

The EC50 of propofol with different doses of dexmedetomidine during gastrointestinal endoscopy A double-blind, placebo-controlled trial

Hong-Chun Xu, MMed^a, Qin Ye, MMed^b, Le Wu, MMed^a, Tian-Tian An, B.S.Nurs^a, Fang-Jun Wang, MD^{a,*}

Abstract

Purpose: The goal of this study was to evaluate the dose-response relationship between dexmedetomidine and propofol in sedating patients and to determine the optimal dosage of dexmedetomidine during gastrointestinal endoscopy.

Methods: One hundred fifty patients were divided into 5 groups, each receiving a loading dose of dexmedetomidine (0.4, 0.6, 0.8, 1.0 µg/kg) or saline, with propofol for sedation. The median effective concentration (EC50) of propofol was calculated using the modified Dixon up-and-down approach. Adverse effects, vital signs, procedure, and recovery times were recorded.

Results: The EC50 of propofol in groups NS, D0.4, D0.6, D0.8, and D1.0 were 3.02, 2.44, 1.97, 1.85, and 1.83 μ g/mL, respectively. Heart rate in the dexmedetomidine groups decreased more than the NS group (P < .001). The mean arterial pressure (MAP) in the NS group experienced a decline compared to groups D0.8 and D1.0 when the plasma concentration and effect-site concentration reached equilibrium. Additionally, the respiratory rate was found to be lower in groups NS, D0.4, D0.6, and D0.8 (P < .05). Recovery time in groups D0.8 and D1.0 was longer than the NS group (P < .05). Bruggemann comfort scales score was higher in group D1.0 (P < .05). No significant difference was found in the incidences of hypotension and bradycardia, and the dose of ephedrine and atropine. Respiratory depression was significantly reduced in groups D0.8 and D1.0 compared to the NS group.

Conclusion: A single dose of 0.6 to 0.8 µg/kg of dexmedetomidine should be recommended in combination with propofol for gastrointestinal endoscopy. And the EC50 of propofol is 1.97 to 1.85 µg/mL.

Abbreviations: BCS = Bruggemann comfort scales, EC50 = the median effective concentration of 50% patients, HR = heart rate, MAP = mean arterial pressure, PACU = post anesthesia care unit, TCI = target-controlled infusion.

Keywords: dexmedetomidine, dose relationship, EC50, gastrointestinal endoscopy, optimal dose, propofol

1. Introduction

As public health awareness grows, regular medical examinations, such as gastrointestinal endoscopy, have become essential for diagnosing and treating gastrointestinal diseases.^[1] Gastrointestinal endoscopy, an effective and widely used procedure, involves the insertion of a flexible camera-equipped tube into the digestive tract to assess the condition of the gastrointestinal system.^[2] While this procedure may cause some discomfort, a variety of sedative and anesthesia options are available to alleviate pain and anxiety, ensuring patient comfort and safety.

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

^a Department of Anesthesiology, Affiliated Hospital of North Sichuan Medical College, Nanchong, China, ^b Department of Anesthesiology, Zi-Gong Fourth People's Hospital, Zigong, Sichuan, China. Currently, a common sedative protocol involves the use of propofol combined with opioids.^[3] Nevertheless, these substances can adversely affect the respiratory and circulatory systems, potentially leading to hypotension and respiratory depression, especially when used together.^[4] Other potential side effects of opioids include nausea, vomiting, drowsiness, and confusion.^[5] Consequently, the exploration of alternative sedatives or anesthesia techniques is a viable approach to mitigate these risks. Therefore, the exploration of alternative sedatives or anesthesia techniques is a viable approach to mitigate these risks.

Received: 27 March 2024 / Received in final form: 6 May 2024 / Accepted: 9 May 2024

http://dx.doi.org/10.1097/MD.00000000038421

This study, approved by the Ethics Committee of the Affiliated Hospital of North Sichuan Medical College (2019ER(R)095-1) and registered with the Chinese Clinical Trial Registry on December 17th, 2019 (http://www.chictr.org. cn/; Registration Number: ChiCTR1900028279), adhered to the Declaration of Helsinki and CONSORT Standards. After obtaining informed consent, 150 patients, aged 18 to 60, with an American Society of Anesthesiologists (ASA) physical classification status of I-II, for elective gastrointestinal endoscopy at the Affiliated Hospital of North Sichuan Medical College were enrolled. The study was conducted from December 2019 to April 2020.

^{*} Correspondence: Fangjun Wang, Department of Anesthesiology, Affiliated Hospital of North Sichuan Medical College, Nanchong, 637000, China (e-mail: wfjlxy006@nsmc.edu.cn).

