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Manual versus target-controlled infusion of balanced propofol during diagnostic colonoscopy – A prospective randomized controlled trial

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SUMMARY

Introduction There is an increasing interest in balanced propofol sedation (BPS) for colonoscopy in outpatient settings. Propofol is a potent anesthetic agent for this purpose and has a narrow therapeutic range, which increases a risk of cardiovascular and respiratory complications in case of improper administration.

Objective The aim of this study was to compare patients' safety and comfort of endoscopists in two methods of BPS targeting deep sedation – propofol target-controlled infusion (TCI) and manual intravenous titration technique (MT) – during colonoscopy.

Methods This prospective randomized controlled trial included 90 patients (class I or II of the American Society of Anesthesiologists) deeply sedated with propofol, coadministered with small doses of midazolam and fentanyl. Propofol was given by MT technique (45 patients) or by TCI (45 patients). The following adverse effects were recorded: hypotension, hypertension, bradycardia, tachycardia, hypoxemia, bradypnea, apnea, hiccupping, and coughing, as well as endoscopist's comfort during colonoscopy by means of a questionnaire.

Results The MT group compared to the TCI group had a lower mean arterial pressure in the 10th minute after the beginning ($p = 0.017$), and at the end of colonoscopy ($p = 0.006$), higher oxygen saturation in the fifth minute ($p = 0.033$), and in the 15th minute ($p = 0.008$) after the beginning of colonoscopy, and lower heart rate at the beginning of the procedure ($p = 0.001$). There were no statistically significant differences in adverse events. Endoscopist's comfort during colonoscopy was high 95.6% in the TCI group vs. 88.9% in the MT group ($p = 0.069$).

Conclusion MT is clinically as stable as TCI of propofol for deep sedation during colonoscopy, and endoscopists experienced the same comfort during colonoscopy in both groups. Thus, both combinations are suitable for deep sedation during diagnostic colonoscopy.

Keywords: balanced propofol sedation; deep sedation; colonoscopy; endoscopist's comfort; target-controlled infusion

INTRODUCTION

Colonoscopy is an important invasive procedure, but an uncomfortable, painful, and unpleasant experience for a lot of patients [1]. For colonoscopy in outpatient settings, deep sedation in spontaneously breathing patients is increasing in popularity, despite a relatively high incidence of cardiovascular and respiratory suppression [2].

Propofol is increasingly used for sedation during colonoscopy due to its pharmacological properties – rapid onset of action and short recovery profile, moderate antiemetic, analgesic, and amnestic effect [3, 4, 5]. However, propofol induces respiratory and cardiac depression which is dose-dependent and may put patients at risk. Therefore, there is an increasing interest in balanced propofol sedation (BPS) – with addition of benzodiazepines and/or opioids in small doses, the dose of propofol may be reduced [6, 7].

Propofol has narrow therapeutic range and the current standard administration technique in colonoscopy is intermittent administration of propofol bolus [8], according to desired sedation depth [4]. Among various methods which are now available for administration of propofol, target-controlled infusion (TCI) is one of the most sophisticated ones [9]. The basic principle of TCI is that anesthesiologist sets and then adjusts target concentrations of propofol. The infusion rate is adjusted automatically according to a validated pharmacokinetic model (Marsh's or Schnider's) [10, 11], and TCI maintains present concentration of propofol in the plasma (Cp) or the brain (Ce).

OBJECTIVE

The aim of this clinical study was to compare patients' safety and endoscopists' comfort in two methods of BPS targeting deep sedation – propofol TCI with manual intravenous (i.v.) titration technique (MT) during colonoscopy.

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METHODS

We conducted a prospective randomized controlled clinical trial which included 90 patients, comparing patients' safety and endoscopists' comfort of the two different administration techniques of propofol to patients receiving concomitantly small doses of midazolam and fentanyl. The patients were one-to-one randomized into two groups – MT and TCI group – using a random-numbers table. The study took place at the Endoscopy Department of the Clinic for Gastroenterology and Hepatology, Clinical Centre of Serbia, Belgrade, during a period of six months (from April through October, 2013). Seven expert endoscopists with similar clinical experience performed colonoscopies in the trial. Propofol administration and dose adjustments were carried out by one anesthesiologist, with the help of trained nurses. The study was approved by Institutional Ethics Committee of the Clinical Centre of Serbia (No. 4183/01.08.2012.) and written informed consent was obtained from all the patients.

