Effect of different doses of dexmedetomidine on the median effective concentration of propofol during gastrointestinal endoscopy:a randomized controlled trial

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Abstract

Background: Dexmedetomidine could be an ideal adjuvant to propofol during gastrointestinal endoscopy because it provides both analgesia and sedation without respiratory depression. This study investigates the effect of different doses of dexmedetomidine on the median effective concentration of propofol during gastrointestinal endoscopy. Methods: 90 adult patients were randomly assigned to Group Control , Group DEX0.5 (0.5 μg/kg dexmedetomidine), or Group DEX1.0 (1.0 μg/kg dexmedetomidine) . Anaesthesia during endoscopy was implemented by plasma target-controlled infusion (TCI) of propofol with different doses of dexmedetomidine. TCI concentration of the first patient for each group was 2.5 μg/ml and the consecutive adjacent concentration gradient was 0.5 μg/mL. EC50 of TCI propofol for gastrointestinal endoscopy was determined by using the modified Dixon's up-and-down method. Cardiovascular variables were also measured. Results: EC50 of TCI propofol and 95% confidence interval (CI) for gastrointestinal endoscopy were, 3.77 (3.48-4.09), 2.51 (2.27-2.78) and 2.10 (1.90-2.33) μg/mL in Group Control, Group DEX0.5 and Group DEX1.0. The average percent change from baseline in HR was 2.8 (8.9), -7.4 (7.7) and -10.5 (8.8) (P¡0.001), and the average percent change from baseline in MAP was -10.6 [-24.7; 3.5], -9.5 [-29.2; 11.4] and -4.0 [-27.3; 15.5] (P = 0.034) in Group Control, Group DEX0.5 and Group DEX1.0, respectively. Conclusions: Dexmedetomidine reduced the EC50 of TCI propofol. A 0.5-1 μg/kg dexmedetomidine caused a decrease in HR without bradycardia. The decrease in dosage of propofol with increasing doses of dexmedetomidine caused more stable MAP. Dexmedetomidine is an ideal adjuvant drug to propofol during gastrointestinal endoscopy.

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Running Title: EC_{50} of propofol with dexmedetomidine

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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT -

1. Propofol is a popular drug for gastrointestinal endoscopy. However, Propofol may result in hypotension, bradycardia, and respiratory depression.

2. Dexmedetomidine, a α_2 receptor agonist, provides analgesia and sedation but does not cause respiratory depression.

3. Co-administration could improve anaesthetic effectiveness and reduce the incidences of adverse events caused by a single drug.

WHAT THIS STUDY ADDS -

1. Combination medication of propofol with dexmedetomidine reduced the EC_{50} of TCI propofol during gastrointestinal endoscopy compared with administration of propofol without dexmedetomidine.

2. A 0.5-1 μg/kg dexmedetomidine caused a decrease in HR without bradycardia. The decrease in dosage of propofol with increasing doses of dexmedetomidine caused more stable MAP.

3. Dexmedetomidine is an ideal adjuvant drug to propofol during gastrointestinal endoscopy.

Abstract

Background : Dexmedetomidine could be an ideal adjuvant to propofol during gastrointestinal endoscopy because it provides both analgesia and sedation without respiratory depression. This study investigates the effect of different doses of dexmedetomidine on the median effective concentration of propofol during gastrointestinal endoscopy. **Methods** : 90 adult patients were randomly assigned to Group Control , Group DEX0.5 (0.5 μg/kg dexmedetomidine), or Group DEX1.0 (1.0 μg/kg dexmedetomidine) . Anaesthesia during endoscopy was implemented by plasma target-controlled infusion (TCI) of propofol with different doses of dexmedetomidine. TCI concentration of the first patient for each group was 2.5 μg/ml and the consecutive adjacent concentration gradient was 0.5 μg/mL. EC_{50} of TCI propofol for gastrointestinal endoscopy was determined by using the modified Dixon's up-and-down method. Cardiovascular variables were also measured. **Results** : EC_{50} of TCI propofol and 95% confidence interval (CI) for gastrointestinal endoscopy were, 3.77 (3.48-4.09), 2.51 (2.27-2.78) and 2.10 (1.90-2.33) μg/mL in Group Control, Group DEX0.5 and Group DEX1.0. The average percent change from baseline in HR was 2.8 (8.9), -7.4 (7.7) and -10.5 (8.8) (P ¡0.001), and the average percent change from baseline in MAP was -10.6 [-24.7; 3.5], -9.5 [-29.2; 11.4] and -4.0 [-27.3; 15.5] ($P = 0.034$) in Group Control, Group DEX0.5 and Group DEX1.0, respectively. **Conclusions:** Dexmedetomidine reduced the EC_{50} of TCI propofol. A 0.5-1 μg/kg dexmedetomidine caused a decrease

