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EDITORIAL

Deep Sedation with Propofol and Pethidine versus Moderate Sedation with Midazolam and Fentanyl in Colonoscopic Procedure

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ABSTRACT

AIM: To compare and evaluate the clinical efficacy of the combination of propofol and pethidine (PP) versus midazolam and fentanyl (MF) for moderate sedation in colonoscopic procedure.

METHODS: 1032 patients were randomly assigned to group PP (518) and group MF (514). Primary outcome variable was the successfully completed colonoscopy. Secondary outcome variables were patient tolerance, discomfort during insertion, patient and endoscopist satisfaction, procedural pain, recovery time and sedation-related complications during and immediately after procedure.

RESULTS: All endoscopies were completely successful except 33 patients in group MF and 11 patients in group PP (p=0.019). Additional propofol dose, procedural pain and recovery time in group MF was significantly higher than in group PP. Tolerability of the patient, comfort during insertion, patient and endoscopist satisfaction and sedation-related complications in group MF were significantly lower than in group PP. No serious complications were observed in both gropus.

CONCLUSION: The efficacy of propofol and pethidine for deep sedation shows an advantage over midazolam and fentanyl for moderate sedation used for colonoscopy in term of procedure completion rate, ease of endoscopy, as well as patient's and endoscopist's satisfaction. However, the combination of propofol and pethidine for deep sedation produces a higher complication rate than in the combination of midazolam and fentanyl for moderate sedation.

Key words: Deep sedation; Colonoscopy; Propofol; Pethidine; Midazolam; Fentanyl

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INTRODUCTION

Colonoscopy is generally considered a highly invasive procedure that causes considerable discomfort to the patients. Therefore, routine administration of sedative and analgesic drugs is widely provided for this procedure. Combination of benzodiazepines and opiates is the most common practice[1]. Consequently, multi-drug regimens exist including opioids, benzodiazepines and propofol. In Thailand, most of diagnostic and therapeutic gastrointestinal endoscopies are performed with intravenous sedation[2-4]. Midazolam is frequently used because it has potent amnestic properties, some anxiolytic effect and a short elimination half-life[5]. Fentanyl is a more potent opioid than pethidine, and is associated with a faster onset of action, fewer adverse events, higher sedative effect, and it is cleared more rapidly[1]. Propofol is a strong hypnotic drug with short duration of action and more rapid recovery time for the patient compared with midazolam[6]. Generally, the anesthesiologists commonly use propofol for moderate and deep sedation for endoscopic procedures. In contrast, the non-anesthetic personnel usually use benzodiazepine and/or opioid for these procedures. At Siriraj GI Endoscopy Center, most colonoscopic procedures are performed with moderate and deep sedation. There have been different practices in regards to the use of the sedative agents. The study, therefore, was designed to compare and evaluate the clinical efficacy of the combination of midazolam and fentanyl for moderate sedation versus propofol and pethidine for deep sedation in colonoscopy procedure.

MATERIALS AND METHODS

Patients

The study was conducted from February 2006 to January 2008 at a large tertiary care referral center, Siriraj Hospital, Bangkok, Thailand. Patients with age of at least 18 years of age who presented

for colonoscopy were eligible for the study. Exclusion criteria included severe cardio-respiratory instabilities, any clinical evidence of hepatic encephalopathy, ASA physical status of class IV or V, pregnancy, and refusal to participate in the study. A total of 5832 colonoscopy procedures were performed for the study period. Of these, 1032 consecutive patients were eligible and randomized for the study. The study was approved by the Institutional Review Board of the Faculty of Medicine Siriraj Hospital. All patients provided written informed consent for the study and the procedure.