We included 90 patients, who signed the informed consent, of both sexes, 18–65 years old (body weight from 50 kg to 120 kg), classified into group I or II according to the American Society of Anesthesiologist (ASA), recruited from the practices and scheduled for diagnostic outpatient colonoscopy with deep sedation. Indications for colonoscopy were as follows: screening for colorectal cancer, diarrhea, constipation, and bleeding. The following patients were excluded from the study: those allergic to the study drugs, patients with previous problems with anesthesia or sedation, patients with history of stridor, snoring or sleep apnea, patients with neck abnormalities, and those classified into groups III or IV of Mallampati classification [12], patient with neuropsychiatric, cardiac, respiratory, renal disorders, those in pregnant state, and with history of large-bowel surgery. If, for any reason, the endoscopist could not complete the procedure, the patient was excluded from the final analysis.

All the patients underwent an overnight fast and bowel cleansing by drinking 4 l of polyethylene glycol electrolyte solution (Fortrans, Beaufour Ipsen Industrie, Dreux, France). In the endoscopy room, intravenous access was obtained and each patient received 8 ml/kg/h of isotonic saline solution in the form of infusion. Oxygen was supplemented with a mask (6 l/min.). Pre-induction medication for all the patients was as follows: midazolam (Dormicum, Roche Pharma, Reinach, Switzerland, 5 mg/5 ml) in a bolus of 2 mg for the patients up to 70 kg, and 3 mg for those over 70 kg, and fentanyl (Fentanyl, Janssen-Cilag, Baar, Switzerland, 0.05 mg/ml) in a bolus of 1 ml for the patients between 50 kg and 60 kg, 1.5 ml for the patients between 60 kg and 80 kg, and 2 ml for those over 80 kg. Both drugs were administrated slowly (>60 seconds), two minutes before propofol. The patients in the MT group (n = 45) received propofol intravenously (Diprivan, Astra-Zeneca, Stocholm, Sweden, 10 mg/ml), in a bolus of 0.5 mg/kg, and then 10–20 mg were titrated every one to two minutes. The TCI group (n = 45) received propofol with TCI pump (Alaris PK, Cardinal Health, Dublin, OH, USA), according to the Schnider's pharmacokinetic model, with the initial Ce of 2.5 μg/ml. This concentration was increased or decreased by 0.5–1 μg/ml until the deep level of sedation was achieved. After the deep sedation level had been achieved, colonoscopy was performed. The Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale was used to document the patients' responsiveness scores [13]. The patients who lost response to verbal commands and eyelash reflex (MOAA/S = 2) were considered to be in deep sedation.

Administration of propofol was stopped at the end of the colonoscopy by reaching the base of cecum and seeing the landmark of ileocecal valve.

The patients were monitored at five-minute intervals; heart rate, systolic and diastolic arterial pressure, then mean arterial blood pressure were measured automatically using patient monitor (Mec-1000, Mindray Medical International Limited, Shenzhen, China), as well as blood oxygen saturation (SpO_2) using pulse oximeter (Oxipac, Draeger, Lübeck, Germany); respiration rate per minute was recorded by visual inspection and palpation. Endoscopist used Olympus (Olympus Corporation, Tokyo, Japan) and Pentax (Pentax Corporation, Tokyo, Japan) video-endoscopes. The following observed adverse events in both groups (MT and TCI) were recorded and compared [14]: hypotension [mean arterial pressure (MAP) < 60 mmHg], hypertension (MAP > 105 mmHg), bradycardia [heart rate (HR) < 45 beats/min.], tachycardia (HR > 115 beats/min.), hypoxemia (blood oxygen desaturation, SpO_2 < 92% for longer than 30 seconds), bradypnea (number of respirations < 6/minute), apnea (cessation of breathing) and other adverse events related to colonoscopy sedation (coughing, hiccupping) [15]. Each use of the following maneuvers was also registered: lifting the chin, increase in oxygen flow, placement of an oropharyngeal airway, assisted ventilation with bag-mask, and endotracheal intubation.