in HR without bradycardia. The decrease in dosage of propofol with increasing doses of dexmedetomidine caused more stable MAP. Dexmedetomidine is an ideal adjuvant drug to propofol during gastrointestinal endoscopy.

Keywords : The median effective concentration, Propofol, Dexmedetomidine, Gastrointestinal endoscopy.

Introduction

Gastrointestinal endoscopy plays a very important role in the diagnosis and treatment of gastrointestinal diseases. To facilitate the work of the gastroenterologist and provide patient comfort, patients are given sedation during the endoscopic procedures [1,2]. Propofol is a popular drug during gastrointestinal endoscopy because of its rapid onset, short duration of action, and minimal adverse effects [3-7]. However, propofol may result in sedation-related adverse events such as, respiratory depression and hypotension [8]. Adjuvants are usually needed in endoscopic procedures in order to decrease the propofol dosage and adverse events [9,10]. Dexmedetomidine, a $\alpha_2$receptor agonist, could be an ideal adjuvant to propofol for endoscopy because it provides both analgesia and sedation without respiratory depression [11]. However, the bradycardia caused by dexmedetomidine was often reported [12-16]. Nonaka T *et al.* [16] demonstrated that that the incidence of bradycardia (defined as a pulse rate [?] 45 bpm) in the combination of dexmedetomidine with propofol group was higher than that in the propofol alone group (37.9% vs. 10.3%). Whether dexmedetomidine is an ideal adjuvant drug to propofol during gastrointestinal endoscopy is worthy of our further study.

In the present study, we hypothesized that dexmedetomidine could reduce the median effective concentration (EC_{50}) of TCI propofol during gastrointestinal endoscopy. The primary endpoint was to determine the EC_{50} of TCI propofol with different doses of dexmedetomidine. The secondary endpoint was to compare the effects of different doses of dexmedetomidine on heart rate (HR) and mean arterial pressure (MAP) during gastrointestinal endoscopy.

Materials and Methods

Study design

The Ethics Committee of Shidong Hospital of Yangpu District in Shanghai approved this study. The registration number of this randomized clinical trials is ChiCTR2100054402 (The URL is http://www.chictr.org/cn/). Each patient signs the informed consent before endoscopy. A total of 90 adult patients undergoing gastrointestinal endoscopy between December 2021 and February 2022, were enrolled in this study.

Inclusion and exclusion criteria

Patients undergoing gastrointestinal endoscopy, aged 18 to 65 years old; ASA I to III; and body mass index19 to 27 kg/m^2 were enrolled in this study.

Patients with (1) allergy to either dexmedetomidine or propofol; (2) history of long-term opioid use or alcohol abuse; (3) history of psychological problems or psychiatric disease; (4) heart failure (ejection fraction <40%); significant ischemic heart disease; (5) hypotension or bradycardia; (6) history of unregulated hypertension; (7) severe respiratory disease; (8) hepatic or renal insufficiency were excluded from this study.

Anesthesia protocol

A total of 90 adult patients were randomly assigned to Group Control (saline solution)), Group DEX0.5 (0.5 μg/kg dexmedetomidine), or Group DEX1.0 (1.0 μg/kg dexmedetomidine). The gastroenterologists, anesthesiologist and patients, were blinded to the grouping.