Study design

The study is a prospective, randomized control study. Patients were randomized into either the propofol-pethidine (PP) group or the midazolam-fentanyl (MF) group by using computerized generated randomization numbers placed in sealed envelopes. The endoscopists and the patients were blinded to the randomization procedure. Randomization took place in the pre-procedure room, separate from the procedure room and the recovery room. All sedation was performed in the procedure room by the anesthetic personnel. The blinded research assistant was presented in the recovery room to collect procedural data and other research or questionnaire data. Successful completion of the endoscopic procedure was the primary outcome measured. Successful endoscopic procedure was defined as completion of the procedure as intended without additional bolus propofol once the procedure started. The decision for additional bolus propofol (as long as the sedative dose had not exceeded the specified limit) rested on the anesthesiologist performing the sedation. The secondary objective was to assess patient and endoscopist satisfaction, patient tolerance to the procedure, endoscopist perception of patient tolerance to the procedure, ease of endoscopy, and complications both during and immediately after the procedure.

The colonoscopic procedure was performed by either gastroenterology fellow supervised by staff attending physician or by the staff endoscopist. Olympus video (CF-Q 180AL, Olympus Corporation, Tokyo, Japan) was used for all colonoscopic procedures. Each patient was monitored in standard manner for blood pressure, heart rate, heart rhythm with single lead electrocardiogram, and oxygen saturation with pulse oximetry. No other premedications were administered before the procedure.

Sedation technique

All sedation was administered by the nurse anesthetist or anesthesiology resident supervised by the staff anesthesiologist in the procedural room. Patients in group PP received i.v. 1.0 mg/kg of pethidine initially. An additional i.v. dose of pethidine was given up to a cumulative dose of 2.0 mg/kg, if needed, and 0.5-1.0 mg/kg of propofol i.v. was also given. After the bolus dose of propofol, DS was maintained by using $\leqslant$6 mg/kg/hr of propofol i.v. infusion continuously. If the patient did not tolerate the procedure after the maximum dose of propofol infusion, a supplemental bolus dose of propofol (20-30 mg) was given.

Patients in group MF received intravenous (i.v.) 0.02-0.03 mg/kg of midazolam initially. An additional i.v. dose of midazolam was given up to a cumulative dose of 0.08 mg/kg, if needed, and 0.001 mg/kg of fentanyl i.v. was also given. An additional i.v. dose of fentanyl was given up to a cumulative dose of 0.003 mg/kg, if needed. If the patient did not tolerate the procedure, a supplemental bolus dose of propofol (20-30 mg) was given.

Assessment of sedation efficacy

The level of sedation was assessed by the anesthetic personnel using a sedation score[7] (5=not arousable, 4=arousable to stimuli, 3=arousable to command, 2=drowsy, 1=awake). The sedation score was observed and maintained at the level 3 in group MF and at the level 4 in group PP. The time to recover from sedation was assessed every 5 minutes after the procedure by using the modified Aldrete score[8]. This score represents an established post-anesthetic recovery score, and range is 0-10. The recovery time was defined as the time after completion of the endoscopic examination until the modified Aldrete score $\geqslant$9. At 30 minutes after the endoscopic procedure, the recovery score was also assessed.

Procedural and post-procedural assessment

The endoscopist doing the procedure was blinded to the sedation technique. After the start of the procedure, the research assistant would rate the ease of intubation of the endoscope as follow: 1, effortless; 2, easy; 3, fair; and 4, difficult. The research member would also note whether additional bolus propofol was given. Immediately after the procedure, the endoscopist was asked to fill out a questionnaire to rate patient tolerability to the procedure and rank his/her satisfaction of the procedure. The endoscopist rated patient tolerance to the procedure as follow: 1, exceptional; 2, well; 3, fair; 4, poor. The endoscopist's satisfaction to the sedation for the procedure was ranked as follow: 1, very satisfied; 2, satisfied; 3, neutral; and 4, unsatisfied. Procedural vital signs were monitored and recorded by the blinded nurse anesthetist or anesthesiology resident.

