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SCIENTIFIC ARTICLE

Sedation-Analgesia in Elective Colonoscopy: Propofol-Fentanyl versus Propofol-Alfentanil

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Abstract

Background and objectives: Sedation-analgesia is recommended for comfortable colonoscopy procedures, which are invasive and can be painful. This study aimed to compare the combinations of propofol-alfentanil and propofol-fentanyl for sedation-analgesia in elective colonoscopy patients.

Methods: This prospective and randomized study was planned in ASA I-II groups and included 80 patients between the ages of 18 and 65 years. Sedation-analgesia induction was performed as 1 $\mu g.kg^{-1}$ fentanyl, 1 $mg.kg^{-1}$ propofol in the propofol-fentanyl group (Group PF) and 10 $\mu g.kg^{-1}$ alfentanil, 1 $mg.kg^{-1}$ propofol in the propofol-alfentanil group (Group PA). Patients' scores were limited to 3-4 values on the Ramsey Sedation Scale (RSS) by 0.5 $mg.kg^{-1}$ bolus additional doses of propofol in sedation-analgesia maintenance. We recorded demographical data, heart rate, mean arterial pressure (MAP), oxygen saturation of hemoglobin (SpO2), RSS value, colonoscopy time, total dose of propofol, complications, recovery time, and discharge time, as well as colonoscopist and patient satisfaction scores.

Results: MAP at the 15^{th} minute in Group PA was significantly higher than in Group PF ($p = 0.037$). Group PA's beginning mean heart rate was higher than the mean heart rate at subsequent readings ($p = 0.012$, $p = 0.002$). The mean total propofol dose of Group PA was significantly higher than the total dose of Group PF ($p = 0.028$). The mean recovery time of Group PA was significantly longer than that of Group PF ($p = 0.032$).

Conclusion: Fentanyl provides better operative conditions and reduces the need for additional propofol doses. These advantages cause a shorter recovery time. Therefore, propofol-fentanyl is superior to the propofol-alfentanil for sedation-analgesia in colonoscopy.

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Introduction

Due to the frequency of colorectal malignancies in industrial countries, diagnostic and therapeutic colonoscopy rates have increased dramatically. Colonoscopy-induced pain and anxiety affects both patient and colonoscopist comfort [1]. The best sedation/analgesia type for gastrointestinal endoscopic procedures is still not clear [2]. Although some studies recommend that the colonoscopy procedure can be performed without sedation, various other studies have reported this is not possible and that sedation administration before the procedure is safer for both patient and colonoscopist [3-5]. Both anesthesia and sedation-analgesia are options for colonoscopy procedures [6], but conscious sedation is recommended [1]. Conscious sedation allows the patient to give responses to verbal or tactile stimulation and provides the attendance of respiratory and cardiovascular functions [1].

Doctors performing colonoscopy screenings throughout the world tend to prefer sedation-analgesia. Midazolam, propofol and/or alfentanil or pethidine combinations, α-agonists, and neuroleptics are used for sedation-analgesia [6,7].

This study aimed to compare the hemodynamic effects, recovery and discharge times, patient-colonoscopist satisfaction, and complications of propofol-fentanyl and propofol-alfentanil combinations in elective colonoscopy procedures.

Material and Methods

After obtaining the Ethics Committee's approval and the patients' written informed consents, this prospective and randomized 80-patient study proceeded in Şişli Etfal Training and Research Hospital, Istanbul, Turkey. The research team selected a group of ASA I-II patients between 18 and 65 years scheduled for elective colonoscopy screening. Researchers verified the status of patients' 8-hour fasting period and the absence of alcohol or sedative drug use 24 hours before the colonoscopy procedure. The same anesthesiologist administered sedation-analgesia on all patients. The exclusion criterions of this study were pregnancy, gastrointestinal hemorrhage, known or predicted airway difficulty, alcohol or drug addiction, neuropsychiatric disease, severe heart or respiratory insufficiency, and sedative drug allergy.

