Comparison of the effects of bispectral index-controlled use of remifentanil on propofol consumption and patient comfort in patients undergoing colonoscopy

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Abstract

Background and study aims : **In endoscopic procedures, propofol can be safely administered either alone or in conjunction with remifentanil. The aim of the study is to compare the effects of the administration of propofol alone and the administration of remifentanil in addition to propofol on patient and endoscopist satisfaction, preoperative hemodynamic response, and propofol consumption.**

Materials and methods : **A totally 60 patients were enrolled in the study. Propofol group (Group 1) : A 0.4-mg/kg propofol bolus and 1 mg/kg/h maintenance infusion of propofol until a bispectral Index value of 70-75 was achieved. Propofol + remifentanil group (Group 2) received a 0.4 mg/kg propofol bolus dose and maintained with a 0.5 mg/kg/h infusion of propofol + 0.2 mcg/kg/min infusion of remifentanil. The infusion dose of remifentanil was maintained, and the propofol infusion dose was titrated until a BIS value of 70-75 was achieved.**

Results : **In Group 1 (colonoscopic intervention 1 and 5 min) and Group 2 (colonoscopic intervention 10 min.), main blood pressure (MBP) value has a significant decrease. Hypotension occurred in 6 patients in group 1, while 12 patients in group 2. No significant difference was found between the Patient's endoscopist' satisfaction, MBP and heart rate. Propofol consumption was greater in group 1 than in group 2. When the Ramsay sedation levels of Group 1 and Group 2 were compared, a statistically significant difference was observed.**

Conclusion : **The addition of remifentanil to propofol may be an alternative to the use of alone propofol for sedation in colonoscopic interventions.** (Acta gastroenterol. belg., **2015**, 78, **314-318**).

Key words : propofol, remifentanil, colonoscopy, sedation, patient satisfaction.

Introduction

Clinicians use an endoscopic approach to diagnose and treat gastrointestinal diseases. Endoscopic intervention is often an obtrusive and stressful procedure for patients (1). Sedation and analgesia are an essential component of endoscopic procedures because they help patients to overcome their concerns and comfortably tolerate the intervention. Pain and vasovagal reactions that require the administration of sedative and analgesic agents occur frequently in endoscopic procedures (2). The addition of amnesia to sedoanalgesia gives patients no memory of their colonoscopy and any negative or unpleasant experiences that may occur during the procedure.

Sedation and analgesia also have disadvantages, such as prolongation of the hospital stay, hypotension, and respiratory depression (3,4). The sedation applied has 4 phases : mild, moderate, deep, and general anaesthesia. Endoscopic procedures usually require a moderate sedation phase. While creating sedation, the anaesthesiologist must consider the patient's physical condition and the properties of the drugs administered (5). Bispectral index (BIS) monitoring is commonly used to measure the depth of patient sedation (6). Bispectral analysis may decrease awareness during anaesthesia. At the same time, it can reduce resource usage since it requires less medication to produce amnesia and therefore facilitates a fast wake-up (7).

Propofol has been widely used in endoscopic procedures. While the drug has no analgesic properties, it can provide sedation and amnesia depending on the dose. Opioid agents can also be added to prevent pain and propofol overdose in patients during colonoscopic interventions. However, when used in combination with opioids, the sedative activity of propofol increases, so medical professionals must be vigilant to recognise respiratory depression in patients receiving these drugs (5,8,9).

Opioids bind to specific receptors located in all parts of the central nervous system and other tissues. Although opioids provide some sedation, their analgesic effects are more pronounced. The endoscopy team should choose an anesthesia and sedation technique that will provide comfort and safety as well as a fast recovery of all psychomotor functions of a patient (3). Remifentanil is a short-acting opioid receptor agonist with an elimination period of less than 10 minutes. Its biotransformation is rapid and complete, so its infusion duration has very little effect on the patient's wakeup time (10). Many studies have reported the advantages of using remifentanil in interventions that require sedation (11-13).

In this study, BIS-controlled sedation was provided during colonoscopic procedures ; the aim was to compare the effects of the administration of propofol alone and the administration of remifentanil in addition to propofol on patient and endoscopist satisfaction, perioperative hemodynamic response, and propofol consumption.

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Patients/materials and methods

For this study, institutional ethics committee consent was obtained from Abant Izzet Baysal University, Clinical Ethics Committee (Ethics Committee No. 2012/264). During their preanaesthetic evaluation, 60 patients aged 50 to 75 years with American Society of Anesthesiologists (ASA) risk classifications of II-III who were scheduled to undergo elective colonoscopic procedures were enrolled in the study. Data were collected from January 2014 to May 2014. We excluded patients with known allergies to any of the medications used in the study, opioid-dependence, severe pulmonary, cardiac, renal, or liver disease that is a constant threat to life (patients in ASA 4 status), and those who had taken a sedative drug in the last 24 hours or who refused to take part in the study.

