the patients were taken to the endoscopy room, HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean blood pressure (MBP), respectively, SpO_2 and $EtCO_2$ monitoring was initiated. The mixture of medications in the syringe, prepared by the anesthesiologist in charge of this study, was administered to the patient as a 0.15 mL/kg IV push by the anesthetist following the patient. After the response to verbal stimuli decreased and the corneal reflex disappeared, the gastroenterologist was allowed to begin the procedure. During the procedure, the degree of the patients' sedation was targeted to be >4 according to the Ramsay Sedation Scale (RSS). In cases of RSS <4, an additional dose of 0.05 mL/kg of the anesthetic medication was administered as an intermittent bolus.

Follow-Up Assessments

The basal values of HR, $EtCO_2$, IPI, and SpO_2 were obtained before the procedure, and the instantaneous trend data were recorded. SBP, DBP, and MBP values before the procedure (the baseline value), at the 1st, 5th, 10th, 15th, 20th, 25th, 30th minutes of the procedure and at the end of the procedure were recorded. Other parameters including $EtCO_2$, IPI, SpO_2 and HR were obtained as instant data output from the Capnostream 6™ Portable Respiratory Monitor and recorded.

Hypertension was defined as MBP higher than 20% of the initial value during or after the procedure. If the patient developed hypertension, signs of superficial anesthesia (eye-opening, movement) were initially evaluated. If the anesthesia was found to be superficial (RSS <4), an additional dose of 0.05 mL/kg IV of the anesthetic medication was administered. If hypertension persisted for more than one minute despite an additional dose, it was concluded that the anesthesia was not superficial and perlinganit 50-100 µg IV was administered. The perlinganit dose was repeated when necessary. A 20% lower MBP value than the initial value was accepted as hypotension. When the patient developed hypotension, ephedrine 5 mg IV was administered, and the dose of ephedrine was repeated when necessary. A HR of <45 beats/min was considered as bradycardia, and bradycardia was treated with atropine 0.5 mg IV. In cases of HR >100 beats/min, superficial anesthesia findings were re-evaluated. In cases of superficial anesthesia (RSS <4), an additional dose of 0.05 mL/kg IV of anesthetic medication was given. When it was concluded that the anesthesia was not superficial, 5-10 mg esmolol was administered IV. The dose of esmolol was repeated when necessary.

The duration of anesthesia was measured from the time of the first dose of propofol or ketofol until the patient's eyes opened. The duration of the procedure was determined by recording the time from the beginning to the end of the process. Induction, additional doses, and total medication doses were recorded. In addition, the time of spontaneous eye opening following the procedure and the time of Modified Aldrete Score (MAS) >9 were recorded.

At the conclusion of the procedure, the patients were given oxygen through a mask and monitored in the observation room with the emergency equipment at hand. HR, MBP, and SpO_2 were recorded at the 5th, 10th, 20th, and 30th minutes after the procedure. Complications (hypertension, hypotension, bradycardia, bronchospasm, allergic rash, nausea, vomiting, cough, dizziness, diplopia, agitation, desaturation, apnea, airway obstruction, laryngospasm, aspiration) during and after the procedure were recorded.

Statistical Analysis

Sample size calculation was based on the primary outcome variable. Mean arterial pressure (82.1±15.1 mmHg) measured 5 minutes after the start of sedation in a pilot study of 10 patients receiving propofol was used for the sample size calculation. This frame was chosen because hemodynamic stability was achieved and endoscopy was initiated. Since a 10% change in mean arterial pressure was considered significant, 44 participants were calculated as required for each group in this study with an alpha level of 0.05, a beta level of 0.10 and power level of 0.95. To account for potential drop-outs, a decision was made to include a minimum of 50 patients per group.

Statistical analysis was performed using IBM SPSS v23 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). The Student's t-test was used to compare the means between the two groups. Conformity to normal distribution was examined using the Kolmogorov-Smirnov test. A two-way analysis of variance was used to compare parameters according to their group and time. The results of the analysis are presented as mean ± standard deviation for quantitative data, and a p-value of <0.05 was considered statistically significant.