Patient's assessment

After the procedure, the patient was discharged to the recovery room, where all vital signs continued to be monitored for the next two hours. The blinded research assistant interviewed the patient with questionnaire evaluating for the patient satisfaction to the procedure and procedural pain. The patient satisfaction was divided into four responses as follow: 1, very satisfied; 2, satisfied; 3, neutral; and 4, unsatisfied. The procedural pain was evaluated by using a visual analog scale (VAS, 0-10) with 0 being none and 10 being unbearable. The complications during and immediately after the procedure were recorded. Alteration in vital signs was considered as a complication if any of the following was observed: hypertension or hypotension (increase or decrease in blood pressure by 20% from baseline), tachycardia or bradycardia (increase or decrease in heart rate by 20% from baseline), and oxygen desaturation (SpO_2 <90%). In addition, other symptoms such as dizziness, abdominal pain, nausea, or vomiting were also recorded as complications.

Statistical analysis

The study was designed to test the null hypothesis that deep sedation with the combination of propofol and pethidine would offer better sedation than moderate sedation with the combination of midazolam and fentanyl for colonoscopic procedure. In the reported literature, the success rates of sedated colonoscopy ranged from 55-98%[9]. To detect a 5% difference in the success rate 95%, the estimated sample size was calculated to 435 patients per arm. The power of the test was 0.8. Additionally, α was set to 0.05 for all comparisons. Results were expressed as mean±SD or percentage (%), when appropriate. The statistical software package SPSS for Windows Version 11 (SPSS Inc., Chicago, IL) was used to analyze the data. All statistical comparisons were made at the two-sided 5% level of significance.

RESULTS

Of the total 1032 patients randomized, 514 patients were randomized to group MF while 518 patients were randomized to group PP. Table

1 summarizes the clinical characteristics of the two groups. The mean ages in both groups were similar: 58.3±14.3 years in group MF and 58.6±13.2 years in group PP (p=0.845). There were no significant differences in gender, weight, height, ASA physical status, prior sedated colonoscopy and indications of procedure. Sedation time in group MF was significantly longer than in group PP (p=0.001).

Table 1 Characteristics of patients, sedation time, prior sedated colonoscopy and indication of procedure (mean, SD and percentage).

	Group MF (n=514)	Group PP (n=518)	*P* value
Age (yr) (mean, SD)			0.845
Gender (%):			
Male	58.3 (14.3)	58.6 (13.2)	0.133
Female	232 (45.1)	258 (49.8)	
Weight (kg) (mean, SD)	282 (54.9)	260 (50.2)	0.300
Height (cm) (mean, SD)	56.5 (11.4)	60.3 (11.8)	0.073
ASA physical status (%):			
I	158.3 (8.1)	160.3 (7.8)	
II	163 (31.7)	178 (34.4)	0.166
III	299 (58.2)	304 (58.7)	
Sedation time (min) (mean, SD)	52 (10.1)	36 (6.9)	0.001 [1]
Prior sedated colonoscopy (%)	36.1 (18.3)	31.0 (15.4)	0.583
Indication (%)	288 (56.0)	299 (57.7)	
Lower gastrointestinal hemorrhage	100 (19.5)	98 (18.9)	0.827
Colorectal cancer	89 (17.3)	92 (17.8)	0.851
Bowel habit change	71 (13.8)	74 (14.3)	0.827
Surveillance	40 (7.8)	38 (7.3)	0.786
Abdominal pain	38 (7.4)	36 (6.9)	0.783
Colon polyp	38 (7.4)	36 (6.9)	0.783
Constipation	26 (5.1)	23 (4.4)	0.641
Anemia	22 (4.3)	24 (4.6)	0.783
Others	90 (17.5)	97 (18.7)	0.612

Group MF: Midazolam-Fentanyl; Group PP: Propofol-Pethidine;
[1] considered to be of statistical significance.