Patients were randomised into two equal groups using the closed envelope method. During the preoperative assessment, all participants were given information about the method of anaesthesia, and the Verbal Rating Scale (VRS), which consists of 10 units, including patient satisfaction, Ramsay sedation scoring (RSS) (1 Patient is anxious and agitated or restless, or both, 2 Patient is cooperative, oriented, and tranquil, 3 Patient responds to commands only, 4 Patient exhibits brisk response to light glabellar tap or loud auditory stimulus, 5 Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus, 6 Patient exhibits no respons) and a nausea and vomiting scale, was explained to them. The patients also provided verbal and written consent to participate in this study.

Standard monitoring was performed on patients taken to the intervention room. Electrocardiogram (ECG), heart rate (HR), MBP, and peripheral oxygen saturation (SpO_2) were assessed. All patients were monitored using BIS (Bispectral Index A-2000, AspectMedical Systems, Netherlands) to measure the depth of sedation. After intravenous access was achieved using a 20-gauge intracath, 0.9% NaCl was administered at a rate of 5-8 ml kg/hr. Patients received 2 L/min of O_2 by nasal cannula ; a 0.4-mg/kg propofol bolus dose was administered to the group that was given propofol alone (1% propofol Lipuro, B. BraunIrengun, Istanbul, Turkey). Group 1 : Maintenance treatment was provided by a 1-mg/kg/h infusion of propofol. Throughout the intervention, the infusion dose of propofol was increased by titration until a BIS value of 70-75 was achieved. Group 2 received a 0.4-mg/kg propofol bolus dose initially, and then patients were maintained with a 0.5-mg/kg/h infusion of propofol + a 0.2-mcg/kg/min infusion of remifentanil (Ultiva, Glaxo Smith Kline, Istanbul, Turkey). Throughout the intervention, the infusion dose of remifentanil was maintained, and the propofol infusion dose was titrated by increasing the amount until a BIS value of 70-75 was reached.

Before and throughout the intervention, the patients' systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), KAH, SpO_2, and BİS values were measured and recorded at 0, 5, 10, 15, 20, and 30 min. An SBP drop below 90 mmHg or a reduction of 20% compared to baseline values measured before the intervention was considered hypotension. Fluid resuscitation was the treatment for hypotension, and 5 mg of ephedrine hydrochloride (ephedrine 0.05 g/ml, Osel, Istanbul, Turkey) was on hand if the patient failed to respond. An HR of less than 50 beats/min was evaluated as bradycardia, which was treated with 0.5 mg of atropine sulphate (Atropine Sulphate Vial Galen, Istanbul, Turkey). In case of respiratory depression (SpO_2 dropping below 85% for more than 60 seconds), patients received supplemental oxygen, and their heads were brought to extension and their chins raised. Mask ventilation was used if persistent desaturation occurred. During and after the intervention, we recorded all side effects, including hypotension, hypertension, tachycardia, bradycardia, desaturation, nausea, vomiting, itching, and complications induced by anaesthesia and the colonoscopic procedure. A 4-point nausea and vomiting scale was used to assess nausea and vomiting. After the intervention, the patients' levels of sedation and pain were rated by the Ramsay Sedation Scale and the VRS scale, respectively. Both patient satisfaction and endoscopist satisfaction were evaluated after the intervention.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS 15.0) software was used to perform statistical calculations. Descriptive variables including age, height, weight, heart rate (HR), mean arterial pressure (MAP), and intervention time are shown as mean ± standard deviation. A Kolmogorov-Smirnov test was conducted to determine whether the data fit a normal distribution. An independent-samples t-test was used to analyse normally distributed variables between groups, while the Mann-Whitney U test was carried out for those not normally distributed. In the case intragroup comparison, a paired simple t-test was used for normally distributed data, and a wilcoxon test was employed for data that were not distributed normally. The chi-squared and Fisher's exact test were used to analyse categorical variables. A p-value less than 0.05 ($p < 0.05$) was considered statistically significant.