RESULTS

There was no difference between the groups in terms of their age, gender, height, weight, ASA classification, duration of anesthesia, and duration of procedure (endoscopy + colonoscopy) (p>0.05) (Table 1).

The MBP values of group P and group K during the procedure and in the observation room are shown in Table 2. The mean values of MBP at 1st, 5th, 10th, 15th, 20th minutes, at end of procedure and post-procedure 5th min differed between the groups (p<0.05).

The RSS values of group P and group K are shown in Table 3. The RSS mean values at 1st, 5th, 10th, 15th, 20th, and 25th minutes differed between the groups (p<0.001).

Table 1. Demographic characteristics of the groups

	Group K, (n=50), Mean ± SD/n (%)	Group P, (n=50), Mean ± SD/n (%)	p
Age (years)	50.2±13.9	51.2±10.2	0.700
Gender			
Male	20 (40)	20 (40)	1.000
Female	30 (60)	30 (60)	
Height (cm)	164.4±9.4	164.7±9.3	0.848
Weight (kg)	76.4±12.6	76.8±14.1	0.893
ASA I/II/III	12 (24)/32 (64)/6 (12)	12 (24)/32 (64)/6 (12)	1.000
Comorbidities			
- Hypertension	34 (89.5)	32 (84.2)	0.978
- Diabetes mellitus	9 (23.7)	8 (21.1)	
- Coronary artery disease	6 (15.8)	6 (15.8)	
- Bronchial asthma	4 (10.5)	3 (7.9)	
- COPD	3 (7.9)	5 (13.2)	
Duration of anesthesia (min)	24.6±3.6	24.8±4.2	0.859
Duration of procedure (min)	22.6±3.6	22.8±4.2	0.820

ASA: American Society of Anesthesiologists; COPD: Chronic obstructive pulmonary disease, SD: Standard deviation, min: Minimum.

Table 2. Mean blood pressure values of the groups

Time	Group K, (mmHg), Mean ± SD	Group P, (mmHg), Mean ± SD	p
Beginning of the procedure	100.8±12.8	99.8±13.2	0.707
1st min	92.7±10.3	82.2±15	**<0.001**
5th min	94.2±12.2	80.2±15.2	**<0.001**
10th min	90.6±11.3	78.4±16.4	**<0.001**
15th min	91.7±10.7	84.3±13.4	**0.003**
20th min	93.6±10.5	83.7±13.8	**<0.001**
25th min	94.0±7.5	85.2±17.3	0.083
30th min	99.5±0.7	76.5±15.2	0.100
End of the procedure	93.5±8.5	89.3±11.4	0.035
After the procedure 5th min	94.7±7.2	90.3±11.0	**0.021**
After the procedure10th min	94.9±7.2	92.5±8.9	0.136
After the procedure 20th min	95.6±6.8	94.7±8.8	0.548
After the procedure 30th min	97.3±7.4	95.9±11.5	0.470

SD: Standard deviation, min: Minute.

Table 3. Ramsey Sedation Scale of the groups

Time	Group K, Mean ± SD	Group P, Mean ± SD	p
Beginning of the procedure	1.2±0.4	1.3±0.4	0.339
1st min	4.9±0.3	4.4±0.6	**<0.001**
5th min	4.8±0.5	3.9±0.7	**<0.001**
10th min	4.4±0.6	3.7±0.8	**<0.001**
15th min	4.6±0.6	4.1±0.6	**<0.001**
20th min	4.8±0.5	4.3±0.5	**<0.001**
25th min	4.7±0.5	4.3±0.7	**<0.001**
30th min	4.5±0.7	4.6±0.5	0.846
End of the procedure	4.6±0.6	4.7±0.5	0.348

SD: Standard deviation, min: Minute.

HR was found to be statistically significant between the groups at the beginning, 0-5 minutes, 5-10 minutes, 10-15 minutes, 15-20 minutes, 20-25 minutes, 25-30 minutes and >30 minutes ($p<0.05$) (Table 4).