After colonoscopies we asked the endoscopists to assess the degree of difficulty of colonoscopy with an 11-point (0–10) rating scale, with 0 being "very easy" and 10 "extremely difficult". The endoscopists also assessed the patients' sedation using verbal scale for the quality of sedation (excellent, good, fair, poor) [16], and patients' comfort based on the observation of defensive reactions during colonoscopy [17]. The movement was rated as none (no movement), mild (face grimacing or small movement), moderate (movement without the need to discontinue the procedure) or severe (movement requiring discontinuation of the procedure). We also asked the endoscopists to assess the overall satisfaction with procedure using a five-point verbal scale for comfort (excellent, very good, good, fair, poor) [18].

Statistical analysis

The calculation of sample size was made for two independent samples, with equal number of patients in each group (1:1). Probability of type 1 statistical error (alpha) was set to 0.05, and power of the study to 80%. The effect size was calculated from the observed difference in time to opening of the eyes after target-controlled versus manually-

controlled infusion of propofol in the study of Passot et al. [19] (4.6 ± 2.0 minutes vs. 6.8 ± 2.5 minutes). The sample size was calculated by G*Power software version 3.0.10 (Heinrich Heine University Düsseldorf, Düsseldorf, Germany) [20], and it turned out to be 45 patients per group.

Numeric variables were described by central tendency measures (the mean) and by measures of statistical dispersion (the standard deviation). Categorical variables were described by percentages. The Student's t-test was used for comparison of the study groups after confirming normal distribution of data within the groups. Pearson's χ^2 test was used for testing differences in categorical variables among the study groups. The differences were considered significant if probability of null hypothesis was less than 0.05. All calculations were performed by IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Ninety patients in total were enrolled in the study, and 45 of them were allocated to each of the two groups. Baseline characteristics of the patients were similar in both groups, and are shown in Table 1. The duration of colonoscopy in the MT group was 10.33 ± 5.16 minutes, and in the TCI group 9.66 ± 5.18 minutes (p = 0.543). Total dose of propofol in the MT and TCI groups were 155.77 ± 52.63 mg and 148.97 ± 58.46 mg, respectively (p = 0.563). Changes in MAP, HR, respiration rate, oxygen saturation and levels of sedation during colonoscopy are presented in Table 2. The MAP values before sedation and during colonoscopy were similar in both groups. However, in the 10th minute during colonoscopy, the MAP in the MT group was significantly lower in comparison to the TCI group (86.50 ± 9.04 vs. 92.39 ± 6.37 mmHg, p = 0.017), and the same was observed at the end of the colonoscopy (86.55 ± 9.28 vs. 91.50 ± 7.05 mmHg, p = 0.006). HR at the beginning of colonoscopy was significantly higher in the MT group in comparison to the TCI group (79.55 ± 11.17 vs. 71.80 ± 10.61 beats/minute, p = 0.001), but during the procedure the difference in HR between the groups disappeared. In both groups oxygen saturation during the procedure was in the range from 97% in the MT to 100% in the TCI group. The saturation was significantly lower in the MT group, compared with the TCI group, in the fifth (98.84 ± 1.67 vs. 99.48 ± 0.82%, p = 0.033) and the 15th minute (97.38 ± 2.26 vs. 99.60 ± 0.51%, p = 0.008) of the procedure. In regard to the respiration rate, it was lower in the TCI group in the fifth minute (12.26 ± 2.75 vs. 15.42 ± 4.0 min^{-1}, p = 0.000) and at the end of the procedure (13.28 ± 2.17 vs. 15.1 ± 3.0 min^{-1}, p = 0.001).