Each patient did not receive pre-medication. A 20-G intravenous catheter was inserted into the right or left antecubital region for fluids and medicationsHR, MAP, Electrocardiogram, noninvasive systolic arterial pressure, respiration rate, and peripheral oxygen saturation (SpO_2) were monitored (Philips IntelliVue). All patients were given oxygen by nasal catheter (the oxygen flow of 3-5 L/min) during procedure.

A nurse who did not participate in this study diluted the dexmedetomidine solution to 20 mL. After pre-oxygenation, patients were given different doses of dexmedetomidine: saline solution (Group Control), 0.5 μg/kg dexmedetomidine (Group DEX0.5), or 1.0 μg/kg dexmedetomidine (Group DEX1.0). The same volume (20 mL) of dexmedetomidine solutions or saline solution was administered in 5 min. Then, propofol was given by Graseby 3500 TCI Syringe Pump with the Marsh parameters. The plasma target-controlled concentration of the first patient for each group was 2.5 μg/mL. Once the target concentration on the TCI pump was achieved, gastroenterologists started gastroscopy. In our endoscopy center, patients underwent gastroscopy followed by colonoscopy in one anaesthetic treatment. Target-controlled infusion of propofol is maintained until the end of colonoscopy. A stable sedation without patient body movements is necessary to enhance the precision and swiftness of the gastrointestinal endoscopy and enhance the patient satisfaction and the gastroenterologist satisfaction. The flow chart of the Dixon's up-and-down methodology was shown in Figure 7. Whether the patients were "responsive" is determined by the anesthesiologist who does not know the grouping and dexmedetomidine dose (saline solution). .

Emergency equipment was always on standby. Ephedrine 6-10 mg was administered in case MAP dropped blow 60 mmHg or 30% less than the baseline, and atropine 0.25 mg was given in case HR were lower than 50 beats per minute. Appropriate nitroglycerin was administered in case MAP were over 120 mmHg. If SpO_2 $< 92\%$ for more than 5 seconds, ventilation support was performed by the anesthesiologist when necessary.

Measurements

In this study, baseline of HR and MAP are defined as the measured values at 5 min after the patient was brought to the endoscopic room. HR, MBP and SpO_2 were monitored and recorded at the designated time points: T_0: baseline values; T_1: 2.5 min after administration of dexmedetomidine; T_2: 5 min after administration of dexmedetomidine (Dexmedetomidine administration is over); T_3: when propofol target plasma concentration reached the target; T_4: at scope intubation; and $T_{5\text{-}X}$: by 3 min intervals.

The endoscopic time were recorded. We defined the recovery time as the interval time from cessation of TCI propofol to the time when patients could respond readily to name spoken in normal tone (that is Observer's Assessment of Alertness/Sedation scale (OAA/S) = 5). Sedation-related adverse events, such as postoperative nausea and vomiting, respiratory depression, bradycardia, and hypotension, were also recorded.

The satisfaction of gastroenterologists (scored by 4, excellent; 3, good; 2, fair; and 1, poor) and the satisfaction of patients (4, no discomfort; 3, slightly uncomfortable; 2, extremely uncomfortable; 1,unacceptable) were assessed immediately after procedure and 30 minutes after procedure, respectively. [7,10].

The average percent change from baseline in HR and MAP, were compared among three groups. In this study, we defined the calculation formula of percent change from baseline at the fixed time points = ($HR_{T1\text{-}x}$ –HR_{T0})/ HR_{T0}* 100 and ($MBP_{T1\text{-}x}$ – MBP_{T0})/ MBP_{T0}*100. [7,10].

Statistical analysis

. The sample size calculation, using the method described by Eberl et al. [17], was based on the retrospective sedation database of our hospital, in which the propofol requirement for gastrointestinal endoscopy was 300 (100) mg, presented as mean (standard deviation). Given power of 0.80 and type I error of 0.05, we will need to study 28 subjects per group to decrease propofol requirement by about 25%. And taking into consideration a potential dropout rate of 10%, 30 patients for each group will be required, thus a total of 90 adult patients should be randomly assigned.