The mean SpO_2 value was 98.1±2% in group K and 96.8±3.4% in group P. A statistically significant difference was found in the mean SpO_2 values ($p<0.05$) (Table 5). The mean $EtCO_2$ level in our study was 34.4±5.6 mmHg in group K and 29.6±9.3 mmHg in group P, and this difference was statistically significant ($p<0.05$).

The mean IPI value was 9.4 in group K and 7.3 in group P, which was statistically significant ($p<0.05$). When the interaction between group and time was analyzed, the mean IPI of the ketofol group at baseline was 9.6, and it was 9.2 for the propofol group. The highest mean onset time was observed in the ketofol group (Table 6).

The mean time to reach MAS >9 in the recovery period was 242.4±54.6 sec in group K, while it was 250.4±50.1 sec in group P ($p=0.447$). Spontaneous eye opening was observed at an average of 171.6±17.8

Table 4. Multiple comparison results of heart rate by group and time

	Beginning	0-5 minute	5-10 minute	10-15 minute	15-20 minute	20-25 minute	25-30 minute	>30 minute	Total
Group K, (beat/min.)	$88.9±18.4^{A,K,I,F}$	$91.3±13.7^{I}$	$88.7±11.8^{H}$	$83.8±12.7^{E}$	$83.8±12.8^{E}$	$83.7±13.7^{E}$	$81.8±12.2^{C}$	$86.4±9.6^{A}$	86.2±13.2
Group P, (beat/min.)	$92.6±16.7^{K,I,H}$	$89.4±16^{K}$	$86.7±14.9^{A}$	$83.3±14.4^{G}$	$82.3±14.7^{C}$	$81.3±16.4^{F}$	$79.2±16.6^{D}$	$73.7±8.9^{B}$	84.4±15.6
Total, (beat/min.)	$90.7±17.6^{f}$	$90.4±14.9^{f}$	$87.7±13.5^{e}$	$83.5±13.6^{d}$	$83±13.8^{c}$	$82.5±15.1^{b}$	$80.6±14.6^{a}$	$82±11.1^{a}$	85.3±14.5

$^{A-K}$: There is no significant difference between values with the same letter, $^{a-f}$: There is no significant difference between main effects with the same letter.

Table 5. Multiple comparison results of peripheral oxygen saturation by group and time

	Beginning	0-5 minute	5-10 minute	10-15 minute	15-20 minute	20-25 minute	25-30 minute	>30 minute	Total
Group K, (%)	$99.2±1.2^{L}$	$98±2.4^{K}$	$97.8±2.1^{H}$	$98.2±1.7^{EF}$	$98.3±1.9^{C}$	$98.4±1.7^{C}$	$98.3±1.9^{C,F}$	$96.5±2.2^{A}$	98.1±2
Group P, (%)	$98.6±2^{K,E,F,C}$	$96.8±3.7^{I}$	$96.1±4.3^{G}$	$96.9±3.2^{B}$	$97.2±2.8^{E}$	$97.1±2.9^{D}$	$96.9±3.3^{B,I}$	$96.3±3.1^{A,G}$	96.8±3.4
Total, (%)	$98.9±1.7^{f}$	$97.4±3.2^{e}$	$96.9±3.5^{d}$	$97.6±2.7^{a}$	$97.7±2.4^{c}$	$97.7±2.5^{c}$	$97.5±2.8^{b}$	$96.3±2.9^{a}$	97.5±2.9

$^{A-L}$: There is no significant difference between values with the same letter, $^{a-f}$: There is no significant difference between main effects with the same letter.

Table 6. Comparison of integrated pulmonary index values according to group and time

	Beginning	0-5 minute	5-10 minute	10-15 minute	15-20 minute	20-25 minute	25-30 minute	>30 minute	Total
Group K	$9.6\pm0.7^{B,F,I}$	9.3 ± 1^{F}	9.5 ± 0.8^{I}	9.4 ± 1^{B}	9.3 ± 1^{F}	9.4 ± 0.9^{B}	$9.5\pm0.9^{B,J}$	$9.5\pm0.7^{B,J}$	9.4 ± 1
Group P	$9.2\pm1^{B,F,I}$	7.6 ± 2.7^{K}	7.3 ± 2.8^{H}	7.1 ± 2.7^{G}	7.1 ± 2.6^{E}	7.5 ± 2.2^{D}	7.2 ± 2.2^{C}	6.1 ± 2.4^{A}	7.3 ± 2.6
Total	9.4 ± 0.9^{f}	8.4 ± 2.2^{c}	8.4 ± 2.3^{a}	8.3 ± 2.4^{e}	8.2 ± 2.3^{d}	8.5 ± 1.9^{c}	8.3 ± 2.1^{b}	7.3 ± 2.5^{a}	8.3 ± 2.2