In group MF, 481 patients (93.6%) successfully completed the procedure as intended as compared to 501 patients (96.7%) in group PP (p=0.019). The additional bolus propofol in group MF was 86.97 ±19.60 (range 50-140) mg and in group PP was 38.82±17.64 (range 20-90) mg. There was statistically significant difference between the two groups (p<0.001). Of the successful procedures, mean total dose and range of midazolam and fentanyl used in group MF was 0.08± 0.05 (range 0.01-0.36) mg/kg/hr and 0.003±0.002 (range 0.000-0.012) mg/kg/hr. Additionally, mean total dose and range of propofol and pethidine used in group PP was 5.98±2.67 (range 0.97-20.36) mg/kg/hr and 1.74±1.05 (range 0.39-11.4) mg/kg/hr. Procedural pain was minimal in both groups. However, procedural pain in group MF was significantly greater than in group PP (p<0.001). Recovery time in group MF was significantly longer than in group PP (p<0.001). At 30 min post-procedure, the recovery score was more than 9.00 in both groups. However, the recovery score at 30 min post-colonoscopy in the propofol and pethidine group was significantly higher than in the midazolam and fentanyl group (p<0.001, Table 2).

Response to patient satisfaction and patient tolerance as assessed by the blinded researcher as well as the ease of endoscopy and endoscopist satisfaction as assessed by blinded endoscopist is shown in table 3. More patients in group PP responded as being very satisfied with the procedure as compared to those in group MF, 90.4% vs. 59.9% (p<0.001). More patients in group MF responded as being neutral or unsatisfied to the endoscopic procedure as compared to those in group PP, 6.7% *vs*. 3.8% and 0.8% *vs*. 0% (p<0.001), respectively.

Table 3 Patient satisfaction and patient tolerance (n, %) as assessed by blinded researcher as well as the ease of endoscopy and endoscopist satisfaction (n, %) as assessed by blinded endoscopist.

	Group MF (n=481)	Group PP (n=501)	*P* value
Patient satisfaction			
Very satisfied	288 (59.9)	453 (90.4)	<0.001 [1]
Satisfied	157 (32.6)	29 (5.8)	
Neutral	32 (6.7)	19 (3.8)	
Unsatisfied	4 (0.8)	0	
Patient tolerance			
Exceptional	126 (26.2)	299 (59.7)	
Well	309 (64.2)	179 (35.7)	<0.001 [1]
Fair	44 (9.2)	23 (4.6)	
Poor	2 (0.4)	0	
Ease of endoscopy			
Effortless	191 (39.7)	318 (63.5)	
Easy	225 (46.8)	165 (32.9)	<0.001 [1]
Fair	58 (12.0)	18 (3.6)	
Difficult	7 (1.5)	0	
Endoscopist satisfaction			
Very satisfied	242 (50.3)	389 (77.6)	
Satisfied	203 (42.2)	96 (19.2)	<0.001 [1]
Neutral	36 (7.5)	16 (3.2)	
Unsatisfied	0	0	

Group MF: Midazolam-Fentanyl; Group PP: Propofol-Pethidine;
[1] considered to be of statistical significance.

Endoscopist rated perception of patient tolerance to the procedure as exceptional occurred in more patients in group PP as compared to those in group MF (p<0.001). Moreover, the endoscopist rated satisfaction as very satisfied in more patients in group PP as compared to those in group MF (p<0.001). Data on ease of endoscopy is also shown in Table 3. More patients in group PP had the endoscopy rating as effortless, compared to those in group MF (p<0.001).

Table 4 showed the sedation-related complications during and immediately after colonoscopy procedure. An overall number of complications occurred in 60 patients (13.2 %) in group MF and 280 patients (55.9%) in group PP (p<0.001). Most of the sedation-related complications were hemodynamic alterations, including hypotension, 7.7% in group MF and 48.3% in group PP; hypertension, 2.0% in group MF and none in group PP; bradycardia, 2.4% in group MF and 4.0% in group PP; and arrhythmia, 0.7% in group MF and 1.0%

Table 2 Endoscopy success (n, %), total additional propofol dose, total sedatives dose, procedural pain, recovery time and recovery score at 30 min post-procedure (mean, SD; range).

