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Original Article

Comparison of the effects of adding fentanyl or remifentanil to propofol in colonoscopy sedoanalgesia on visual analog scale and recovery: A prospective double-blind study

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Abstract

Aim: In this study; our aim is to compare the effects of fentanyl or remifentanil combinations added to propofol in sedoanalgesia of colonoscopy on the visual analog scoring (VAS) and recovery of the patient.

Material and Methods: Seventy patients aged between 18 and 65 who had colonoscopy were included in the study. 1 mg/kg propofol and 1 mcg/kg fentanyl, and 1 mg/kg propofol and 1 mcg/kg remifentanil were given as bolus to Group PF and Group PR, respectively. The respiratory and hemodynamic data during the procedure, and additionally pain and recovery criteria evaluated by VAS and Observer's Assessment of Alertness/Sedation Scale (OAA / S) scores were compared at the end of the procedure.

Results: There was a significant difference between the groups at 5th, 15th and 30th minutes in terms of VAS scores ($p < 0.001$). There was a significant difference between the groups in terms of OAA / S scores at 5th and 15th min ($p < 0.001$). The OAA / S scores were similar in both groups at 30th min and there was no difference ($p = 1.00$).

Conclusion: Combination of propofol with fentanyl or remifentanil in sedoanalgesia of colonoscopy provides a safe and comfortable examination. Early recovery in both groups is advantageous as they provide early discharge.

Keywords: Sedoanalgesia; Colonoscopy; Fentanyl; Remifentanil; Pain; Recovery.

INTRODUCTION

Colonoscopy is one of the standard procedures for the diagnosis of the lower gastrointestinal system. Anxiety of the patient is high and air insufflation into the bowel causes pain during the procedure. For these reasons, sedatives and analgesics are frequently used (1). In addition to ensuring the safety of the patient, providing rapid recovery and direct discharge from the colonoscopy unit are the desirable features of the used sedative and analgesics (2).

The air that remain in the bowel after colonoscopy causes abdominal distension and abdominal pain. Early recovery and mobilization of the patient is necessary for get rid of pain, therefore sedoanalgesics with short duration of action are also important for early mobilization.

Propofol is a general anesthetic that is frequently used for sedation in colonoscopy with its rapid onset and termination of action. Propofol does not have pain relief effect and is recommended to be used with an adjuvant agent to reduce its side effects like respiratory depression, hypoxia and hypotension (3). Adding narcotic analgesic to propofol reduces both the dose of propofol as well as the side effect, and also improves patient comfort by contributing to pain management.

Remifentanil that has a powerful narcotic analgesic is a preferred analgesic due to its rapid onset of action and quick elimination (8-10 minutes) (4). The potency and rapid onset of fentanyl is similar to remifentanil, however it has long-acting time than remifentanil(5). In our study, we aimed to compare the effect of combination of propofol / fentanyl and propofol / remifentanil on sedoanalgesics for colonoscopy on visual analog scores (VAS) and recovery of patients.

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MATERIAL and METHODS

The prospective clinic study was conducted after the approval of the Local Ethics Committee of the Inonu University Medical Faculty (2019/16). After obtaining written consent from all patients, 70 patients between the ages of 18 and 65, who were as ASA class I- II-III, and who were scheduled to colonoscopy with sedoanalgesia, were enrolled in the study.

A simple randomization method was used based on a web-based randomization generation sequence. Patients were divided into two groups as Group PF (propofol and fentanyl administered) and Group PR (propofol and remifentanil administered). The exclusion criteria were; presence of severe cardiac and respiratory insufficiency, severe sleep apnea, psychiatric disorders using psychiatric drugs, alcohol and drug addiction. Preoperative evaluation and colonoscopy preparation were performed to patients before colonoscopy.