Results

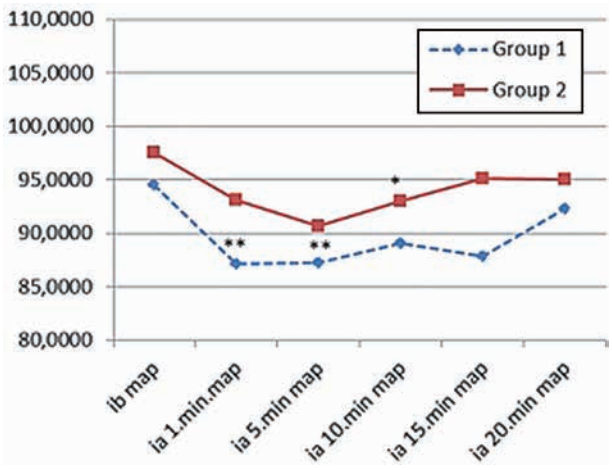
Our study included 60 patients who were scheduled for elective colonoscopy. In order to induce sedation during the intervention, 30 patients received propofol alone, and 30 patients were given both propofol and remifentanil. No significant difference was found between the patients' demographic data and the intervention times ($p > 0.05$) (Table 1).

In Group 1, when the MBP value before the colonoscopic intervention was compared with MBP values at intraoperative 1 min and 5 min, a significant decrease

Table 1. — **The demographic characteristics of patients, propofol and remifentanil consumption**

	Group 1	Group 2	P value
Age (year)	60 ± 4.84	58 ± 5.39	P = 0.14
Weight (kg)	73 ± 12.14	69 ± 11.19	P = 0.25
Gender (M / F)	17/13	15/15	P = 0.61
Duration of intervention (min)	14 ± 3.71	13 ± 2.58	P = 0.25
ASA (II/III)	1/29	2/28	P = 0.55
Propofol (mg)	117 ± 43.29	89 ± 43.34	P = 0.01*
Remifentanil (μg)	0	180 ± 48.59	

(M/F) Male/ Female, ASA : American Society of Anesthesiologists.
* p value of comparison between groups, $p < 0.05$.
Values are expressed as mean ± SD, n.
ASA, American Society of Anesthesiologists.



ib mbp = intervention before mean arterial pressure, ia 1,5,10, 15,20.min mbp, = intervention after 1,5,10,15,20.min. mean arterial pressure value.
** Group 1, $p < 0.05$.
* Group 2, $p < 0.05$.

Fig. 1. — Comparison of mean arterial pressure values between groups.

was observed ($p < 0.05$) (Fig. 1). In Group 1, transient hypotension occurred in 12 patients, and normotension was achieved with fluid resuscitation. When the HR value before induction was compared with the values at 1 min, 5 min, 10 min, 15 min, and 20 min into the intervention in this same group of patients, no significant reduction was noted ($p > 0.05$).

In Group 2, when the pre-intervention MBP value was compared with values at 10 min into the colonoscopic intervention, a significant decrease was observed ($p < 0.05$) (Fig. 1). In Group 2, 6 participants experienced transient hypotension, and normotension was achieved with fluid resuscitation. When the pre-intervention HR values were compared with HR values at 1 min, 5 min, 10 min, 15 min, and 20 min into the intervention, no significant difference was observed ($p > 0.05$). A comparison of MBP and HR values between the groups also produced no significant difference ($p > 0.05$) (Fig. 1).

The mean amount of propofol administered in Group 1 was 117 ± 43.29 mg. Group 2 received average propofol and remifentanil doses of 89 ± 43.34 mg and 180 ± 48.59 μg, respectively (Table 1).

When the RSS of Group 1 and Group 2 were compared, a statistically significant difference was observed ($p = 0.04$). The median RSS at the after the intervention were significantly higher in Group 1 median value, than in Group 2 median value (Group 1 : 3 (1-6) ; Group 2 : 2 (2-5)) ($p < 0.05$).

When VRS scores were evaluated by patient satisfaction (Very poor (0), Poor (1), Good (2), Very good (3)) and endoscopist satisfaction (Very poor (0), Poor (1), Good (2), Very good (3)), no significant difference was observed between the groups ($p > 0.05$). Desaturation was not noted in any of the groups.

In Group 1, 1 patient experienced nausea and vomiting, while 2 patients in Group 2 reported vomiting and nausea. The 3 patients with nausea and vomiting were treated with metoclopramide HCl.

Discussion

Our study included 60 patients who were scheduled to undergo colonoscopic intervention. To achieve sedation, we administered propofol alone to 30 patients, and propofol in conjunction with remifentanil was given to 30 patients. Our main findings in this study were that the addition of remifentanil to propofol reduced the dose of propofol required, did not cause hemodynamic instability by providing sufficient analgesia for the intervention, and allowed sedation to be safely maintained under BIS control.

