Journal of

Gastroenterology and Hepatology Research

Online Submissions: http://www.ghrnet.org/index./joghr/
doi:10.17554/j.issn.2224-3992.2015.04.553

Journal of GHR 2015 July 21 4(7): 1689-1693
ISSN 2224-3992 (print) ISSN 2224-6509 (online)

ORIGINAL ARTICLE

Clinical Efficacy of Combination of Propofol and Ketamine (Ketofol) for Deep Sedation in Colonoscopic Procedure

Somchai Amornyotin, Siriporn Kongphlay

Somchai Amornyotin, Department of Anesthesiology and Siriraj GI Endoscopy Center, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand

Siriporn Kongphlay, Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand

Correspondence to: Amornyotin Somchai, Associate Professor of Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Email: somchai.amo@mahidol.ac.th

Telephone: +66-2-4197990 Fax: +66-2-4113256

Received: April 16, 2015 Revised: July 6, 2015

Accepted: July 7, 2015

Published online: July 21, 2015

ABSTRACT

AIM: To compare and evaluate the clinical efficacy of the combination of propofol and ketamine (ketofol) versus propofol alone when each regimen is used as sedative agents for colonoscopy.

METHODS: 100 patients who underwent colonoscopy in two years, were randomly assigned to PN and PK groups. 50 patients in group PN received propofol and normal saline and 50 patients in group PK received propofol and ketamine for deep sedation. All patients were premedicated with 0.02-0.03 mg/kg of midazolam. Immediately after the procedure, the endoscopist was asked to rate tolerability for the patient, discomfort during insertion and satisfaction. As well, a blinded member of the research team evaluated the patient satisfaction, procedural pain, recovery time and recovery score. The primary outcome was the successfully completed colonoscopic procedure. The secondary outcome variables were patient tolerance, discomfort during insertion, patient and endoscopist satisfaction, recovery time and recovery score, hemodynamic parameters, as well as adverse events during and immediately after procedure.

RESULTS: All endoscopies were completely successfully. Mean total dose of midazolam in group PK and PN was 0.027±0.005 mg/kg and 0.026±0.005 mg/kg, respectively (p=0.469). Mean total dose of propofol in group PK and PN was 7.28±3.03 mg/kg/h and 8.02±2.99 mg/kg/h, respectively (p=0.451). Mean total dose of ketamine in group PK was 1.49±0.61 mg/kg/h. There were no significant differences in the patient and endoscopist satisfaction, procedural pain and recovery time, but the recovery score at 30 min post-procedure in group PK was significantly lower than group PN (p=0.025). Tolerability of the patient and comfort during insertion in group PN were statistically significantly lower than the patients in group PK. Overall and sedation-related adverse event rate in group PN were also significantly higher than in group PK. However, these adverse events were transient and easily treated with no sequelae.

CONCLUSION: Deep sedation in both regimens provided effective and safe for colonoscopy. No serious adverse events were observed. However, the combination of propofol and ketamine (ketofol) used as sedative agents for deep sedation had significantly higher efficacy than the propofol alone.

Key words: Ketofol; Ketamine; Propofol; Deep sedation; Colonoscopy; Efficacy; Safety

Amornyotin S, Kongphlay S. Clinical Efficacy of Combination of Propofol and Ketamine (Ketofol) for Deep Sedation in Colonoscopic Procedure. *Journal of Gastroenterology and Hepatology Research* 2015; 4(7): 1689-1693 Available from: URL: http://www.ghrnet.org/index.php/joghr/article/view/1263

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, ketmine and propofol. Ketamine is a more potent anesthetic drug[2]. Propofol is a strong hypnotic drug with short duration of action and more rapid recovery time for the patient compared with midazolam[3,4].

The combination of propofol and ketamine (ketofol) stabilizes the hemodynamic response[5]. There have been few studies directly comparing the combination of propofol and ketamine versus propofol alone for deep sedation in patients undergoing colonoscopy. At Siriraj GI Endoscopy Center, most colonoscopic procedures are performed with 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 propofol and ketamine (ketofol) versus propofol alone when each regimen is used as the sedative agents for deep sedation for colonoscopic procedures.