SPSS 13.0 or the software R was performed for statistical analysis. We used the modified Dixon's up-and-down methodology, described in 1965 [18], to determine the EC_{50} of TCI propofol with different doses of dexmedetomidine. We performed a chi-squared test for categorical variables, ANOVA test for continuous values and Kruskal-Wallis rank sum test for discrete values as appropriate. Data were presented as number (n), mean (standard deviation, SD), or median [Min, Max]. A 0.05 was set as the threshold of rejecting the null hypothesis.

Results

The study flow diagram was showed in Figure.1. There was no statistical significance in preoperative laboratory values and characteristics of patients (Table 1).

EC_{50} of TCI propofol and its 95% confidence interval (CI) for gastrointestinal endoscopy were 3.77 (3.48-4.09), 2.51 (2.27-2.78) and 2.10 (1.90-2.33) μg/mL in Group Control, Group DEX0.5 and Group DEX1.0 (Table 2). EC_{50} of TCI propofol in Group DEX0.5 and Group DEX1.0 was reduced by 33.4% and 44.3% compared with Group Control. Figure 2 to 4 showed that the TCI concentrations of propofol for consecutive patients and their "responsive" or "non-responsive" during gastrointestinal endoscopy.

The average percent change from baseline in HR was 2.8 (8.9), -7.4 (7.7) and -10.5 (8.8) (P ¡0.001), and average percent change from baseline in MAP was -10.6 [-24.7; 3.5], -9.5 [-29.2; 11.4] and -4.0 [-27.3; 15.5] ($P = 0.034$) in Group Control, Group DEX0.5 and Group DEX1.0, respectively (Table 3). Figure 5 and Figure 6 showed the time course of percent change from baseline in HR and MAP. The decrease in dosage of propofol with increasing doses of dexmedetomidine caused more stable MAP. Dexmedetomidine caused a decrease in heart rate. However, there was no bradycardia in our study.

Recovery time were 10.9 (2.5), 9.3 (2.9), and 11.6 (3.3) min ($P = 0.015$) in Group Control, Group DEX0.5 and Group DEX1.0 (Table 3). The recovery time of Group DEX0.5 was significantly shorter than that of the other groups.

This study was completed without any serious adverse events, such as the need for tracheal intubation or termination of the endoscopy. Major sedation-related adverse events were showed in Table 3.

Satisfactions of patients and gastroenterologists were showed in Table 3.

Discussion

We determined the EC_{50} of TCI propofol with different doses of dexmedetomidine during gastrointestinal endoscopy. The EC_{50} of TCI propofol when co-administration with 0.5 or 1.0 μg/mL dexmedetomidine was reduced by 33.4% and 44.3% compared with Group Control. We dermonstrated that the increasing doses of dexmedetomidine with propofol caused more stable MAP. Dexmedetomidine caused a decrease in heart rate. However, there was no bradycardia in our study.

In our previous study [10], we investigated the effect of different doses of esketamine on the EC_{50} of TCI propofol in the elderly population, and obtained the corresponding data for users' reference. Due to the different mechanisms of action and different pharmacological characteristics of dexmedetomidine and esketamine, different combinations will have different methods of administration and pharmacological outcome. Therefore, we decided to use the same research method and statistical method to study the combination of propofol and dexmedetomidine for gastrointestinal endoscopy anesthesia in adults. This study differs from our previous studies in the following ways: (1) There are a separate application for ethics and a separate clinical registration in this study. (2) The subjects of the study were also re-recruited; the elderly (over 65 years old) were recruited in the previous study, and the adults (18-65 years old) were recruited in this study. (3) The adjuvant drugs involved in this study (dexmedetomidine) are also completely different from those in the previous study (esketamine); the administration method is also different from the previous study.

We used the modified Dixon's method to determine the EC_{50} of TCI propofol with different doses of dexmedetomidine. This method has a long history [18-20]. Pace NL*et al.* demonstrated that up-and-down methodology could make full use of the data provided by fewer cases and obtain results quickly and accurately [21]. It was reported that 20 or more patients each group could show statistically significant differences in the EC_{50} using the Dixon's methodology. So the sequential methodology is often used in anesthesia researches [9,10,22].