$^{A-K}$: There is no significant difference between values with the same letter, $^{a-f}$: There is no significant difference between main effects with the same letter.

sec in group K and 213.4±48.8 sec in group P, and this difference was statistically significant (p<0.001). For anesthesia onset, the procedure start time was 71.5±9.2 sec in group K and 76.6±13.6 sec in group P, and this difference was statistically significant (p=0.031).

The mean values of propofol used in induction did not differ between the groups (group K: 113.8±15.8 mg vs. group P: 121.2±24.2; p=0.089). The additional dose of propofol was 39.4±18.4 mg in group K and 163.1±55.3 mg in group P, this difference was statistically significant (p<0.001). The average total amount of propofol used per patient was 140.2±26.9 mg in group K and 284.1±60.8 mg in group P, which was statistically significant (p<0.001).

An additional dose was administered in 68% (n=34) of the patients in the group K, an additional dose was given to all patients (n=50) in the group P. There was a statistically significant difference between the groups in terms of additional doses in maintenance (p<0.001). While no complications developed in group K during the procedure, hypotension requiring intervention was observed in 2 patients, bradycardia in 1 patient, and respiratory depression in 12 patients in group P.

DISCUSSION

This study demonstrated that ketofol has better effects on hemodynamics and respiratory parameters when compared to propofol use alone and also ketofol did not cause delayed recovery time. Ketofol can be prepared in a single injector by combining ketamine and propofol in the desired proportions. It is frequently used in clinics because it is convenient to use these two medications in the same injector, it is safe in terms of dose titration, and it provides high-quality sedation. Concomitant use reduces the side effects of each medication compared to their use separately and enables the use of lower doses of these medications. Due to its short recovery time, absence of respiratory suppression, and ability to provide effective analgesia, ketofol can be used safely, particularly in the elderly and in those patients with co-morbidities.[6,7,11]

To minimize the risk of complications in endoscopic procedures performed under sedoanalgesia, the patient's level of sedation is vital. In patients undergoing colonoscopy, Türk et al.[12] compared the combination of propofol and ketamine to the combination of propofol and alfentanil and found that RSS was higher in the ketamine group. David and Shipp[13] administered sedation to patients in the emergency department, and reported that ketofol provided better sedation quality and depth when compared to propofol. In our study, the depth of sedation was also evaluated with RSS. Accordingly, while there was no statistically significant difference between the groups in terms of their baseline RSS values before the procedure, it was found that the mean RSS values at the 1st, 5th, 10th, 15th, 20th, and 25th minutes were significantly higher in the ketofol group. A more statistically significantly profound sedation was achieved in those patients in the ketofol group. This was attributed to the hypnotic and sedative effects of ketamine administered with propofol and its analgesic properties. In addition, the rapid onset and short duration of the effect of propofol alone necessitated the need for more than one additional dose for maintenance during the procedure in group P. In our study, additional doses were given to 34 patients in the ketofol group during the procedure, while more than one additional dose was required in all patients in the propofol group.

In their study, Smischney et al.[14] examined the effect of propofol and ketofol as induction agents on hemodynamics. They reported that ketofol provided better hemodynamic stability in the first 10 minutes after induction. Aberra et al.[15] investigated the effects of propofol and ketofol on laryngeal mask placement conditions and hemodynamic stability in pediatric patients and observed that mean blood pressure and HR were higher in the ketofol group. At the same time, there was a significant decrease in mean blood pressure and HR in the propofol group. As a result, they reported that ketofol could be used as an alternative to propofol in pediatric anesthesia. Tosun et al.[16] compared the effects of propofol-ketamine and propofol-fentanyl combinations in 90 pediatric patients who underwent upper GIS endoscopy. The authors observed that the patients in the propofol-ketamine group tolerated endoscopy better, and the HR and mean blood pressure values of the patients in this group were more stable.