	Group MF (n=514)	Group PP (n=518)	*P* value
Endoscopy success (%)	481 (93.6)	501 (96.7)	0.019 [1]
Total additional propofol dose (mg)	86.97 (19.60), 50-140	38.82 (17.64), 20-90	<0.001 [1]
Total midazolam dose (mg/kg/hr)	0.08 (0.05), 0.01-0.36		
Total fentanyl dose (mg/kg/hr)	0.003 (0.002), 0.000-0.012		
Total propofol dose (mg/kg/hr)		5.98 (2.67), 0.97-20.36	
Total pethidine dose (mg/kg/hr)		1.74 (1.05), 0.39-11.04	
Procedural pain (VAS)	2.41 (1.23), 0-6	0.86 (1.18), 0-4	<0.001 [1]
Recovery time (min)	26.36 (10.73), 10-40	23.63 (7.83), 10-40	<0.001 [1]
Recovery score at 30 min post-procedure [2]	9.38 (0.80), 7-10	9.77 (0.49), 8-10	<0.001 [1]

Group MF: Midazolam-Fentanyl; Group PP: Propofol-Pethidine; VAS: Visual analog scale 0-10 (0=none and 10=unbearable); [1] considered to be of statistical significance; [2] assessed by using the modified Aldrete score (0-10).

in group PP. These alterations were transient and did not require any specific interventions. The respiratory-related complications including upper airway obstruction in group PP were significantly higher than in group MF (p=0.049). All upper airway obstruction patients were easily treated by using nasopharyngeal airway. No serious complications were occurred. Nausea and vomiting occurred in 8 patients in group MF and 3 patients in group PP (p=0.126). Dizziness occurred in 2 patients both in group MF and PP (p=0.994). Abdominal pain occurred in 4 patients in group MF and 3 patients in group PP (p=0.315).

Table 4 Sedation-related complications during and immediately after colonoscopy (n, %).

	Group MF (n=481)	Group PP (n=501)	P value
Overall	60 (13.2)	280 (55.9)	<0.001 [1]
Cardiovascular-related	58 (12.7)	267 (53.3)	<0.001 [1]
Hypotension	35 (7.7)	242 (48.3)	<0.001 [1]
Hypertension	9 (2.0)	0	0.002 [1]
Bradycardia	11 (2.4)	20 (4.0)	0.170
Arrhythmia	3 (0.7)	5 (1.0)	0.566
Respiratory-related	2 (0.4)	13 (2.6)	0.007 [1]
Hypoxia	0	4 (0.8)	0.056
Upper airway obstruction	2 (0.4)	9 (1.8)	0.049 [1]
Others	11 (2.4)	5 (1.0)	0.127
Nausea/vomiting	8 (1.7)	3 (0.6)	0.126
Dizziness	2 (0.4)	2 (0.4)	0.994
Abdominal pain	1 (0.2)	0	0.315

Group MF: Midazolam-Fentanyl; Group PP: Propofol-Pethidine;
[1] considered to be of statistical significance.

DISCUSSION

Colonoscopy is a painful and unpleasant procedure with high discomfort without sedation. Opiates, benzodiazepines, and propofol in various combinations are administered to the patients to provide sedation[1,7,10,11]. The synergistic effect of midazolam and fentanyl is more apparent and has proven to be safe and effective. Many reports have favored the use of propofol for sedation during gastrointestinal endoscopy[5,7,10-12]. However, propofol also has some disadvantages. It induces a deeper level of sedation and causes more severe cardio-respiratory depression than midazolam. Additionally, patients sometimes complain of pain during injection. The combination of propofol and low dose opioid or benzodiazepine reduces the total dose of these sedatives and reduces serious adverse effects.