Propofol, acting at the GABAA receptors [23] and the N-methyl-D-aspartate subtype of glutamate receptors [24], is popularly used during endoscopic procedure because of its properties of fast onset of action, short duration of action, and minimal side effects [3-7]. However, propofol may cause dose-dependent reduced

myocardial contractility and systemic vascular resistance [25-27], which resulted in dose-dependent hemodynamic changes, such as hypotension and bradycardia [28]. It was reported that transient hypotension occurs in 4% to 7% of cases and transient hypoxia occurs in 3% to 7% of cases using propofol sedation in an anesthesia and sedation guideline in gastrointestinal endoscopy[29]. Some medication strategies of propofol for endoscopic procedure were explored in some studies. Clinically, considering that drugs with different mechanisms of action may have synergistic effects, anesthesiologists tried various combinations of analgesic and sedative medications to reduce the total amount of individual medications and reduce complications [9,17, 30-32]. It was showed that the propofol EC_{50} was decreased when co-administration with fentanyl 1.0 μg/kg during colonoscopy in elderly patients [9]. Recently, it was reported that low-dose esketamine reduced the propofol requirement during ERCP without affecting respiratory or cardiovascular adverse events in ASA I-II patients, when compared with alfentanil[17,32]. In our other previous study [10], we confirmed that combination of propofol and esketamine could reduce the EC_{50} of TCI propofol during gastrointestinal endoscopy compared with propofol alone in elderly patients.

Dexmedetomidine is a highly selective alpha2-adrenoceptor agonist. It was reported that dexmedetomidine provided sedativeand analgesic [33] without the risk of respiratory depression [11,34,35]. In the past few years, some studies demonstrated that dexmedetomidine alone in digestive endoscopic sedation has no significant advantages in recovery time, haemodynamic stability, and patient's and gastroenterologist's satisfaction, compared with propofol or midazolam [3,36,37]. Recently, some researchers have studied the efficacy and safety of using dextromethorphan as an adjuvant to propofol [16,38,39]. A synergistic effect on sedation was observed in all these studies, in which the total propofol requirement in the dexmedetomidine group was significantly reduced. In our this study, we demonstrated that combination of propofol and dexmedetomidine decreased the EC_{50} of TCI propofol during gastrointestinal endoscopy. As dexmedetomidine suppresses neuronal activity and facilitates vagal activity by α_2 receptor activation in the central nervous system; and propofol acts at the GABAA receptors and the NMDA receptors. Therefore, we think the sedative effect of dexmedetomidine and propofol would be synergistic.

The bradycardia caused by dexmedetomidine was often reported [12-16]. Recently, it was reported that the incidence of bradycardia (defined as a pulse rate [?] 45 bpm) in the combination of dexmedetomidine with propofol group was higher than that in the propofol alone group (37.9% vs. 10.3%, $P = 0.029$) in the study by Nonaka T [16], in which the dexmedetomidine was administrated a loading dose of 1 μg/kg in 10 min and a maintenance infusion at the rate of 0.5 μg/kg/h. In our study, the HR average percent change from baseline of dexmedetomidine-propofol co-administration group (Group DEX0.5 and Group DEX1.0) was significantly lower than that of Group Control (propofol alone) (Table 3, Figure 6), which is consistent with the pharmacological properties of dexmedetomidine itself. Dexmedetomidine caused a decrease in heart rate. However, there were no cases of bradycardia (HR ¡ 50 bpm) in the study. There were two possible reasons why there was no bradycardia:(1) Compared to other studies [40,41], our total dose of dexmedetomidine was not high. We just administered a single dose of dexmedetomidine of 0.5 or 1.0 μg/kg for 5 minutes without maintenance infusion. (2) The dose-dependent depression of propofol on the heart rate was weaken, owing to the decrease in dosage of propofol.