Regarding hemodynamic data, our study yielded similar outcomes to those of the aforementioned studies. A crucial finding from this study was that, despite being under control, hypertensive patients were present in both groups. Antihypertensive agents with a variety of mechanisms of action can be used to treat hypertension. Consequently, the hemodynamic responses of these patients to anesthetics were not uniform. Even though the number of hypertensive patients in our study was comparable between groups, this may be considered a limitation of this study.

In a meta-analysis involving five studies and 1,250 patients in which propofol and ketofol were used in the procedural sedation of adults in the emergency department, the incidence of respiratory side effects was found to be lower in the ketofol group when compared to the propofol group, and the peripheral oxygen saturation values of those patients in the propofol group were found to be lower than those in the ketofol group.[17] In a prospective study by Elkalla and El Mourad[18] comparing the sedation efficiency and safety of propofol, dexmedetomidine and ketofol for drug-induced sleep endoscopy in patients with sleep apnea, dexmedetomidine and ketofol were found to provide a safe respiratory profile without significant hemodynamic side effects. During the procedure, our study recorded peripheral oxygen saturation values as instantaneous trend data. The difference between the mean SpO_2 values of 98.1% in the ketofol group and 96.8% in the propofol group was statistically significant. There was no significant decrease in SpO_2 values in the ketofol group compared to the baseline value. In terms of peripheral oxygen saturation, our study's findings were comparable to those of the studies discussed previously.

In a study by Turan et al.[19] in which capnography monitoring was added to oxygen saturation monitoring for better monitoring of the respiratory parameters, 30 patients who were sedated for a gastroscopy/colonoscopy procedure with an IPI monitor were evaluated, and a decrease in the SpO_2 value was detected in only two patients, despite the fact that five patients required ventilation with a mask (IPI score of 1-3). The authors reported that IPI monitoring could detect respiratory problems which may develop in patients earlier than pulse oximetry could and this may provide benefits for the patient and the anesthesiologist. Gozal and Gozal[20] used IPI monitoring in children who underwent deep sedation and observed that the IPI monitor could detect all respiratory problems with 98% specificity. In addition, the authors stated that for less experienced healthcare professionals, an IPI monitor might be helpful in the follow-up of pediatric patients undergoing sedation.

In our study, we found the mean IPI values for group K and group P to be 9.4 and 7.3 respectively, with the difference being statistically significant. In the ketofol group, the IPI values were similar to the baseline. In contrast, the IPI values of the propofol group decreased significantly relative to the baseline value and were statistically significantly lower than those of the ketofol group at all times. Although SpO_2 was normal in 12 patients in group P, respiratory depression requiring intervention occurred and IPI values remained low during apnea episodes in these patients. Respiratory depression and apnea episodes requiring intervention were not observed in any patient in group K. In our study, we found that the IPI monitor was a superior early indicator to pulse oximetry for patient intervention in emergency situations, consistent with the findings of the aforementioned studies.

Anderson et al.[21] evaluated the role of capnography in the detection of respiratory involvement in pediatric patients who received propofol prior to orthopedic procedures. They found that while all of the patients who developed apnea were detected by capnography, none of them were detected by clinical follow-up and pulse oximetry. The authors reported that continuous measurement with capnography during the procedure is superior to clinical observation and pulse oximetry for detecting adverse respiratory and airway events. Hypopneic hypoventilation is a type of hypoventilation that is difficult to detect except through capnography in the follow-up of sedated patients. Remarkably, Langhan et al.[22] reported that all hypoventilation episodes, or hypopneas, have an $EtCO_2$ of 30 mmHg or less. Hypopnea's low $EtCO_2$ levels are caused by an increase in dead space as tidal volume decreases. Numerous studies have focused on the definitions of apnea and bradypnea, but their commentary on this type of breathing is limited. Changes in respiratory rate allow for the detection of bradypnea and apnea. Hypopnea, on the other hand, cannot be detected through physical examination or the conventional monitoring of the respiratory tract.