Table 1. Demographic characteristic of the patients

Demographic characteristics	MT group (n = 45)	TCI group (n = 45)	p
Sex (male/female), n	15/30	19/26	0.384[b]
Age (years), mean ± SD	49.02 ± 11.91	50.35 ± 11.21	0.586[a]
Weight (kg), mean ± SD	75.06 ± 14.54	73.60 ± 13.51	0.621[a]
Height (cm), mean ± SD	173.31 ± 9.12	173.02 ± 8.76	0.879[a]
BMI (kg/m^2), mean ± SD	24.88 ± 3.90	24.47 ± 3,24	0.586[a]
Alcohol consumption (yes/no), n	0/45	3/42	0.078[b]
Smoking (yes/no), n	18/27	21/24	0.523[b]
ASA (I/II), n	29/16	25/20	0.389[b]

MT – manual technique; TCI – target-controlled infusion; BMI – body mass index; ASA – American Society of Anesthesiologists; n – number in group; SD – standard deviation; [a]Student's t-test; [b]χ^2 test; statistical significance p < 0.05

Table 2. Monitored parameters before and during colonoscopy

Measuring points		Immediately before sedation (basic value)	Start of colonoscopy	During colonoscopy after 5 min.	During colonoscopy after 10 min.	During colonoscopy after 15 min.	During colonoscopy after 20 min.	The end of colonoscopy
MAP (mmHg)	MT group (n = 45)	110.16 ± 13.61	87.00 ± 9.31	87.55 ± 9.73	86.50 ± 9.04	78.12 ± 11.63	82.50 ± 8.66	86.55 ± 9.28
	TCI group (n = 45)	105.12 ± 10.93	88.77 ± 7.69	88.26 ± 8.17	92.39 ± 6.37	86.00 ± 4.59	85.00 ± 5.00	91.50 ± 7.05
	p	0.066[a]	0.327[a]	0.719[a]	0.048[a]	0.066[a]	0.677[a]	0.001[a]
HR (beats/ min.)	MT group (n = 45)	87.17 ± 17.15	79.55 ± 11.17	71.66 ± 10.83	70.30 ± 7.34	81.50 ± 8.43	69.00 ± 6.92	73.15 ± 11.03
	TCI group (n = 45)	82.28 ± 15.04	71.80 ± 10.61	68.30 ± 10.00	69.33 ± 8.15	74.18 ± 8.86	75.00 ± 0.00	68.77 ± 10.92
	p	0.154[a]	0.000[a]	0.146[a]	0.685[a]	0.088[a]	0.203[a]	0.062[a]
Oxygen saturation (%)	MT group (n = 45)	98.95 ± 1.41	99.22 ± 1.37	98.84 ± 1.67	98.70 ± 1.80	97.38 ± 2.26	98.50 ± 0.70	98.93 ± 1.83
	TCI group (n = 45)	98.93 ± 1.75	99.51 ± 0.69	99.48 ± 0.82	99.47 ± 0.66	99.60 ± 0.516	100.00 ± 0.00	99.35 ± 0.77
	p	0.947[a]	0.213[a]	0.038[a]	0.062[a]	0.01[a]	0.095[a]	0.159[a]
Respiration rate per minute	MT group (n = 45)	17.06 ± 2.91	14.00 ± 3.81	15.42 ± 4.05	14.80 ± 3.07	14.50 ± 2.77	15.00 ± 3.46	15.11 ± 3.03
	TCI group (n = 45)	15.95 ± 3.05	12.66 ± 2.79	12.26 ± 2.75	12.95 ± 3.24	15.20 ± 3.42	14.00 ± 3.46	13.28 ± 2.17
	p	0.081[a]	0.062[a]	0.000[a]	0.064[a]	0.647[a]	0.721[a]	0.000[a]
MOAA/S score	MT group (n = 45)	5*	2.24 ± 0.43	2.15 ± 0.36	2.00 ± 0.00	2.00 ± 0.00	2.00 ± 0.00	/
	TCI group (n = 45)	5*	2.00 ± 0.00	2.00 ± 0.00	2.00 ± 0.00	2.00 ± 0.00	2.00 ± 0.00	/
	p	/	0.000[a]	0.056[a]	/	/	/	

MT – manual technique; TCI – target-controlled infusion; MAP – mean arterial pressure; HR – heart rate; SD – standard deviation; MOAA/S – Modified Observer's Assessment of Alertness/Sedation, scale being as follows: 6 = agitated; 5 = responds to name in normal tone; 4 = lethargic response to name in normal tone; 3 = responds to name called loudly; 2 = responds to mild prodding/shaking; 1 = does not respond to mild prodding/shaking; and 0 = does not respond to deep-stimulus "sternal rub"
* immediately before sedation (base value) = 5; measured values refer to the measured points from the start until the end of the colonoscopy
[a] Student's t-test;
Values are mean ± SD; statistical significance p < 0.05.