Copyright © 2024 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Xu H-C, Ye Q, Wu L, An T-T, Wang F-J. The EC50 of propofol with different doses of dexmedetomidine during gastrointestinal endoscopy: A double-blind, placebo-controlled trial. Medicine 2024;103:23(e38421).

Dexmedetomidine, a highly selective $\alpha 2$ receptor agonist, has demonstrated sedative, analgesic, and antisympathetic effects without significant respiratory side effects.^[6,7] It has been utilized in various clinical settings, including general anesthesia^[8,9] and gastrointestinal endoscopy,^[10] reducing the need for other anesthetics and analgesic drugs. However, high doses of dexmedetomidine can lead to bradycardia and hypotension.^[8,11,12]

The optimal dose of dexmedetomidine for gastrointestinal endoscopy remains uncertain, particularly in balancing the desired sedation level while minimizing side effects. This uncertainty highlights the need for further research and investigation. So, we propose conducting a randomized, double-blinded, and controlled study to explore the dose relationship between dexmedetomidine and propofol in gastrointestinal endoscopy. By administering varying doses of dexmedetomidine with propofol and comparing the EC50 of propofol in each group, we aim to determine the optimal dexmedetomidine dose when combined with propofol for sedation during gastrointestinal endoscopy.

2. Materials and methods

This study, approved by the Ethics Committee of the Affiliated Hospital of North Sichuan Medical College (2019ER(R)095-1) and registered with the Chinese Clinical Trial Registry on December 17, 2019 (http://www.chictr.org.cn/; Registration Number: ChiCTR1900028279), adhered to the Declaration of Helsinki and CONSORT Standards.

After obtaining informed consent, 150 patients, aged 18 to 60, with an American Society of Anesthesiologists physical classification status of I to II, for elective gastrointestinal endoscopy at the Affiliated Hospital of North Sichuan Medical College were enrolled. The study was conducted from December 2019 to April 2020. Patients with allergies to propofol or dexmedetomidine; cardiovascular disease (arrhythmia, aortic stenosis, ischemic heart disease, severe hypertension, heart failure, ejection fraction < 30%), liver disease (Child-Pugh C), renal disease; history of abdominal surgery; recent use of sedatives and opioids; obstructive sleep apnea syndrome (OSAS), alcoholism; history of drug addiction were excluded. Those experiencing intraoperative bowel perforation or a procedure exceeding 1 hour were withdrawn from the study.

Patients were randomly assigned to 1 of 5 groups using SPSS software, Patients were categorized based on their surgical sequence, with unique codes from 1 to 150 assigned to each. Following this, patients were assigned random numbers, which were used to sort and group them. Each receiving varying doses of dexmedetomidine or an equivalent volume of 0.9% saline. The groups were designated as follows: D0.4 (0.4 µg/kg dexmedetomidine), D0.6 (0.6 µg/kg dexmedetomidine), D0.8 (0.8 µg/kg dexmedetomidine), and NS (0.9% saline).

Upon the patient's arrival in the operating room, an anesthetist nurse prepared the test drug based on the allocation assigned by the SPSS software. The nurse loaded the drug into the infusion pump and established a target-controlled concentration of propofol. To mitigate potential bias in drug distribution influenced by the numerical values visible on the pump's screen, the screen was concealed. The same anesthetist, who was blinded to the treatment allocation, sedated all patients and did not participate in patient monitoring or data collection. This process was designed to maintain the treatment allocation unknown to both patients and anesthetists.

The "up-and-down" method was used to determine the EC50 of propofol, which inhibits the movement response during gastrointestinal endoscopy.^[13,14] Before the procedure, patients were instructed to fast and undergo bowel preparation. Upon entering the endoscopy suite, peripheral venous access was established and 10 mL/kg/h Ringer lactate solution was infused. The nasal catheter oxygen inhalation was administered with a

flow rate of 3 L/min (FiO2: 33%). Patients were continuously monitored for electrocardiogram, noninvasive blood pressure (NIBP), respiratory rate (RR), and oxygen saturation (SpO₂). Rescue medications and materials were prepared.