In our study, the mean $EtCO_2$ value was 34.4 mmHg in group K and 29.6 mmHg in group P, and a statistically significant difference was observed between the two groups. While mean $EtCO_2$ values in the propofol group were significantly lower than the baseline value, the mean $EtCO_2$ value in the ketofol group was statistically insignificantly higher and more stable than the baseline value. We believe the low $EtCO_2$ values in the propofol group were due to $EtCO_2$ being ≤30 mmHg in almost all of the hypoventilation attacks, that is, hypopneic hypoventilation. Although peripheral oxygen saturation was normal in 12 patients in this group, respiratory depression occurred and $EtCO_2$ could not be measured during the apnea episodes in these patients, which caused the average $EtCO_2$ values to be low. Respiratory depression and apnea episodes requiring intervention were not observed in any patient in the ketofol group.

In a study evaluating side effects, Willman and Andolfatto[23] reported that no patients administered propofol and ketamine experienced hypotension, bradycardia, vomiting, laryngospasm, or any side effects at discharge. In the study conducted by Amornyotin et al.[24] in which colonoscopy was performed under anesthesia, hypotension was observed in 16 (32%) patients and bradycardia was observed in one patient in the propofol group. In comparison, hypotension was observed in 7 (14%) patients in the ketofol group. The authors reported the ketofol combination as having fewer cardiovascular side effects. In a meta-analysis by Jalili et al.[25], the authors reported that ketofol may cause less respiratory depression requiring intervention and less bradycardia and hypotension than propofol alone, and the authors suggested ketofol as an alternative to propofol. In our study, none of the patients in the ketofol group developed complications during the procedure. However, in the propofol group, we observed two patients with hypotension which required intervention, one patient with bradycardia, and twelve patients with respiratory depression.

Study Limitations

This study had a number of limitations. This study did not utilize BIS monitoring in conjunction with the Ramsey sedation score for sedation monitoring. With the application of BIS, more objective sedation values could be predicted. Secondly, the study population included patients with controlled hypertension. Although the number of hypertensive patients in both groups was comparable, the different mechanisms of action of the drugs used by these patients may have altered the effects of the anesthesia. Thirdly, in the concomitant use of propofol and ketamine, the literature-recommended ratio of 1:2 was used, and no other ratios were employed.

CONCLUSION

In comparison to the propofol group, the hemodynamic and respiratory parameters were more stable in the ketofol group, the side effects were less frequent, and ketofol use did not result in prolonged recovery. However, it would be appropriate to support this study with more extensive randomized, controlled series and comparative studies of ketofol administered at different rates. In addition, we believe that making IPI and non-invasive end-tidal carbon dioxide monitoring routine among the standard infrastructure and equipment in non-operating room anesthesia applications can be advantageous for both the patient and the anesthesiologist, as respiratory problems and other potential complications can be detected more accurately than when pulse oximetry is used alone.

MAIN POINTS

- It is preferred that the anesthetic agent used in endoscopic procedures be efficient, not interfere with hemodynamic and respiratory data, and not prolong the recovery time.
- Ketofol was more reliable in terms of hemodynamic and respiratory data when compared to propofol, and its side effects were less common.

- In non-operating room anesthesia, IPI and non-invasive $EtCO_2$ monitoring are reliable in detecting respiratory problems and potential complications in patients.

ETHICS

Ethics Committee Approval: This study was approved by the University of Health Sciences Türkiye, Samsun Training and Research Hospital Institution Ethics Evaluation Board (approval number: 2019/4/32).

Informed Consent: This for study written informed consent was obtained from each participant.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.A., H.K.Ç., Concept: A.A., H.K.Ç., Design: A.A., H.K.Ç., Z.D., Data Collection or Processing: A.A., Analysis or Interpretation: A.A., H.K.Ç., Z.D., Literature Search: A.A., H.K.Ç., Writing: A.A., H.K.Ç.

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