Table 3. Endoscopist's comfort and judgment of patient's comfort

Questions		MT group (n = 45)	TCI group (n = 45)	p
How would you rate difficulty of colonoscopy (mean ± SD), rating scale (0–10)		5.20 ± 1.75	5.5 ± 2.37	0.422a
What was patient's sedation for colonoscopy like, n (%)	Excellent	41 (91.1)	43 (95.6)	0.536b
	Good	3 (6.7)	2 (4.4)	
	Fair	1 (2.2)	/	
	Poor	/	/	
What was patient's comfort during colonoscopy like, n (%)	No movements	40 (88.9)	43 (95.6)	0.375b
	Mild movements	2 (4.4)	2 (4.4)	
	Moderate movements	1 (2.2)	/	
	Severe movements	2 (4.4)	/	
What was your comfort during colonoscopy like, n (%)	Excellent	40 (88.9)	43 (95.6)	0.069b
	Very good	/	2 (4.4)	
	Good	3 (6.7)	/	
	Fair	2 (4.4)	/	
	Poor	/	/	

MT – manual technique; TCI – target-controlled infusion; SD – standard deviation;
[a]Student's t-test; [b]χ^2 test; statistical significance $p < 0.05$

Table 4. Procedure-related time and sedative doses

Procedure/sedation times	MT group (n = 45) (mean ± SD)	TCI group (n = 45) (mean ± SD)	p
Induction time (min.)	3.31 ± 0.55	3.28 ± 0.62	0.859[a]
Time of deeper sedation (min.)	11.86 ± 5.21	10.93 ± 5.25	0.400[a]
Total sedation time (min.)	19.55 ± 5.25	18.4 ± 5.67	0.319[a]
Early eye-opening time, (min.)	5.91 ± 1.12	5.44 ± 1.40	0.086[a]
Duration of colonoscopy (min.)	10.33 ± 5.16	9.66 ± 5.18	0.543[a]
Propofol (mg)	155.77 ± 52.63	148.97 ± 58.46	0.563[a]
Midazolam (mg)	2.60 ± 0.49	2.53 ± 0.50	0.529[a]
Fentanyl (mL)	1.59 ± 0.36	1.52 ± 0.40	0.415[a]

MT – manual technique; TCI – target-controlled infusion; SD – standard deviation;
[a]Student's t-test; statistical significance $p < 0.05$

Values of MAP, HR, SpO_2 and respiration rate per minute in both groups were significantly above the minimum acceptable values of 60 mmHg, 45 beats/minute 92% and six breaths per minute, respectively. Great majority of the patients from both groups reached the desired level of sedation (MOAA/S score = 2), from the start until the end of colonoscopy, but the patients in the TCI group in the fifth minute during the colonoscopy had deeper sedation level than the patients in the MT group (2.00 ± 0.00 vs. 2.24 ± 0.43, p = 0.001). Deep sedation level was achieved in both groups without risk of oxygen desaturation. None of the patients required increase in oxygen flow, placement of an oropharyngeal airway, the assisted ventilation with bag-mask, or endotracheal intubation. However, the chin had to be lifted in one patient from the MT group.

Occurrence rate of adverse events related to sedation were similar in both groups, with only one hiccupping in the TCI group and two in the MT group (p = 0.554) and without coughing in both groups.

Endoscopists' comfort during colonoscopy and their judgment of patients' comfort is shown in Table 3. All endoscopists completed the questionnaire. There were no statistical differences between the groups. Difficulty rate of colonoscopy was 5.2 ± 1.7 in the MT group vs. 5.5 ± 2.37 in the TCI group (p = 0.422). Endoscopists registered five patients (11%) with movements in the MT group, whereas in TCI there were two patients with movements (p = 0.375). The overall satisfaction with patients' sedation was high, 91.1% described it as „excellent" in the MT group vs. 95.6% who described it as „excellent" in the TCI group (p = 0.536). Also, endoscopists' assessment of their own comfort was high, 95.6% in the TCI group vs. 88.9% in the MT group (p = 0.069).