They were monitored prior to colonoscopy. Anesthetic monitoring was applied with noninvasive blood pressure (NIBP), heart rate (HR), electrocardiograph (ECG), and peripheral oxygen saturation (SpO2). Peripheral venous access was obtained using a 22-G intravenous (i.v.) catheter from right hand because patients will lie on the left side and 0.9% NaCl infusion was started.

Anesthetic drugs were prepared and labeled before procedure. Propofol (Propofol® Lipuro, B Braun AG, Melsungen, Germany) was prepared as 10 mg/mL. 0.5 mg/kg lidocaine was given by IV prior to the first injection of propofol in both groups for propofol injection pain. Fentanyl (Talinat ®, Vem, Istanbul, Turkey) and remifentanil (Ultiva®, Glaxo Smith Kline, Istanbul, Turkey) were kept readily available in the injector as 10 mcg/mL. For Group PF, firstly fentanyl 1 mcg/kg IV was given as slow bolus. Then, 0.5 mg/kg lidocaine and 1 mg/kg propofol were given. For Group PR, firstly remifentanil 1 mcg/kg IV was given as slow bolus (in 90 seconds), then, 0.5 mg/kg lidocaine and 1 mg/kg propofol were given. Patient's disruptive movements, duration of the procedure and dose of additionally administered propofol were recorded for both groups. Our primary aim was to compare the groups in terms of VAS and OAA/S scores.

The hemodynamic data of patients were recorded at basal, after drug administration, 5th, at the end of the procedure, at also after procedure 5th, 15th and 30th minutes . Patients received oxygen with inflow of 7 L/min via a face mask. Atropine sulfate 0.5 mg/mL and ephedrine 5 mg/mL (for cases when the blood pressure decreased by more than 50% relative to baseline) were kept readily available in the injector for possible bradycardia (pulse <50 beats/min).

Jaw-thrust maneuver and required mask ventilation were performed when SpO2 is <90 after sedoanalgesia.

Pain was evaluated by VAS scores (visual analog scale; 0: no pain, 100: intolerable pain). 5 scale OAA/S (Observer's Assessment of Alertness/Sedation Scale; 1. Does not respond to nudging or shaking, 2. Responds after mild nudging or shaking, 3. Responds after name is spoken loudly, 4. Lethargic response to name spoken in normal tone, 5. Responds readily to name in normal tone) was used for recovery at 5, 15 and 30 minutes after the procedure. Patients were asked whether remember the colonoscopy procedure after recovery. Patients were discharged from the colonoscopy unit accompanied by a relative, after they were observed to be completely recovered.

The anesthetists who managed the anesthesia and collected the data were different.

Statistical Analysis

The minimum sample size required to detect a significance difference p VAS-5 using this test should be at least 3 in each group, (6 in total), considering type I error (alfa) of 0.05, power (1-beta) of 0.8, effect size of 4.01 and two-sided alternative hypothesis.

The data were expressed as mean with standard deviation, median (min-max) values or frequency (percentage) for overall variables. Normality distribution was assessed using Shapiro Wilk test. Quantitative data were analyzed by independent samples t test and Mann Whitney U test. Qualitative data were analyzed with Yates corrected chi-square or Fisher's exact test as appropriate. IBM SPSS Statistics version 25.0 for Windows was used for statistical analyses.

RESULTS

A total of 70 patients were included in the study, no patients were excluded. There was no significant difference in the demographic data of the patients of the two groups (Table 1). There was no significant difference between the groups in terms of duration of procedure and additional propofol requirement (Table 1).