An independent nurse performed randomization by sequentially opening numbered opaque envelopes with group allocation cards in a random computer generated sequence. Patients were not informed of the group in which they were included.

We explained the oral scoring system to the patients, which is on a scale of 1 to 10 and necessary to evaluate the patient satisfaction. After patients were admitted to the gastrointestinal endoscopy unit, intravenous (IV) catheterization was performed with 18-gauge IV catheters and a 0.9% NaCl infusion was started; patients received no premedication. The lateral positioned patients were monitored with noninvasive systemic mean arterial pressure (MAP), 3-channel ECGs, and pulse oximetry (SpO_2). Patients received 3L.min^{-1} oxygen by nasal catheter.

The research team performed sedation-analgesia induction as 1 μg.kg^{-1} fentanyl and 1 mg.kg^{-1} propofol in Group PF and 10 μg.kg^{-1} alfentanil and 1 mg.kg^{-1} propofol in Group PA. After the beginning of the colonoscopy screening, the patients' scores were limited to 3-4 values on the Ramsey Sedation Scale (RSS) (Table 1) by 0.5 mg.kg^{-1} bolus additional doses of propofol in sedation-analgesia maintenance. We recorded heart rate, MAP, SpO_2, and RSS values before the procedure, at the beginning of the colonoscopy screening, and at 5-minute intervals during the procedure.

We established colonoscopy time as the time from induction to the end of the colonoscopy screening. The recovery time was the time from induction until the RSS scores progressed to value 2. We recorded total propofol doses and complications. After the procedure, patients with scores of 9 or greater, according to the Aldrete Score (Table 2), were discharged. After recovery, patients orally scored satisfaction on a scale of 1 to 10 (1: not satisfied, 10: very satisfied). Colonoscopist satisfaction was scored with 10 cm visual analog scale. We recorded colonoscopist and patient satisfaction scores.

We recorded anesthesia and endoscopy-related complications that appeared during or after procedure, such as allergic reactions, bradycardia, tachycardia, hypotension, hypertension, respiratory depression, desaturation, perforation, bleeding, nausea and vomiting. Desaturation was defined as the decrease of oxygen saturation to below 85%.

Table 1 - Ramsay Sedation Scale.

Definition	Score
Patient is anxious and agitated or restless, or both	1
Patient is cooperative, oriented and calm	2
Patient responds to commands only	3
Patient exhibits brisk response to light glabellar tap or loud auditory stimulus	4
Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus	5
Patient exhibits no response	6

Table 2 - Aldrete Score.

	Definition	Score
Activity	Able to move 4 extremities voluntarily or on command	2
	Able to move 2 extremities voluntarily or on command	1
	Able to move 0 extremities voluntarily or on command	0
Respiration	Able to deep breath and cough freely	2
	Dyspnea or limited breathing	1
	Apnea	0
Circulation	Blood Pressure < ± 20% of Preanesthetic level	2
	Blood Pressure < ± 20-50% of Preanesthetic level	1
	Blood Pressure < ± 50% of Preanesthetic level	0
Consciousness	Fully Awake	2
	Arousable on calling	1
	Not responding	0
O_2 Saturation	Maintains > 92% on room air	2
	Needs O_2 inhalation to maintain O_2 saturation > 90%	1
	Saturation < 90% even with supplemental oxygen	0

We calculated the sample sizes with the assumption of at least 30% possible difference in our study between any two groups. Therefore, we allocated 40 patients into each group to obtain an alpha error of 5% and statistical power of 80%.

For data evaluation and descriptive statistics (mean, standard deviation), researchers used paired variance analysis for repeated measures of the groups and the Newman-Keuls multiple comparison test for subgroups. We used an independent t-test for comparisons between the two groups and the chi-square test for comparison of qualitative parameters. Results were considered statistically significant when the p value was under 0.05.

Results

Age, sex, weight, ASA values, colonoscopy times, and complication rates were similar in both groups (Table 3). Complications were apparent in 21 patients. Although there was no respiratory depression, 8 patients from Group PF, and 12 from Group PA experienced desaturation. These patients did not need endotracheal intubation or mask ventilation; vocal or tactile stimuli produced adequate recovery from desaturation. Only one patient had nausea and vomiting; this patient was in Group PA. All of the patients that experienced complications were discharged safely. We did not see endoscopy-related complications.