Mean values of propofol, midazolam, fentanyl doses, administered to the study groups, and the parameters of sedation and procedural time are shown in Table 4. The observed differences were not significant. In the TCI group, Ce_{min} = 1 μg/ml, Ce_{max} = 4.5 μg/ml, and mod = 2.3 (TCI range of propofol: 1 μg/ml – 4.5 μg/ml, mod = 2.3)

DISCUSSION

As far as we know, this is the first randomized, prospective study which compared administration of propofol by titration with TCI following intravenous administration of midazolam and fentanyl for achieving deep sedation in diagnostic colonoscopy. However, despite numerous publications describing propofol use in colonoscopy, there are limited data studying the incidence of cardiorespiratory complications of BPS targeted to deep sedation. Our study shows that although several cardiopulmonary parameters were more stable numerically in the TCI group, the MT group also maintained the values sufficiently above the lower limit indicated. No patients in both groups required additional oxygen, oropharyngeal airway, endotracheal intubation, or assisted ventilation. Seven endoscopists participated in the study, and their comfort was the same in both groups.

Our results of endoscopists' comfort are similar to those of Chiang et al. [21]: they compared the propofol administration by TCI using Schnider's model with manually

controlled propofol infusion, with both groups premedicated with alfentanil, for the same-day bidirectional endoscopy in deep sedation. They reported high endoscopists' satisfaction score in both groups, but nurse anesthetists had to additionally assist the upper airways throughout the procedure for the group of patients with manually controlled propofol infusion. This result is in correlation with ours: the chin had to be lifted in one patient, and four patients' movements were registered in the MT group. Unlike our research, in this study the TCI with propofol gave less haemodynamic and respiratory adverse events than manually controlled propofol infusion.

The question whether sedation technique influences endoscopist's comfort was investigated by Mazanikov et al. [22] Anesthesiologist-managed propofol sedation with constant propofol infusion in deep sedation had no impact on the degree of gastroenterologist's satisfaction when compared with patient-controlled moderate sedation with propofol/remifentanil in endoscopic retrograde cholangiopancreatography [22]. Also, the study of Stonel et al. [23] showed that endoscopists had similar satisfaction during colonoscopy, compared with patient-controlled sedation using TCI of propofol with anesthesiologist-administered propofol bolus technique targeting moderate sedation.

Advantage of TCI over manual regimen was shown in the study of Chan et al. [17], in which they compared TCI with propofol using Marsh's pharmacokinetic model with intermittent bolus of sedative cocktail (midazolam + alfentanil + small doses of propofol) during deep sedation for colonoscopy; the TCI group produced less hypoxia, hypotension and bradycardia than with intermittent bolus of sedative cocktail. The advantages of the TCI were also shown in the study of Absalom et al. [24] with closed-loop control of moderate sedation for colonoscopy by using bispectral index. None of the patients became apneic, required airway support or became hemodinamically unstable while sedated. On the other hand, Eberl et al. [25] reported less hemodynamic stability with combination of alfentanil and TCI of propofol than when alfentanil alone or combination of midazolam and fentanyl were used for achieving moderate sedation during colonoscopy. The propofol group experienced more hypotensive events, but less oxygen desaturation episodes, similar as with the „opioid-only" group.

Both propofol alone and propofol in combination with opiates and/or benzodiazepines are frequently used during colonoscopy to achieve moderate levels of sedation [3]. Lee et al. [7] found no significant differences between the balanced propofol sedation and conventional groups (midazolam and meperidine) with regard to the rates of cardiopulmonary complications, but BPS provided significantly higher level of endoscopist's satisfaction. Increasing interest in BPS titrated to deep sedation is shown in the study of Ho et al. [26]: comparing alfentanil and fentanyl in BPS during gastroscopy and colonoscopy they reported the same safety profile.