The MAP average percent change from baseline of Group DEX1.0 was significantly higher than that of Group Control and Group DEX0.5 (Table 3, Figure 5). The possible reason why increasing doses of dexmedetomidine caused more stable haemodynamics was that the dose-dependent depression of propofol on the circulation was weaken duing to the decrease in dosage of propofol. Furthermore, Figure 5 showed that the hemodynamics (MAP) of dexmedetomidine-propofol co-administration group (Group DEX0.5 and Group DEX1.0) were more stable. In the control group (propofol alone), MAP rebounded at T_4 time point (at scope intubation); but in the co-administration group, MAP did not increased at T_4time point, which may be due to the analgesic effect of dexmedetomidine. This steady blood pressure and appropriately reduced heart rate (but not bradycardia) in co-administration group may benefit the heart in maintaining the balance of oxygen supply and demand.

In the meanwhile, it should be motioned that the loading dose of dexmedetomidine was infused within 10 min

in many previous studies [11,39,42], while we tried to infuse dexmedetomidine single dose within 5 min under close monitoring [43-45]. It was showed that no hypotension, bradycardia, tachycardia and hypertension took place after receiving these doses of dexmedetomidine within relatively shorter time (5 min).

Recovery time was widely concerned by endoscopists and anesthesiologists [9,17,30,32,46]. Rapid recovery is important for patients and hospitals. Using dexmedetomidine for sedation may cause prolonged recovery in term of pharmacological properties, as dexmedetomidine has a relatively long elimination half-life (approximately 2 h) [33,47,48]. It was demonstrated that dexmedetomidine caused prolonged recovery time in outpatient shock wave lithotripsy, compared with midazolam/fentanyl combination [48]. Arain and Ebert et al. demonstrated that a prolonged sedative effect occured after intraoperative use of dexmedetomidine compared with propofol [49]. Arzu ET *et al* . [50] demonstrated that there was a slower recovery in dexmedetomidine-propofol combination group, than in ketamine-propofol combination group. However, in some other studies, it was found that the use of dexamethasone did not prolong the recovery time. In Takashi Nonaka1's study [16], there were no significant difference in recovery times between Combination group (dexmedetomidine and propofol) and Propofol alone group during gastric endoscopic submucosal dissection. The median (ranges) of recovery time was 7 (3-23) min in Combination group and 5 (3-20) min in Propofol alone group. Even Senem Koruk *et al.* [39] demonstrated that a shorter recovery time with the dexmedetomidine-propofol co-administration for ERCP patients, compared with the midazolam-propofol co-administration. In our study, we found the recovery time of Group DEX0.5 was significantly shorter than that of the other groups. There are two possible reasons: one is that we just gave the single dose of dexmedetomidine (0.5 μg/kg dexmedetomidine in 5 min) without continuous administration, which single dose was unlikely to cause drug accumulation and prolong awakening time; the second is that the decrease in the EC_{50} of TCI propofol is also conducive to rapid recovery. However, on the other hand, there was no difference in recovery time between Group DEX1.0 (1.0 μg/kg dexmedetomidine within 5 min) and Group Control (propofol alone).

There was one limitation in our study. Although we require gastroenterologists with the same qualifications and experience to perform endoscopy, there are inevitably differences in operating techniques and skills between different gastroenterologists, which may cause patients to respond differently to the same depth of anesthesia.

Conclusions

Dexmedetomidine decreased the EC_{50} of TCI propofol during gastrointestinal endoscopy. The decrease in dosage of propofol with increasing doses of dexmedetomidine caused more stable MAP. A 0.5-1.0 μg/kg dexmedetomidine caused a decrease in heart rate without bradycardia and did not cause prolonged recovery time. We believe dexmedetomidine is an ideal adjuvant drug to propofol during gastrointestinal endoscopy.