The MAP mean at the 15th minute in Group PA was significantly higher than in Group PF (p = 0.037), but there were no differences between the two groups at all other times of MAP (Table 4). Similar to Group PA, Group PF showed no significant differences when the beginning MAP mean was compared with the mean at all other times.

There was no difference in mean heart rate between the two groups at any time. Although mean heart rates were similar in Group PF for all recording times, significant differences were found in Group PA (p = 0.0001). Group PA's beginning mean heart rate was significantly higher than the mean heart rates for all other recording times (p = 0.002, p = 0.012), which were similar to each other (Table 5). There were no significant differences between the two groups in mean oxygen saturation values (Figure 1).

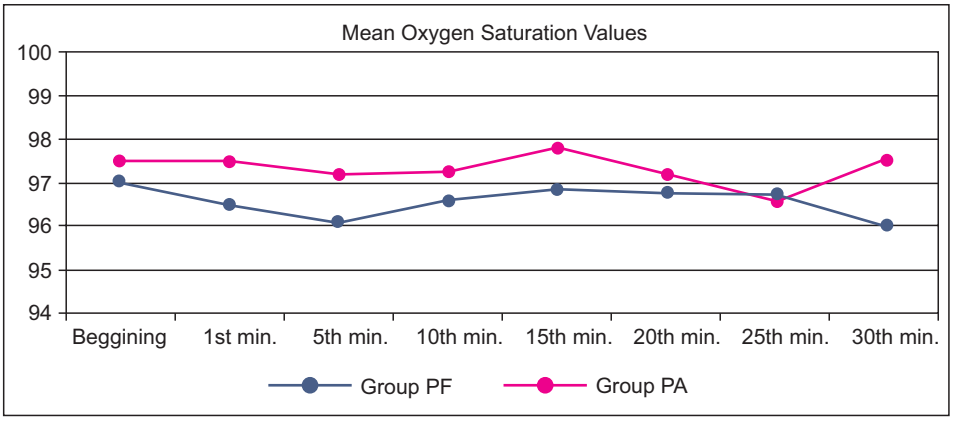

Figure 1 - Mean Oxygen Saturation Values of the Groups.

Table 3 - Distributions of Age, ASA, Sex, Weight, Complications and Colonoscopy Times in Groups.

		Group PF	Group PA	p
Age (year)		51.8 ± 12.65	54.5 ± 15.16	0.390
	Female	22 (55%)	23 (57.5%)	
	Male			
Sex		18 (45%)	17 (42.5%)	0.822
Weight (kg)		77.97 ± 14.02	80.03 ± 11.22	0.472
	I	14 (35%)	11 (27.5%)	
ASA	**II**	26 (65%)	29 (72.5%)	0.573
Colonoscopy Time (minute)		17.5 ± 7.39	20.68 ± 10.2	0.115
	Absent	32 (80%)	27 (67.5%)	
Complication	**Present**	8 (20%)	13 (32.5%)	0.204

Table 4 - Mean MAP Values of the Groups.

MAP	Group PF	Group PA	p
Beginning	93.32 ± 18.25	96.7 ± 18.81	0.423
1st Minute	84.2 ± 100.61	72.95 ± 13.24	0.491
5th Minute	75.33 ± 16.29	76.8 ± 15.29	0.681
10th Minute	80.37 ± 14.32	82.81 ± 20.41	0.550
15th Minute	75.95 ± 10.87	85.1 ± 17.76	**0.037***
20th Minute	83.08 ± 13.41	87.09 ± 21.78	0.553
25th Minute	89.4 ± 17.19	86.45 ± 29.69	0.787
30th Minute	81.67 ± 2.52	84.5 ± 25.03	0.854

Table 5 - Mean Heart Rates of the Groups.