Sedation then becomes important in facilitating patient's tolerance the colonoscopic procedure. The importance and efficacy of sedation has been reported in many studies favoring sedation in patients undergoing colonoscopy[5-7,10-12]. However, the potential benefit from the use of unsedated colonoscopy remains controversial[13,14]. Three studies concluded that colonoscopy without sedation reduced the rate of intubation of the cecum and increased the risk of missing adenomas and cancers[15-17]. However, in a prospective study by Takahashi and colleges, it was shown that sedation-free colonoscopy was more cost-effective, rarely caused complications and was well accepted by most patients[13]. In addition, another study by Leung *et al*, also demonstrated the feasibility of unsedated colonoscopy performed by supervised trainees. The unsedated option minimized direct and indirect costs of the procedure[18].

The primary objective of the study was to measure the rate of completion of colonoscopy in the two different combination groups without additional propofol after the start of the procedure. Our result showed that both groups have good overall successful completion rate (94%). Our overall success rate in performing sedated colonoscopy is comparable to that had been reported. In a study involving the outpatient community, the success rate in performing sedated colonoscopy was also 94%[1]. Moreover, many studies reported that propofol based sedation had a more successful completion rate[6,7,12,19,20], and did not increase rate of complication[21] and colonic perforation[22]. In our study comparing the two combination groups, the success rate in the group PP was statistically significantly higher than in the group MF (93.6%, 96.7%, p=0.019). Total sedation time in group PP was significantly lower than in group MF. This might be due to the time to the targeted depth of sedation in group PP was short. In addition, the interruption of procedure for the additional sedative dose in group MF was occurred.

Factors associated with successful completion and methods of reducing discomfort during colonoscopy have been reported. These included female gender, poor bowel preparation, small waist circumference, lower body mass index, smaller endoscope diameter, variable stiffness endoscope, hypnosis, music, audio distraction, or simply allowing the patients to participate in administration of the medication[23,24].

The higher success rate of completed procedure in group PP may be due to two factors. First, the combination use of propofol and pethidine may offer a better and more precise sedation target, the sedation level 4, for deep sedation. In a patient who may already be anxious about the procedure, the titration to sedation level 3, for moderate sedation may not be well tolerated. Second, there is a potential that the level of sedation in the midazolam and fentanyl group will be inadequate according to the study protocol. The total dose of sedative drugs used may be relatively small. An indirect evidence to support the latter explanation is that higher mean additional propofol dose and procedural pain was observed in group MF than in group PP.

Tolerance toward colonoscopy is an important factor that determines patient acceptance, physician acceptance and the adequacy and feasibility of the procedure. In our study, the tolerability to the procedure was well in both groups as measured by patient' s perception of procedural pain and endoscopist's rating of patient tolerance. Additionally, procedural pain was mild in both groups. However, procedural pain in group MF was significantly higher than in group PP. Subsequently, patients who received propofol and pethidine reported higher satisfaction with the procedure. In group PP, endoscopist's perception of patient tolerance was higher exceptional, as well, the endoscopist's satisfaction was also greater than in group MF. Patient's and endoscopist's satisfaction may be related to ease of endoscopy, as more effortless intubation was observed in patients who received propofol and pethidine. This observation is similar to a prior study which showed that patients' perceived satisfaction with their comfort during the endoscopic procedure was an important predictor of patient satisfaction[25,26].