PATIENTS AND METHODS

Patients

The study was conducted 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 cardiorespiratory instabilities, severe hypertension, psychological abnormalities, any clinical evidence of hepatic encephalopathy, ASA physical status class IV or V, pregnancy, and refusal to participate in the study. A total of 100 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, double-blind, controlled study. Patients were randomized into either the propofol-ketamine group (PK) or the propofol-normal saline (PN) 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, separated from the procedure room and the recovery room. Deep 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 any serious adverse events such as severe oxygen desaturation (SpO_2 < 85%) or apnea > 10 sec. The secondary outcome variables were the patient and endoscopist satisfaction, endoscopist perception of patient tolerance to the procedure, ease of endoscopy, and adverse events 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 noninvasive blood pressure, heart rate, heart rhythm with single lead electrocardiogram, and oxygen saturation with pulse oximetry.

Deep sedation technique

All sedation was administered by the nurse anesthetist or anesthesiology resident supervised by the staff anesthesiologist in the procedural room. The targeted depth of sedation level was deep sedation. The level of sedation during the procedure was assessed with the Observer's Assessment of Alertness/Sedation score (OAA/S). All patients in both groups received intravenous (i.v.) 0.02-0.03 mg/kg of midazolam initially. The patients in group PK received i.v. 1.0 mg/kg of ketamine and i.v. 0.5-1.0 mg/kg of propofol. After the bolus dose of propofol, the sedation was maintained and titrated by using propofol i.v. infusion continuously. In addition, the patients in group PN received i.v. of normal saline (equivalent volume to ketamine) and i.v. 0.5-1.0 mg/kg of propofol. After the bolus dose of propofol, the sedation was maintained and titrated by using propofol i.v. infusion continuously.

Assessment of sedation efficacy

The level of sedation was assessed by the anesthetic personnel using the OAA/S score (5=Responds readily to name spoken in normal tone, 4=Lethargic response to name spoken in normal tone, 3=Responds only after name is called loudly and/or repeatedly, 2=Respond only after mild prodding or shaking, 1= Does not respond to mild prodding or shaking). The sedation score was observed and maintained at the level 1 throughout the procedure. The time to recover from sedation was evaluated every 5 minutes after the procedure by using the modified Aldrete score. This score represents an organized 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 colonoscopic 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. Immediately after the procedure, the endoscopist was asked to complete a questionnaire to rate patient tolerability to the procedure and rank his/her satisfaction of the sedation used for 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 allocated into four responses as follow: 1, very satisfied; 2, satisfied; 3, neutral; and 4, unsatisfied. The procedural pain was evaluated by using a verbal rating scale (VRS, 0-10) with 0 being none and 10 being unbearable. The complications during and immediately after the procedure were noted. Alteration in vital signs was considered as an adverse event 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 adverse events.

Statistical analysis

The study was designed to test the null hypothesis that sedation with the combination of propofol and ketamine would offer no better sedation than propofol alone for colonoscopic procedure. 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 Window 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 100 patients randomized, 50 patients were randomized to group PK while 50 patients were randomized to group PN. Table 1 summarizes the patients' characteristics, sedation time, prior sedated colonoscopy, and indication of procedure of the two groups. All colonoscopic procedures were successfully completed. There were no significant differences in mean total dose and range of midazolam and propofol used between the two groups. Procedural pain was minimal in both groups (p=0.213). Recovery time in group PK was relatively longer than in group PN but not statistically different (p=0.102). At 30 min post-procedure, the recovery score was≥9 in both groups. However, the recovery score at 30 min post-colonoscopy in the propofol and ketamine group was significantly lower than in the propofol and normal saline group (p=0.025, Table 2)

The 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. Endoscopist rated perception of patient tolerance to the procedure as exceptional occurred in more patients in group PK as compared to those in group PN (p=0.021). Data on ease of endoscopy is also shown in Table 3. More patients in group PK had the endoscopy rating as effortless, compared to those in group PN (p=0.031).

An overall number of adverse events occurred in 10 patients (20.0%) in group PK and 20 patients (40.0%) in group PN (p=0.029). Most of the adverse events were hemodynamic alterations, including hypotension, 14.0% in group PK and 32.0% in group PN; and bradycardia, none in group PK and 2.0% in group PN. These alterations were transient and did not require any specific interventions. The respiratory-related adverse event including upper airway obstruction was not significantly different between the two groups (p=0.307). Nausea and vomiting as well as dizziness occurred in one patient in group PK and none in group PN (p=0.315). No procedure-related complications were observed (Table 4).