Heart Rate	Group PF	Group PA	p
Beginning	84.98 ± 13.19	89.10 ± 11.64	0.142
1st Minute	81.8 ± 10.87	82.48 ± 13.06	0.802
5th Minute	77.44 ± 9.71	76.88 ± 12.43	0.824
10th Minute	76.59 ± 10.34	77.41 ± 11.51	0.479
15th Minute	77.09 ± 11.83	76.39 ± 11.4	0.828
20th Minute	75.46 ± 13.82	77.05 ± 10.46	0.704
25th Minute	77.6 ± 14.74	77.9 ± 14.17	0.964
30th Minute	79 ± 22.07	78.13 ± 12.15	0.933
P	0.770	**0.0001***	

Table 6 - Mean RSS Values of the Group.

RSS	Group PF	Group PA	p
1st Minute	4.85 ± 0.43	4.8 ± 0.69	0.697
5th Minute	3.93 ± 1.12	3.78 ± 1.03	0.534
10th Minute	3.7 ± 0.91	3.41 ± 1.09	0.207
15th Minute	3.68 ± 1.04	3.35 ± 0.84	0.212
20th Minute	3.29 ± 0.73	3.1 ± 1	0.543
25th Minute	3.1 ± 0.74	3.33 ± 0.87	0.534
30th Minute	2.25 ± 0.5	3 ± 0.82	0.134
P	**0.0001***	**0.017***	

Table 7 - Distribution of Total Propofol Doses, Recovery Time, Discharge Time, and Colonoscopist and Patient Satisfaction Scores in Groups.

	Group PF	Group PA	p
Total Propofol Dose (mg)	148 ± 38.13	170.5 ± 50.95	**0.028***
Recovery Time (minute)	18.88 ± 6.76	23.1 ± 10.2	**0.032***
Discharge Time (minute)	31.37 ± 9.55	35.31 ± 13.06	0.136
Colonoscopist's Satisfaction Score	9.25 ± 0.84	9.33 ± 1.31	0.761
Patient's Satisfaction Score	9.38 ± 0.87	9.48 ± 0.82	0.597

Mean RSS values were similar when comparing the groups. Group PF's mean RSS values differed significantly for recording times (p = 0.0001). Group PF's first and 5th minute mean RSS values were significantly higher than at other times (p = 0.002, p = 0.045) when no differences were noted. Group PA's mean RSS values had significant differences during all the recording times (p = 0.017). Group PA's first-minute mean RSS value was significantly higher than the 15th, 20th, 25th, and 30th minute values (p = 0.002, p = 0.022) (Table 6).

The mean total propofol dose of Group PA was significantly higher than Group PF (p = 0.028) and the mean recovery time of Group PA was significantly longer than the recovery time of Group PF (p = 0.032). Mean discharge times and colonoscopist and patient satisfaction scores were similar in both of the groups (Table 7).

Discussion

Propofol is a short-acting, intravenous hypnotic, which provides rapid and complete recovery from anesthesia. When propofol is used as the sole anesthetic agent for an invasive procedure, very high doses (14.9 $mg.kg^{-1}.h^{-1}$) are required for toleration of the procedure [2]. Both direct myocardial depression and peripheral vasodilation are propofol's cardiovascular depressant effects, which are dose and concentration dependent [7,8]. Complications, such as hypotension, respiratory depression, and decreased upper airway protective reflex activity can appear with the use of high-dose propofol [7]. Because the propofol is insufficient for analgesia, combining propofol with an intravenous opioid is recommended to increase the quality of sedation [7,9].

Both alfentanil and fentanyl can be used safely in colonoscopy procedures. Fentanyl clinical potency is 3-10 times that of alfentanil. Alfentanil, a tetrazole derivative of fentanyl, crosses rapidly to highly perfused tissues like those of the brain, then distributes to the peripheral tissues. Both alfentanil and fentanyl cross the blood brain barrier rapidly. Alfentanil has rapid onset and produces unconsciousness 50 seconds after administration. Respiratory depression and unconsciousness occur at the same time with alfentanil; however, unconsciousness occurs 30-60 seconds after respiratory depression in fentanyl because fentanyl has higher lipid solubility than alfentanil and fentanyl's plasma concentration accumulates in tissue compartments before the onset of sufficient opioid effects. Less accumulation of alfentanil provides greater binding of plasma concentrations to opioid receptors and a more rapid onset of effects [8,10].