The data regarding the safety of the combination of propofol and pethidine as well as of the combination of midazolam and fentanyl for colonoscopy are limited, and there are no large prospective studies that address safety. Although, the respiratory-related complications including upper airway obstruction in group PP were relatively higher than in group MF (p=0.049). However, all upper airway obstruction patients were easily treated by using nasopharyngeal airway. No serious complications were occurred. In addition, the result of our study is comparable to the previous studies. The previous studies have reported no serious adverse events in 2500 patients[27] who had sedated colonoscopic procedures. The observed hemodynamic alterations were transient and did not require any specific interventions. More of these alterations were observed in patients who received propofol and pethidine. These hemodynamic

changes are likely a result of the sedative agents. The significance of these actions with corresponding vital sign changes needs further exploration especially in groups of patient with cardiovascular co-morbid conditions. One single study demonstrated that serious complications occurred in 5.0 per 1000 colonoscopies. Colonoscopy with biopsy or polypectomy was associated with increased risk for complications. Perforation could occur during colonoscopy without biopsy[28]. Although our study did not directly assess procedure-related complications, we did not observe any serious complications during or after the procedures.

There are several limitations in this study. First, our study did not assess pre-procedure anxiety which has been shown to be a factor for successful completion of endoscopic procedures[16,24]. Second, the endoscopic procedures were performed by variety of endoscopists, including fellows in training. Therefore, the varied experience may have biased the result including the successful completion rate and ease of intubation. However, the effect of this may be small given high successful completion of the procedures and an equal number of fellows performed for the completion of the procedures in both groups. Third, we did not utilize psychometric testing to evaluate cognitive recovery which might have been a more objective measure of recovery than the other subjective measures. Our design assessed the more practical outcome of the patient being physically ready for discharge. Fourth, the design of our study aimed that deep sedation level was the target in group PP and moderate sedation level was the target in group MF. This combination technique should not directly be compared. Consequently, the chemical structures and mechanism of interactions between these sedative drugs are completely different. Finally, the study employed ease of endoscopy and satisfaction scales that had not been previously validated. Since these reported scales are secondary outcomes, the result of the primary objective remained unbiased by the used of these scales. Overall, despite these limitations, we are confident, however, that these findings are generalizable to the practice of colonoscopy that used moderate to deep sedation technique.

In conclusion, the efficacy of propofol and pethidine for deep sedation showed a distinct advantage over midazolam and fentanyl for moderate sedation used for colonoscopy. The combination use of these sedative agents in either group is safe and effective with rarely observed serious complications. The ease of applying and titrating the combination of propofol and pethidine to the directed target depth likely contributes to better sedation resulting in a higher procedure completion rate, higher ease of endoscopy, and higher patient' s and endoscopist's satisfaction. However, the sedation-related complications in group PP were significantly higher than in group MF.