Sedation and analgesia are widely used both alone (midazolam, diazepam, propofol, ketamine, droperidol, fentanyl, remifentanil) and in combination (3,8,14) to produce sedation and analgesia in colonoscopic interventions. In endoscopic procedures, propofol can be safely administered either alone (15) or in conjunction with

Table 2. — **Patient and endoscopist satisfaction, Ramsey sedation score, Verbal rating scale**

	Group 1	Group 2	P value
Patient satisfaction			
Sedation quality Very well well Moderate poor	 28 (93.3%) 2 (6.6%) 0 (0%) 0 (0%)	 30 (100%) 0 (0%) 0 (0%) 0 (0%)	 p > 0.05
VRS No pain Mild pain Moderate pain Severe pain	 27 (90%) 3 (10%) 0 (0%) 0 (0%)	 29 (96.6%) 1 (3.3%) 0 (0%) 0 (0%)	 p > 0.05
RSS	3.7 ± 1	2.6 ± 0.7	p = 0.01*
Endoscopist satisfaction			
Sedation quality Very well well Moderate poor	 27 (90%) 2 (6.6%) 1 (3.3%) 0 (0%)	 27 (90%) 3 (10%) 0 (0%) 0 (0%)	 p > 0.05

VRS, Verbal rating scale ; RSS, Ramsay sedation scale.
* The p values for comparisons between groups, $p < 0.05$.
Values are expressed as mean ± SD, n or n (%).

remifentanil (16). The addition of an opioid analgesic to an agent yielding sedation and amnesia may improve patient satisfaction (17). Mandel *et al*. (18) compared a propofol-remifentanil sedation protocol administered for a colonoscopy with midazolam-fentanyl and reported that recovery from sedation produced with propofol-remifentanil was faster, and patient satisfaction was better (18). In our study, patients' recovery times were not measured. The post-intervention sedation levels of patients were rated over 6 points (Ramsay sedation score). At the end of the intervention, a lower Ramsay sedation score was obtained for the group that received propofol and remifentanil, which may be an indicator of a faster recovery. In our study, 90% of the patients in Group 1 had no pain, whereas 96.6% of patients in Group 2 reported no pain. In both groups, high patient and endoscopist satisfaction were achieved, and there was no significant difference between the groups. Previous studies have reported a high degree of patient satisfaction with the use of propofol alone (19). In our study, 93.3% of patients in the group receiving propofol alone rated their level of sedation as good or very good, while this percentage reached 100% in the group that was co-administered remifentanil.

The targeted level of sedation in endoscopic and colonoscopic procedures is generally one that will allow the intervention to be tolerated without jeopardizing patient safety. For this purpose, the BIS monitor is often used in endoscopic procedures (6). BIS values range from 0 to 100 : (0, no cortical activity or coma ; 100 fully awake). A score between 40 and 60 is considered general anaesthesia, 60 and 70 as deep sedation, and 70 and 90 as mild/moderate sedation. In our study, the BIS value was 75.2 ± 6.6 for Group 1 patients, while it was 75.4 ± 6.8 for Group 2 patients. Controlled sedation can be achieved by titrating sedative drugs by the targeted BIS value.

Studies have assessed the safety of sedation by investigating respiratory depression (SpO_2 remaining below 85% for more than 60 seconds), endotracheal intubation, aspiration, hypotension, and cardiopulmonary complications such as bradycardia (15,20). The risk of developing cardiorespiratory complications has been reported to be 0.01% in patients who underwent colonoscopy (21). In our study, no respiratory depression developed in either group, and no statistically significant difference was found between the two groups in terms of blood pressure changes. When propofol is administered alone during endoscopic procedures, higher doses may be required for the patient to tolerate the procedure. Depending on the dose administered, hypoventilation, hypotension, and bradycardia may develop (22). When the patients in our study were examined hemodynamically, the blood pressures in both groups decreased. However, this decrease was sharper in the group that received propofol alone (Fig. 1). Hypotension occurred in 12 (40%) patients who were given propofol alone, while it was observed in 6 (20%) patients co-administered remifentanil and propofol. Sudden blood pressure changes are known to cause increased mortality, especially in elderly patients with reduced cardiac performance and unstable cardiovascular conditions (23). Therefore, the propofol dose can be reduced by adding an opioid analgesic (8,17). In our study, the addition of remifentanil reduced the propofol dose by 24%. We believe that the development of hypotension in Group 2 patients was associated with reduced propofol dosage to a lesser extent. Data on the safety of the combination of propofol and remifentanil in endoscopic procedures are controversial. Some studies have

reported that the co-administration of propofol and remifentanil will have a synergistic effect on the respiratory system and cause severe respiratory depression (24), while others claim that this combination is safe and does not cause cardiovascular instability or respiratory depression (25).

As a result, the addition of remifentanil to propofol was determined to be safe in terms of respiratory depression during colonoscopic interventions conducted under BIS monitoring and by creating mid-level sedation. Hypotension developed to a lesser extent in the case of sedation created by this combination and did not lead to cardiac instability. The addition of remifentanil to propofol may be an alternative to the use of alone propofol for sedation in colonoscopic interventions.

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