Because the propofol and alfentanil have rapid onset and are short acting, they are useful for sedation-analgesia [11] and the propofol-alfentanil combination is successful in analgesia [9]. Avramov et al. reported that the propofol-combined opioid provides analgesia and amnesia, as well as reduces incidences of nausea, vomiting, and respiratory depression [12]. In the current study, only one patient had nausea and vomiting; this patient was in Group PA.

Despite the appropriate sedation level achieved in opioid use, colonoscopy patients experienced decreased upper airway protective reflex activity and upper airway management problems [7]. Alfentanil, as a short-acting opioid, was recommended for short procedures but when used as a sole agent, reports indicate that intraoperative and postoperative respiratory depression occurred more frequently [12,13]. In the current study, the incidence of respiratory complications was higher in Group PA than in Group PF. Although there was no respiratory depression, 8 patients from Group PF and 12 from Group PA experienced desaturation. These patients did not need endotracheal intubation or mask ventilation; vocal or tactile stimuli produced adequate recovery from desaturation.

Roseveare et al. suggested that the propofol-alfentanil combination was more short-acting and effective than benzodiazepines were in colonoscopy screening [14]. Külling et al. compared the propofol-alfentanil combination with midazolam and meperidine. They reported that the propofol-alfentanil combination resulted in more rapid recovery and increased patient satisfaction in colonoscopy [15].

In one study of midazolam combinations, researchers compared meperidine, alfentanil, fentanyl, and sufentanil combinations in gastroscopy. Recovery times were reportedly shorter in the sufentanil and alfentanil groups [16]. In Holloway et al.'s study, midazolam combined with alfentanil and fentanyl were compared in colonoscopy. They reported that although alfentanil and fentanyl had similar recovery times, alfentanil provided better operative conditions [17]. The current study compared propofol combined with fentanyl and alfentanil but the results did not confirm the previous studies. Recovery time was shorter and the mean propofol dose was less in Group PF than in Group PA.

The mean colonoscopy times were 20, 68 ± 10, 2 minutes in Group PA and 17, 5 ± 7, 39 minutes in Group PF. Because alfentanil acting time is shorter than the colonoscopy time, additional propofol doses were needed, and the 15th minute MAP values were higher in Group PA than in Group PF. Group PA's beginning mean heart rate was higher than at subsequent recording times, which researchers related to the additional doses of propofol. None of our patients had hypotension or bradycardia.

In our study, we used RSS for the evaluation of sedation level. Mean RSS values were similar in both of the groups. Bispectral Index (BIS) could be used to regulate

the appropriate sedation level and to reduce the dosage of sedatives during endoscopy. There are studies that compare the use of RSS and BIS [18-20]. One of these studies reported that the BIS was the method recommended for monitoring patients under sedation and BIS monitoring could prevent oversedation and related complications [18]. In this study, we consider RSS insufficient to evaluate oversedation [18]. Not using BIS monitoring could be considered the negative side of our study. Nonetheless, there are studies comparing RSS and BIS that reported evaluations of sedation levels and the dosage of sedatives used were similar [19,20]. Since our country is a developing one, acquiring BIS monitor and electrodes is hard and expensive. In similar studies from our country, RSS was used for the evaluation of sedation level [21].

A most significant finding is that the patient/colonoscopist satisfaction scores were similar and high in both of the groups. This emphasizes that sedation-analgesia is the golden key for a comfortable and safe colonoscopy experience.

Because fentanyl has a longer acting time than alfentanil, fentanyl provides better operative conditions and reduces the need for an additional propofol dose, which results in a shorter recovery time. The propofol-fentanyl combination is superior to the propofol-alfentanil combination for sedation-analgesia in colonoscopy procedures.

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