DISCUSSION

Colonoscopy is a painful and unpleasant procedure with high discomfort without sedation. Benzodiazepines and propofol in various combinations are administered to the patients to provide sedation[1,6-8]. The synergistic effect of midazolam and propofol is more apparent and has proven to be safe and effective. Several reports have favored the use of propofol for sedation during gastrointestinal endoscopy (GIE) procedures[3,6-9]. However, propofol also has some disadvantages. It induces a deeper level of sedation and causes more severe cardiorespiratory depression than midazolam. Additionally, patients sometimes complain of pain during injection.

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

	Group PK (n=50)	Group PN (n=50)	P value
Age (yr) (mean, SD)	55.7 (13.3)	56.7 (11.5)	0.280
Gender (%):			0.539
Male	18 (36.0)	21 (42.0)	
Female	32 (64.0)	29 (58.0)	
Weight (kg) (mean, SD)	58.9 (12.5)	60.1 (11.2)	0.621
Height (cm) (mean, SD)	159.7 (6.6)	161.3 (7.8)	0.361
ASA physical status (%)			0.378
I	19 (38.0)	24 (48.0)	
II	26 (52.0)	24 (48.0)	
III	5 (10.0)	2 (4.0)	
Sedation time (min) (mean, SD)	39.8 (13.4)	34.2 (19.8)	0.106
Prior sedated colonoscopy (%)	17 (34.0)	15 (30.0)	0.668
Indication (%)			0.154
Colorectal cancer	9 (18.0)	10 (20.0)	
Colon polyp	9 (18.0)	8 (16.0)	
Surveillance	8 (16.0)	9 (18.0)	
Lower gastrointestinal hemorrhage	4 (8.0)	5 (10.0)	
Chronic diarrhea	4 (8.0)	2 (4.0)	
Bowel habit change	3 (6.0)	4 (8.0)	
Others	13 (26.0)	12 (24.0)	

Group PK: Propofol-Ketamine; Group PN: Propofol-Normal saline.

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 PK (n=50)	Group PN (n=50)	P value
Patient satisfaction			0.062
Very satisfied	36 (72.0)	25 (50.0)	
Satisfied	12 (24.0)	19 (38.0)	
Neutral	2 (4.0)	6 (12.0)	
Unsatisfied	0	0	
Patient tolerance			0.021[1]
Exceptional	16 (32.0)	9 (18.0)	
Well	25 (50.0)	19 (38.0)	
Fair	9 (18.0)	18 (36.0)	
Poor	0	4 (8.0)	
Ease of endoscopy			0.031[1]
Effortless	15 (30.0)	8 (16.0)	
Easy	26 (52.0)	20 (40.0)	
Fair	7 (14.0)	14 (28.0)	
Difficult	2 (4.0)	8 (16.0)	
Endoscopist satisfaction			0.197
Very satisfied	31 (62.0)	22 (44.0)	
Satisfied	13 (26.0)	19 (38.0)	
Neutral	6 (12.0)	9 (18.0)	
Unsatisfied	0	0	

Group PK: Propofol-Ketamine; Group PN: Propofol-Normal saline;
[1] considered to be of statistical significance.

Table 4 Adverse events during and immediately after endoscopy (n, %).

	Group PK (n=50)	Group PN (n=50)	P value
Overall	10 (20.0)	20 (40.0)	0.029[1]
Sedation-related			
Cardiovascular	7 (14.0)	17 (34.0)	0.019[1]
Hypotension	7 (14.0)	16 (32.0)	0.032[1]
Bradycardia	0	1 (2.0)	0.315
Respiratory	1 (2.0)	3 (6.0)	0.307
Upper airway obstruction	1 (2.0)	3 (6.0)	0.307
Others	2 (4.0)	0	0.153
Nausea/vomiting	1 (2.0)	0	0.315
Dizziness	1 (2.0)	0	0.315
Procedure-related	0	0	

Group PK: Propofol-Ketamine; Group PN: Propofol-Normal saline;
[1] considered to be of statistical significance.