Table1. Demographic and clicical parameters in both groups

Characteristics	Group PF (n=35)	Group PR (n=35)	P Value
Age (year)	49.66 ± 12.47	48.74 ± 11.25	0.749
Length (cm)	165.77 ± 7.09	165.37 ± 8.44	0.831
Weight (kg)	75.31 ± 10.24	74.29 ± 12.62	0.709
Sex (female/male)	17 / 18	18 /17	-
ASA (I/II/III)	26/9/0	23/9/3	-
Additional propofol dose (mg)	29 ± 7.84	28 ± 8.67	0.615
Procedure time (min)	15 ± 1	15 ± 1	0.311

Group PF: Group propofol+fentanyl, Group PR: Group propofol+remifentanil, n: number of cases, ASA: American Society of Anesthesiologists. Values are expressed as mean ±standart deviation or number

There was no significant difference between the groups in terms of hemodynamic parameters. There was a decrease in systolic and diastolic blood pressure at after drug administration compared to baseline levels in the both

groups , but this difference was not significant (Group PF = 99.74 ± 7.20 mmHg, 62.71 ± 4.39 mmHg; Group PR = 95.60 ± 9.01 mmHg, 59.46 ± 4.40 mmHg, systolic blood pressure and diastolic blood pressure, respectively).

The HR values were lower following sedation drugs in both groups compared with baseline levels, but this difference was not significant (Group PF=68.17±6.24 beat/min, Group PR=61.46±6.37 beta/min). There was no difference in HR between Group PF and Group PR.

SpO2<90 was observed in both groups following administration of the drugs (Group PF = 42.9%, Group PR = 37.1%), but the difference between the groups was not significant (p = 0.81), (Table 2).

Table 2. Complications associated with sedation during sedoanalgesia

	Group PF (n=35)	Group PR (n=35)	P Value
Bradycardia	0	2 (5.7%)	0.493
SpO_2<90	15 (42.9%)	13 (37.1%)	0.81
Jaw thrust maneuver	15 (42.9%)	13 (37.1%)	0.80
Disruptive movements	0	13 (37.1%)*	<0.001
Amnesia	35 (100%)	35 (100%)	

Values are expressed as mean ±standart deviation or number, SpO_2: Oxygen saturation, *: P< 0.001

Disruptive movement was not seen in any of the patients in the Group PF, but was observed in 37.1% patients in Group PR. This difference was significant (P<0.001). Amnesia occurred similarly in all patients of both groups (Table 2).

There was a significant difference between the groups (p<0.001) in terms of VAS scores at 5th, 15th and 30th minutes (Table 3).

There was a significant difference between the groups in terms of OAA/S scores at 5th and 15th minutes (p<0.001). There was no difference in OAA/S scores at 30th minute, being similar in both groups (p=1.00) (Table 3).

Table 3. VAS and OAA/S scores in both groups

	Group PF (n=35)	Group PR (n=35)	P Value
VAS 5	0 (0-0)*	20 (10-30)	<0.001
VAS 15	0 (0-0)*	20 (10-30)	<0.001
VAS 30	0 (0-0)*	20 (10-30)	<0.001
OAA/S 5	2 (2-3)*	4 (2-5)	<0.001
OAA/S 15	4 (3-4)*	5 (4-5)	<0.001
OAA/S 30	5 (5-5)	5 (5-5)	1.00

VAS: Visual Analogue Scale , OAA/S: Observer's Assessment of Alertness/Sedation scores, n: number of cases, *: p<0.001

DISCUSSION

Colonoscopy is a painful invasive diagnostic procedure in which the patient has high anxiety. Many anesthetic and narcotic analgesic agents use during the procedure as single or combined forms for safety of patient and success of procedure. Combination of sedoanalgesics is preferred more frequently to reduce the side effects and provide rapid recovery (6).

In our clinical study, we compared the efficacy of fentanyl and remifentanil, used as adjuvant agent together with propofol anesthesia during colonoscopy, on recovery in terms of VAS and OAA/S scores in 70 patients. VAS scores was significant lower on in the fentanyl group compared to the remifentanil group. However, this stasistical difference is not important clinically because all VAS scores ≤40 level. OAA/S recovery scores were obtained higher scores in terms of recovery in the remifentanil group at early period.