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Table 1 Characteristics and laboratory values of participants. 30 patients for each group

	Control	**Group DEX0.5**	**Group DEX1.0**	P
Sex (M/F)	8/22	11/19	11/19	0.638
Age (yrs)	54.5 (11.9)	54.1 (8.8)	52.2 (10.3)	0.651
Body mass index (kg/m^2)	23.7 (3.0)	23.4 (3.0)	23.7 (2.6)	0.879
Σερυμ τοταλ βιλιρυβιν (μμολ/Λ)	16.0 (7.8)			

17.8 (10.7)

14.4 (5.1)

0.606

Albumin (g/L)

44.2 (2.3)

42.1 (3.9)

43.1 (3.1)

0.410

Alanine aminotransferase (U/L)

15[11;36]

18[8;32]

29[10;85]

0.562

Aspartate aminotransferase (U/L)

22.5[17;28]

21[15;28]

24[16;48]

0.671

Serum creatinine (mmol/L)

66.9 (13.0)

60.8 (13.3)

60.2 (18.4)

0.557

Blood urea nitrogen (mmol/L)

5.1 (1.2)

4.8 (1.4)

4.8 (1.4)

0.845

International normalized ratio

0.94[0.81;1.09]

0.92[0.83;1.10]

0.95[0.90;1.03]

0.581

Data are number, Median [Min, Max] or Mean (SD).

Table 2. Propofol EC_{50} [95% confidence interval]; 30 patients for each group

Group Control

Group DEX0.5

Group DEX1.0

Προποφολ Ε˜50 (μγ/μΛ)

3.77

2.51

2.10

95% ˜I (μγ/μΛ)

[3.48, 4.09]

[2.27, 2.78]

[1.90, 2.33]

Table 3. Procedure-related time, hemodynamics, and sedation-related adverse events; 30 patients for each group

Group Control

Group DEX0.5

Group DEX1.0

P

Injection site pain(yes/no)

6/24

1/29

0/30

0.008

Procedure time (min)

18.1 (7.3)

18.3 (5.8)

19.6 (6.8)

0.650

Recovery time (min)

10.9 (2.5)

9.3 (2.9)§

11.6 (3.3)

0.015

Mean arterial pressure (%)

-10.6 [-24.7; 3.5]

-9.5 [-29.2; 11.4]

-4.0 [-27.3; 15.5]*

0.034

Heart rate (%)

2.8(8.9)

-7.4(7.7)&

-10.5(8.8)&

¡0.001

Satisfaction of patient

4 [3, 4]

4 [3, 4]

4 [3, 4]

0.24

Satisfaction of gastroenterologist

4 [3, 4]

4 [3, 4]

4 [3, 4]

1

Sedation-related adverse events

Hypotension

2

2

0

-

Respiratory depression

1

0

0

-

Postoperative nausea and vomiting

1

0

0

-

Data are Median [Min, Max] or Mean (SD);

SSCompared with Control and Group DEX1.0, P ¡0.05; *Compared with Control and Group DEX0.5, P ¡0.05;

&Compared with Control, P¡0.05.

Figure legends

Figure 1 . Study flow diagram.

Figure 2 . TCI concentrations of propofol for consecutive patients in control group. The horizontal line at 3.77 μg/mL means the EC_{50} of TCI propofol. The red triangle means "responsive". The blue dot means "non-responsive".

Figure 3 . TCI concentrations of propofol for consecutive patients in DEX0.5 group. The horizontal line at 2.51 μg/mL means the EC_{50} of TCI propofol. The red triangle means "responsive". The blue dot means "non-responsive".

Figure 4 . TCI concentrations of propofol for consecutive patients in DEX1.0 group. The horizontal line at 2.10 μg/mL means the EC_{50} of TCI propofol. The red triangle means "responsive". The blue dot means "non-responsive".

Figure 5 . The time course of percent change from baseline in MAP. T_0: baseline values; T_1: 2.5 min after administration of dexmedetomidine; T_2: Dexmedetomidine administration is over; T_3: when propofol target plasma concentration reached the target; T_4: at scope intubation and $T_{5\text{-}x}$: by 3 min intervals.

Figure 6 . The time course of percent change from baseline in HR. T_0: baseline values; T_1: 2.5 min after administration of dexmedetomidine; T_2: Dexmedetomidine administration is over; T_3: when propofol target plasma concentration reached the target; T_4: at scope intubation and $T_{5\text{-}x}$: by 3 min intervals.

Figure 7 . The flow chart of the Dixon's up-and-down methodology.