Anesthesia induction was standardized. Before induction, all patients received either dexmedetomidine or 0.9% sodium chloride over 10 minutes by an infusion pump, followed by an intravenous injection of fentanyl 0.5 µg/kg. Propofol was then administered with an initial effect-site concentration of 3.0 µg/ mL in each group using a target-controlled infusion (TCI) (the Marsh model).^[15]

The endoscopic procedure commenced after the patient lost consciousness, the eyelash reflex ceased, and an equilibrium was established between the propofol concentration in the effect-site and plasma. Movements of the head or limbs during the procedure were regarded as "responsive."^[13,14] If a patient exhibited purposeful movements, an intravenous bolus of propofol 0.5 to 1.0 mg/kg was administered until the procedure was completed. For the next patient, the effect-site concentration of propofol was increased by 20% times with an adjacent concentration gradient. If patients exhibited "nonresponsive" behavior, a lower-level concentration (20%) was administered with an adjacent concentration gradient for the next patient. Upon reaching the ileocecal valve, intravenous infusion of propofol was discontinued. Patients were then transferred to the postanesthesia care unit (PACU) for further monitoring until they regained a satisfactory level of consciousness. Patients were discharged when the Adrete score was >9.^[16]

Hypotension, defined as a mean arterial pressure (MAP) <60 mm Hg or a decrease in MAP of more than 30% from baseline, was treated with ephedrine 6 mg. Respiratory depression was defined as $\text{SpO}_2 <90\%$ or an apnea lasting more than 15 seconds,^[17] and was treated with assisted ventilation until recovery of breathing. Bradycardia, defined as a heart rate (HR) <50 beats per minute, was managed with a dose of 0.5 mg of atropine. The dosages of ephedrine and atropine were recorded.

The primary endpoint was the concentration of propofol in the effect-site across all patients, which was used to calculate the EC50 of propofol. Secondary endpoints encompassed baseline measurements of HR, MAP, and RR, recorded 5 minutes after the patient's arrival in the endoscopy room. HR, MAP, and RR were continuously monitored at set intervals: T0 baseline values; T1, when the plasma concentration and effect-site concentration reached equilibrium; T2, 1-minute post gastroscopy commencement; T3, 1-minute post colonoscopy start, and T4, upon the patient's awakening. Perioperative adverse events, including hypotension, bradycardia, and respiratory depression, along with propofol dosage, endoscopy duration, recovery time (time from propofol infusion cessation to patient regaining consciousness), Bruggemann comfort scale (BCS: 0, persistent pain; 1, no pain at rest; severe pain when breathing or coughing; 2, no pain at rest; mild pain during breathing or coughing; 3, no pain during deep breathing; 4, no pain during deep breathing and coughing), and Aldrete score, were documented. The Aldrete score was evaluated at 5-minutes intervals postoperatively until it exceeded 9. The time from the patient's arrival to their departure from the endoscopy room was also recorded.

3. Statistical analysis

The Dixon up-and-down method, further refined by Brownlee, necessitates a group size of 20 to 40 patients.^[13,14] Our study estimated a roughly 10% incidence of follow-up failure. Therefore, we decided on a group size of 30 cases. In this study, the up-and-down method was employed to ascertain the EC50 of propofol.

All data were analyzed using the statistical software SPSS20. Categorical variables were analyzed using either the chi-square (χ 2) test or Fisher exact test, applying Bonferroni correction to all pairwise comparisons. Measurement data, expressed as

mean and standard deviation, underwent ANOVA, followed by one-way ANOVA with Bonferroni correction. Then post hoc Bonferroni multiple comparison tests was used to identify vital sign differences among the 5 groups. nonnormally distributed data were analyzed using the U test with adjusted P values, and probability-regression analysis was used to calculate the EC50 of propofol. We considered a P value <.05 as statistically significant.

4. Results

Out of 198 eligible patients were screened, and 150 patients completed the study (Fig. 1). The demographic data and characteristics of the patients are detailed in Table 1. No significant differences were noted across the 5 groups regarding sex, age, height, weight, American society of anesthesiologists physical status, gastrointestinal endoscopy procedure time, and the PACU stay (P > .05) (Table 1).

Propofol plasma concentrations and patient responses during endoscopy are depicted in Figure 2. The EC50 of propofol and the 95% CI for groups NS, D0.4, D0.6, D0.8, and D1.0 were 3.02 (2.75–3.47), 2.44 (1.52–3.09), 1.97 (1.75, 2.23), 1.85 (1.61–2.10), and 1.83 (1.52–2.21) µg/mL, respectively. Groups D0.6, D0.8, and D1.0 showed a significant decrease in EC50 of propofol compared to group NS. No significant differences were found between groups D0.4 and NS or among groups D0.6, D0.8, and D1.0 (P > .05) (Fig. 3). Dexmedetomidine pretreatment significantly reduced propofol requirements (P < .05). Additionally, propofol needs were lower in groups D0.6, D0.8, and D1.0 than in groups D0.4 and NS, with groups D0.8 and D1.0 requiring less propofol than group D0.4 (P < .05). No significant differences in propofol needs were observed among groups D0.6, D0.8, and D1.0 (Fig. 3).