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

	Group PK (*n*=50)	Group PN (*n*=50)	*P* value
Endoscopy success (*n*, %)	**50 (100.0)**	**50 (100.0)**	**1.000**
Total propofol dose (mg/kg/h)	7.28 (3.03), 3.78-20.18	8.02 (2.99), 3.60-17.24	0.451
Total midazolam dose (mg/kg)	0.027 (0.005), 0.016-0.039	0.026 (0.005), 0.016-0.045	0.469
Procedural pain (VRS)	0	0.08 (0.34), 0-2	0.213
Recovery time (min)	28.80 (6.11), 15-45	25.80 (6.34), 15-40	0.102
Recovery score at 30 min post-procedure[2]	9.44 (0.61), 8-10	9.66 (0.48), 8-10	0.025[1]

Group PK: Propofol-Ketamine; Group PN: Propofol-Normal saline; VRS: Verbal rating scale 0-10 (0 = none and 10 = unbearable); [1] considered to be of statistical significance; [2] evaluated by using the modified Aldrete score (0-10).

Ketofol is the combination of ketamine and propofol in various concentrations. It commonly used for several procedures including gastrointestinal endoscopic procedures. The combination of propofol and ketamine reduces the total dose of the sedative drugs and reduces serious adverse effects[5]. Tosun and colleagues evaluated the clinical efficacy and safety of ketofol in the pediatric patients underwent diagnostic upper GIE procedures. They compared the combination of propofol and ketamine with the combination of propofol and fentanyl in 90 pediatric patients. The study demonstrated that ketofol presented effective sedation and stable hemodynamic profiles in the pediatric patients underwent upper GIE procedures[10]. Furthermore, the adjunctive use of smaller dose of ketamine in the ketofol group can minimize the psychomimetic side effects and shorten the time to discharge when compared with the greater dose[11].

The primary objective of the study was to measure the rate of completion of colonoscopic procedure in the two different combination groups. This study showed that the use of propofol-ketamine and propofol alone for deep sedation in colonoscopic patients was relatively safe and effective. Although the adverse events in both regimens were relatively high, these adverse events were mild and transient. Moreover, all endoscopies were completely successfully. Our overall success rate in performing sedated colonoscopy was relatively high to that had been reported.

The higher success rate of completed procedure in both groups may be due to two factors. First, the use of propofol may offer a better and more precise sedation target, the sedation level 1, for deep sedation. Second, there is a potential that the use of midazolam for premedication in both groups creates the synergistic effect. Third, all endoscopic procedures are diagnostic and/or noncomplicated therapeutic procedures. Fourth, the total dose of sedative drugs used in both groups is adequate according to the study protocol.

The tolerance during procedure is an important factor that determines patient and endoscopist acceptance as well as the adequacy and feasibility of the endoscopy. 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 minimal in both groups. Patient's and endoscopist's satisfaction might be related to ease of endoscopy, as more effortless intubation was observed in all patients. However, the patient's satisfaction in the ketofol group was relatively greater than in the propofol alone group. The previous studies also confirmed that the combination of propofol and ketamine could produce more patients' satisfaction than the other regimens during colonoscopy[12].

The data regarding the safety of the combination of propofol and ketamine as well as the propofol alone for colonoscopy are limited, and there are no large prospective studies that report the safety. Generally, we know that sedation-related adverse events are more often associated with cardiorespiratory systems and are commonly transient and of a mild degree[13]. The previous study has been reported no serious adverse events in the colonoscopic patients who had sedated with ketofol. The observed hemodynamic changes were transient and did not require any specific interventions. In addition, the combination of propofol and ketamine is associated with hemodynamic stability and higher satisfaction score[14]. However, colonoscopy with biopsy or polypectomy was associated with increased risk for complications. Perforation could occur during colonoscopy without biopsy[15]. Although our study did not directly evaluate the procedure-related complications, we did not observe any serious complications during or after the procedures. Our previous study also confirmed that colonoscopy under propofol-based sedation did not increase the perforation rate. Serious complications are uncommon[16].

In our study, there were not significantly different in the recovery time, but the recovery score at 30 min post-procedure in the ketofol group was significantly lower than in the propofol alone group. However, the discharge time in both groups was comparable. This was different from the study of Turk and colleagues[17]. Their study compared the ketofol with the combination of alfentanil and propofol in elective colonoscopic patients. The result showed that the ketofol prolonged the discharge time.