Ince studied the analgesic efficacy of fentanyl and remifentanil on child patients who underwent hematological intervention in her thesis. Ince used 2 mg/kg propofol , 0.5 mcg/kg fentanyl and 0.5 mcg/kg remifentanil in her thesis. It was reported that remifentanil provided shorter anesthesia recovery time, and hemodynamic and respiratory parameters were similar on the both groups. In our study, remifentanil, fentanyl and propofol doses were difference from Ince's thesis. However results were similar (7).

Propofol is one of the most frequently preferred sedatives in colonoscopy sedation, because of its short duration of action. However, the incidence of dose-related side effects of propofol included airway obstruction, respiratory and cardiovascular suppression increases in sedation (8). Therefore, using combinations can reduce the used the drug doses and side effects. Chiung-Dan et al. detected a significant difference between the two groups in terms of hemodynamic and propofol consumption in their study in which they used propofol alone and in combination with fentanyl-midazolam in colonoscopy sedation. They concluded that, using the combination drugs in lower doses as 25-50 mcg of fentanyl and 1-2 mg of midazolam, significantly decreases the consumption of propofol while increasing patient safety. In this study, propofol was given by infusion as different from our study (9,10).

Rudner et al. prefered infused 0.2 mcg/kg remifentanil and 0.5 mg/kg propofol doses to maintain a RSS (Ramsay Sedation Score) III (sedated but responds to commands) sedoanalgesia of colonoscopy. However they needed addition doses of propofol (11). Although the combination of propofol with midazolam provides hemodynamically moderate sedation, it is not recommended for the safety of the patient due to high pain scale scores in painful procedures of colonoscopy (12). We also used additional dose of propofol to patients in the both group to prevent disruptive movements.

In a study, fentanyl and ketamine were added to propofol in 60 patients for sedation of colonoscopy, when fentanyl was used at 1mcg/kg and propofol at 0.5 mg/kg doses, OAA/S scores were detected to be 4 level at 15th min. and 5 level at 20th min (13). Turk et al., used a combination of 1 mg/kg propofol and 1 mcg/kg fentanyl for sedation of colonoscopy, it was suggested that fentanyl provided a

better sedation and patient comfort and could be a good alternative compared to alfentanyl (14). Our results was similar with this previous two studies.

Using a bolus dose of remifentanil in short painful processes has been reported as an alternative to infusion when duration of action is considered (15). In the clinical study with two different doses of remifentanil given via patient-controlled intermittent bolus, they used 0.5 and 0.8 mcg/kg doses without combination. VAS score was 34 level and OAA/S score was 4 level in the 0.5 remifentanil group. VAS score was 44 level and OAA/S score was 4 level in 0.8 remifentanil group. Hemodynamic difference was not detected between the groups. Amnesia was only observed in the group of 0.8 (16). Hemodynamic parameters were similiar to in the present study. Presence of pain during the procedure in the intermittent bolus doses of remifentanil may be understood from the VAS scores. In our study, we detected that 1 mcg/kg dose of remifentanil combined with propofol provides a short-term deep sedation and amnesia. Arıcı et al. used combination of remifentanil with midazolam in colonoscopy procedure and achieving high sedation scores in the remifentanil group receiving bolus followed by infusion, it was suggested that it may be a safe alternative (17). Providing amnesia is also important for patient comfort and satisfaction during painful procedures with high anxiety levels like colonoscopy.

The ideal sedoanalgesic combination is not well defined, however propofol is most preferred drug (18). Studies continues to reduce the side effects of propofol, choose the most effective low-dose and increase patient safety.

Limitations

There are a few limitations in the present study. First, infusion was not used in the present study. Because of the short duration of the procedure, we preferred bolus application. Second, BIS monitoring did not use to measure the depth of anesthesia. We could not use BIS due to lack of equipment.

CONCLUSION

Combination of propofol with fentanyl or remifentanil in sedoanalgesia of colonoscopy provided a safe and comfortable situation. These combinations are a good advantageous for early discharge.

Statement of human rights

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Competing interests: The authors declare that they have no competing interest.
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