HR significantly decreased from T1 to T4 in dexmedetomidine groups compared to T0 (P < .001) and was lower than group NS (P < .001). MAP showed a significant reduction in group NS compared to groups D0.8 and D1.0 (P < .05). RR at T1 was lower than baseline in groups NS, D0.4, D0.6, and D0.8 (P < .05) (Fig. 4).

Recovery time was longer in groups D0.8 and D1.0 than in group NS (P < .05), and BCS was higher in D1.0 versus NS (P < .05) (Table 2). Hypotension rates in groups NS, D0.4, D0.6, D0.8, and D1.0 were 46.7%, 36.7%, 20%, 23.3%, and 26.7%, respectively, with no significant difference between groups (P = .152). There was also no significant difference in ephedrine dosage among the groups. Incidences of respiratory depression were 50% in group NS, and 40%, 33.3%, 13.3%, and 10% in groups D0.4, D0.6, D0.8, and D1.0, respectively, with a significant variation across groups (P < .001). Groups D0.8 and D1.0 had significantly fewer cases than groups NS (P = .005 and P = .002, respectively) (Table 2). No significant differences were



Table 1

Demographic data and patients' characters.

	Group NS (n = 30)	Group D0.4 (n = 30)	Group D0.6 (n = 30)	Group D0.8 (n = 30)	Group D1.0 (n = 30)	P value
Gender (M/F)	13/17	14/16	17/13	17/13	12/18	.680
ASA (I/II)	10/20	12/18	11/19	9/21	12/18	.910
Age (yrs)	42.1 ± 8.7	43.6 ± 8.1	44.5 ± 8.7	42.6 ± 8.8	44.2 ± 8.6	.793
High (cm)	163.1 ± 6.7	163.8 ± 6.9	162.2 ± 7.4	164.2 ± 6.2	163.3 ± 8.6	.852
Weight (kg)	60.8 ± 8.2	60.4 ± 10.2	61.0 ± 8.8	63.2 ± 7.3	58.9 ± 9.9	.466

Values are expressed as Mean \pm SD. ASA = American society of anesthesiologists.



Figure 2. Target propofol concentration in group NS (A), group D0.4 (B), group D0.6 (C), group D0.8 (D) and group 1.0 (E). The responses shown were determined using the modified Dixon up-and-down method.

found in bradycardia incidence or atropine dosage among the groups (P > .05).

5. Discussion

In conclusion, the findings of our study revealed the doseresponse relationship between dexmedetomidine and propofol during gastrointestinal endoscopy. Moreover, with an increase in the loading dosage of dexmedetomidine, the EC50 and propofol requirements gradually decreased. This was accompanied by a reduction in respiratory depression, an improvement in BCS scores, and enhanced hemodynamic stability. However, there was a more significant decrease in the HR without an increased risk of bradycardia, and a longer recovery time. A potential ceiling effect may exist in the dose-response relationship between dexmedetomidine and propofol. When the dosage of dexmedetomidine exceeds 0.6 µg/kg, the decrease in EC50 and propofol requirements becomes significantly less pronounced. Similarly, dexmedetomidine dosages of 0.8 and 1.0 µg/kg appeared to have a comparable effect on respiratory depression.

To maintain a steady propofol concentration in the plasma, this study utilized TCI instead of manually controlled infusion (MCI). Previous studies have demonstrated that propofol delivered via TCI results in a more stable hemodynamic and respiratory state, along with a faster recovery compared to MCI methods.^[18,19] However, in this research, 46.7% of patients reported hypotension, and 50% experienced respiratory depression. These findings align with those of Zhou et al,^[20] whose investigation revealed that approximately 32.5% of patients in the propofol group experienced hypotension, while 18% and 10% suffered from moderate and severe hypoxia, respectively. It is essential to implement necessary measures to prevent and mitigate these adverse effects. The adoption of alternative anesthetic procedures or medications can help reduce the likelihood of these undesirable outcomes.

Numerous studies have suggested that the use of dexmedetomidine as an adjuvant medication reduces the need for propofol, opioids, and inhalation anesthetics.^[9,21] For example, Eun et al^[22] discovered that the insertion of an I-gel supraglottic airway device without the use of muscle relaxants, accompanied by a bolus dose of dexmedetomidine at 1.0 µg/kg, resulted in a decrease in the EC50 of propofol from 6.75 to 3.18 μ g/mL. Nevertheless, the administration of dexmedetomidine at high doses has been associated with significant risks, including bradycardia and hypotension. In order to mitigate these risks, the dexmedetomidine dosage in our study was confined to a maximum of 1 μ g/kg.