There are several limitations in this study. First, our study did not assess pre-procedure anxiety which has been influenced the outcome of the study. Second, we did not use the psychometric testing to assess cognitive recovery. Our study design evaluated the more practical outcome of the patient being physically ready for discharge. Third, the design of our study aimed that deep sedation level was the target. It could not be generalized to the other populations who underwent other sedation levels. Fourth, we did not use the capnometry during the procedure. The adverse event rate might be underreported. Fifth, the ease of endoscopy and satisfaction scales had not been previously validated. However, these scales are the secondary outcome variables. The result of the primary outcome continued unbiased by the use of these scales. Overall, despite these limitations, we are confident that these findings are generalizable to the practice of colonoscopy that used the deep sedation technique.

In conclusion, the combination use of these sedative drugs in either group is safe with rarely observed serious adverse events. The combination of propofol and ketamine (ketofol) used as sedative agents for deep sedation for colonoscopic procedure had significantly higher efficacy than the propofol alone. The ketofol regimen likely contributes to better sedation resulting in lower sedation-related adverse event rate and higher ease of endoscopy as well as higher patient tolerance and satisfaction.

CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

REFERENCES

1 Amornyotin S. Sedation and monitoring for gastrointestinal en-

doscopy. *World J Gastrointest Endosc* 2013; **5**: 47-55
2 Amornyotin S. Ketamine: pharmacology revisited. *Int J Anesthesiol Res* 2014; **2**: 42-44
3 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
4 Amornyotin S. Sedative and analgesic drugs for gastrointestinal endoscopic procedure. *J Gastroenterol Hepatol Res* 2014; **3**: 1133-1144
5 Amornyotin S. Ketofol: a combination of ketamine and propofol. *J Anesth Crit Care* 2014; **1**: 00031
6 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
7 Amornyotin S, Songarj P, Kongphlay S. Deep sedation with propofol and pethidine versus moderate sedation with midazolam and fentanyl in colonoscopic procedure. *J Gastroenterol Hepatol Res* 2013; **2**: 885-890
8 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
9 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
10 Tosun Z, Aksu R, Guler G, Esmaoglu A, Akin A, Aslan D, Boyaci A. Propofol-ketamine *vs* propofol-fentanyl for sedation during pediatric upper gastrointestinal endoscopy. *Pediatr Anesth* 2007; 17: 983-988
11 Daabiss M, Elsherbiny M, AlOtibi R. Assessment of different concentration of ketofol in procedural operation. *Brit J Med Pract* 2009; **2**: 27-31
12 Khajavi M, Emami A, Etezadi F, Safari S, Sharifi A, Moharari RS. Conscious sedation and analgesia in colonoscopy: ketamine/propofol combination has superior patient satisfaction versus fentanyl/propofol. *Anesth Pain* 2013; **3**: 208-213
13 Amornyotin S. Sedation-related complications in gastrointestinal endoscopy. *World J Gastrointest Endosc* 2013; **5**: 527-533
14 Aydogan H, Aydogan T, Uyankoglu A, Kucuk A, Yuce HH, Karahan MA, Buyukfrat E, Yalcin S. Propofol-ketamine combination has shorter recovery times with similar hemodynamics compared to propofol alone in upper gastrointestinal endoscopy in adults: a randomized trial. *Acta Medica Mediterranea* 2013; **29**: 259-264
15 Levin TR, Conell C, Seeff LC, Manninen DL, Shapiro JA, Schulman J. Complications of colonoscopy in an integrated health care delivery system. *Ann Intern Med* 2006; **145**: 880-886
16 Amornyotin S, Prakanrattana U, Chalayonnavin W, Kongphlay S, Kachintorn U. Propofol based sedation does not increase perforation rate during colonoscopic procedure. *Gastroenterol Insights* 2010; **2**: 13-16
17 Turk HS, Aydogmus M, Unsal O, Isil CT, Citgez B, Oba S, Acik ME. Ketamine versus alfentanil combined with propofol for sedation in colonoscopy procedures: a randomized prospective study. *Turk J Gastroenterol* 2014; **25**: 644-649

Peer reviewers: Philip H. Gordon, Professor Surgery and Oncology, McGill University and Jewish General Hospital, 3755 Cote St Catherine Road, Montreal Quebec H3T 1E2, Canada; Jason Goh, Consultant Gastroenterologist, GI Medicine, Area 6 office, level 7, Queen Elizabeth Hospital Birmingham, Mindelsohn Way, Edgbaston, Birmingham, United Kingdom.