In our hospital, patients and endoscopists favor a high-quality sedative and pain-free colonoscopy. Therefore, the ASA level of deep sedation (MOAA/S = 2) was set in our research [13, 27]. In a study of 17,999 endoscopic procedures performed over 8 years, the authors concluded that deep sedation during endoscopic procedures is safe and adverse events occurred in a small proportion of patients (4.5%) [28]. In the present study, deep sedation level was achieved in both groups without cardiorespiratory risk. Also, deep sedation showed excellent endoscopists' comfort and low incidence of adverse events such as hiccup and cough [29, 30]. El Chafic et al. [15] reported that the rate of coughing was very low – in 757 patients deeply sedated for endoscopy only 13% had at least one cough and 3% a prolonged cough. Although the patients from both groups were without coughing in our study, hiccupping was more frequent in the MT group (6.7% vs. 3.3%) which did not affect excellent comfort of the endoscopists.

The limitations of our study include the patients' selection bias as they were all of ASA I and II status and below 65 years of age. It should be noted that colonoscopy examinations in Serbia are not routinely done in sedation. They are indicated by gastroenterologist for the patients who are afraid of examination, or have a low pain tolerance, or previous unsuccessful examinations. It is also possible that we missed episodes of hypotension larger than the recorded ones, but the shorter intervals of pressure measuring during the procedure, which approximately lasted 15 to 20 minutes, as well as invasive precise blood pressure monitoring, were inconvenient for the patients. In this study, seven specialists were performing all colonoscopies. Ideally, future studies should be done with a single specialist to insure consistency of the procedure.

CONCLUSION

Both techniques of administration of balanced propofol, MT and TCI, provide the same safety and endoscopist's comfort in deep sedation, thus both combinations are suitable during diagnostic colonoscopy. TCI might have some advantages, since several cardiopulmonary indicators were more stable numerically. For a strategy to be introduced to daily practices, a method has to be not only clinically effective but also cost-effective. From that point of view further observation is warranted regarding cost-effectiveness of TCI in comparison to MT.

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Поређење болусне и циљаном концентрацијом вођене примене пропофола током дијагностичке колоноскопије – проспективна рандомизована контролисана студија

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КРАТАК САДРЖАЈ

Увод Све је веће интересовање за примену балансиране седације пропофолом (*BPS*) током колоноскопије у амбулантним условима. Пропофол је потентан анестетик са малом терапијском ширином, а неправилним интравенским давањем повећава се ризик од кардиоваскуларних и респираторних компликација.

Циљ рада Циљ ове студије је био да се пореди безбедност пацијента и комфор ендоскописте применом две методе *BPS* у дубокој седацији: циљано контролисаном инфузијом (*TCI*) и давањем пропофола у болусима у одређеним временским интервалима (*MT*) током колоноскопије.

Методе рада Ово је проспективна рандомизована контролисана студија са 90 пацијената који су испунили услове за укључивање у студију (класификације I или II Америчког удружења анестезиолога), дубоко седираних пропофолом уз претходно интравенско давање малих доза мидазолама и фентанила. Пропофол је даван *MT* (45 пацијената) или *TCI* (45 пацијената) техником. Бележена су следећа нежељена дејства: хипотензија, хипертензија, брадикардија, тахикардија, хипоксемија, брадипнеа, апнеа, штуцање и кашаљ, а кроз упитник је испитан комфор ендоскописте током колоноскопије.

Резултати *MT* група је у поређењу са *TCI* имала нижи средњи артеријски притисак у десетом минуту после почетка ($p = 0,017$) и на крају колоноскопије ($p = 0,006$), виши степен сатурације у петом минуту ($p = 0,033$) и у петнаестом минуту ($p = 0,008$) после почетка колоноскопије, као и спорији пулс на почетку процедуре ($p = 0,001$). Није било статистички значајне разлике у испољавању нежељених догађаја током примене пропофола на ова два начина. Комфор ендоскописта током колоноскопије је био висок, 95,6% у *TCI* према 88,9% у *MT* групи ($p = 0,069$).

Закључак *MT* је клинички безбедна као и *TCI* пропофола, а комфор ендоскописта током колоноскопије је исти у обе групе, тако да су обе технике адекватне за дубоку седацију током дијагностичке колоноскопије.

Кључне речи: балансирана седација пропофолом; дубока седација; колоноскопија; комфор ендоскописте

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