REFERENCES

1 Hayee BH, Dunn J, Loganayagam A, et al. Midazolam with meperidine or fentanyl for colonoscopy: results of a randomized trial. *Gastrointest Endosc* 2009; **69**: 681-687
2. Amornyotin S, Lertakayamanee N, Wongyingsinn M, Pimukmanuskit P, Chalayonnavin W. The effectiveness of intravenous sedation in diagnostic upper gastrointestinal endoscopy. J *Med Assoc Thai* 2007; **90**: 301-306
3. Amornyotin S, Aanpreung P, Prakanrattana U, Chalayonnawin W, Chatchawankitkul S, Srikureja W. Experience of intravenous sedation for pediatric gastrointestinal endoscopy in a large tertiary referral center in a developing country. *Pediatr Anesth* 2009; **19**: 784-791
4. Amornyotin S, Srikureja W, Pausawasdi N, Prakanrattana U, Kachintorn U. Intravenous sedation for gastrointestinal endoscopy in very elderly patients of Thailand. *Asian Biomed* 2011; **5**: 485-491
5. Reimann FM, Samson U, Derad I, Fuchs M, Schiefer B, Stange EF. Synergistic sedation with low-dose midazolam and propofol for colonoscopies. *Endoscopy* 2000; **32**: 239-244
6. 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**: 1207-1214
7. Paspatis GA, Manolaraki M, Xirouchakis G, Papanikolaou N, Chlouverakis G, Gritzali A. Synergistic sedation with midazolam and propofol versus midazolam and pethidine in colonoscopies: A prospective, randomized study. *Am J Gastroenterol* 2002; **97**: 1963-1967
8. Aldrete JA. The post-anesthesia recovery score revisited. *J Clin Anesth* 1995; **7**: 89-91
9. Mitchell RM, McCallion K, Gardiner KR, Watson RG, Collins JS. Successful colonoscopy; completion rates and reasons for incompletion. *Ulster Med J* 2002; **71**: 34-37
10. Van Natta 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**: 2209-2217
11. 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**: 657-663
12. Sipe BW, Scheidler M, Baluyut A, Wright B. A prospective safety study of a low-dose propofol sedation protocol for colonoscopy. *Clin Gastroenterol Hepatol* 2007; **5**: 563-566
13. Takahashi Y, Tanaka H, Kinjo M, Sakumoto K. Sedation-free colonoscopy. *Dis Colon Rectum* 2005; **48**: 855-859
14. Hoff G. Colonoscopy without sedation. *Scand J Gastroenterol* 2000; **35**: 225-226
15. Petrini JL, Egan JV, Hahn WV. Unsedated colonoscopy: patient characteristics and satisfaction in a community-based endoscopy unit. *Gastrointest Endosc* 2009; **69**: 567-572
16. Aljebreen AM. The completeness rate of colonoscopy in a cohort of unsedated patients. *Saudi J Gastroenterol* 2004; **10**: 150-154
17. Leung FW. Unsedated colonoscopy introduced to ensure access is acceptable to a subgroup of veterans. *Dig Dis Sci* 2008; **53**: 2719-2722
18. Leung FW, Aharonian S, Guth PH, et al. Unsedated colonoscopy: Time to revisit this option? *J Fam Pract* 2008; **57**: E1-4
19. Heuss LT, Schnieper P, Drewe J, Pflimlin E, Beglinger C. Safety of propofol for conscious sedation during endoscopic procedures in high-risk patients-a prospective, controlled study. *Am J Gastroenterol* 2003; **98**: 1751-1757
20. Singh H, Poluha W, Cheung M, Choptain N, Baron KI, Taback SP. Propofol for sedation during colonoscopy. *Cochrane Data Syst Rev* 2008; **4**: CD 006268
21. Amornyotin S, Chalayonnawin W, Kongphlay S. Propofol-based sedation does not increase rate of complication during percutaneous endosopic gastrostomy procedure. *Gastroenterol Res Prac* 2011; doi: 10.1155/2011/134819
22. Amornyotin S, Prakanrattana U, Kachintorn U, Chalayonnavin W, Kongphlay S. Propofol-based sedation does not increase rate of perforation during colonoscopic procedure. *Gastroenterol Insights* 2010; **2**: e4
23. Singh H, Poluha W, Cheung M, Choptain N, Baron KI, Taback SP. Propofol for sedation during colonoscopy. *Dig Dis Sci* 2008; **53**: 1462-1467
24. Hsieh YH, Kuo CS, Tseng KC, Lin HJ. Factors that predict cecal insertion time during sedated colonoscopy: the role of

waist circumference. *J Gastroenterol Hepatol* 2008; **23**: 215-217
25. Schutz SM, Lee JG, Schmitt CM, Almon M, Baillie J. Clues to patient dissatisfaction with conscious sedation for colonoscopy. *Am J Gastroenterol* 1994; **89**: 1476-1479
26. Yacavone RF, Locke GR III, Gostout CJ, Rockwood TH, Thieling S, Zinsmeister AR. Factors influencing patient satisfaction with GI endoscopy. *Gastrointest Endosc* 2001; **53**: 703-710
27. Eckardt VF, Kanzler G, Schmitt T, Eckardt AJ, Bernhard G. Complications and adverse effects of colonoscopy with selective sedation. *Gastrointest Endosc* 1999; **49**: 560-565
28. Levin TR, Zhao W, Conell C, et al. Complications of colonoscopy in an integrated health care delivery system. *Ann Intern Med* 2006; **145**: 880-886

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