In the present study, the EC50 of propofol was assessed in combination with 4 various concentrations of dexmedetomidine, as compared to 0.9% saline. The findings indicated that the EC50 of propofol in the dexmedetomidine groups (0.4, 0.6, 0.8, and 1.0 μ g/kg dexmedetomidine) decreased by 19.20%, 34.77%, 38.74%, and 39.40%, respectively. These findings are in line with prior research conducted by Zhao et al,^[13] which examined the administration of various doses of dexmedetomidine as a pretreatment before induction. The research also



Figure 3. Propofol's EC50 and dosage in groups NS, D0.4, D0.6, D0.8, and D1.0; a P < .05 versus the group NS, b P < .05 versus the group D0.4.

revealed a similar dose-dependent drop in EC50 of propofol. However, the decrease in the EC50 of propofol progressively lessens as the dosage of dexmedetomidine exceed 0.6 µg/kg. Further increases in the dosage of dexmedetomidine may not correspond to the decreases in propofol, indicating a potential ceiling effect in the dose-response relationship between dexmedetomidine and propofol during gastrointestinal endoscopy.

Determining the optimal dosage of dexmedetomidine requires a careful balance between achieving the desired anesthetic effect and minimizing the risk of potential side effects. In this study, we compared both the vital signs and the adverse effects. As shown in Figure 4(B), the MAP curve appeared more stable for the dexmedetomidine groups than for the placebo group. However, there was no statistically significant difference in hypotension incidence or the need for ephedrine doses among the 5 groups. This lack of significant difference could be due to several factors, such as the relatively small sample size of our study, which may have limited our statistical power to detect group differences. Additionally, the side effects of dexmedetomidine on blood pressure regulation could also be a contributing factor.^[8]

The study found that patients administered with dexmedetomidine experienced a significant decrease in HR compared to those who received a placebo. Furthermore, a higher dosage of dexmedetomidine was associated with a lower HR. Importantly, the HR of patients given dexmedetomidine remained above 50 beats per minute. Furthermore, there was no significant difference observed in the incidence of bradycardia and the need for atropine across all 5 groups. These results suggest that a dexmedetomidine loading dose up to 1.0 µg/kg was generally well-tolerated in terms of HR, without a significant increase in bradycardia occurrence. However, it's crucial to closely monitor patients and evaluate individual responses to dexmedetomidine, given the potential risk of bradycardia.

Maintaining spontaneous ventilation is crucial during gastrointestinal endoscopy procedures to ensure patient safety, especially in the outpatient setting.^[23] However, in the placebo group, nearly half of the patients experienced respiratory depression, necessitating airway support. Furthermore, the



Figure 4. Cardiorespiratory variables across the following groups during gastrointestinal endoscopy: NS (\blacksquare), D0.4(\odot), D0.6 (\diamond), D0.8(Δ), and D1.0(\diamond). The variables included HR (A), MAP (B), RR (C), and SpO₂ (D). All data are presented as mean \pm SD. **P* < .05 baseline (T0); #*P* <.05 versus group NS. T0: baseline values; T1: when the plasma concentration and effect-site concentration reached equilibrium; T2: 1 minute after the start of gastroscopy; T3: 1 minute after the start of colonoscopy; and T4: upon awakening of the patient. HR = heart rate, MAP = mean arterial pressure, SpO₂ = oxygen saturation.

Comparison of BCS	, awakening tin	ne, and adverse	e events.

	led	

	Group NS (n = 30)	Group D0.4 (n = 30)	Group D0.6 (n = 30)	Group D0.8 (n = 30)	Group D1.0 (n = 30)	P value
Gastrointestinal endoscopy time (min)	15.7 ± 2.9	14.6 ± 4.0	14.7 ± 2.9	16.0 ± 3.4	16.2 ± 3.6	.369
PACU time	41.9 ± 10.7	43.4 ± 10.4	41.9 ± 8.3	38.5 ± 9.3	37.5 ± 10.9	.118
BCS	3.3 ± 0.5	3.6 ± 0.6	3.7 ± 0.4	3.7 ± 0.4	3.8 ± 0.4^{a}	.034
Recovery time (min)	3.9 ± 1.2	5.2 ± 2.1	5.3 ± 2.0	5.9 ± 2.5^{a}	6.1 ± 2.3^{a}	.001
Adverse events						
Hypotension (Y) (%)	14/16 (46.7)	11/19 (36.7)	6/24 (20)	7/23 (23.3)	8/22 (26.7)	.152
Ephedrine dose (mg)	3.8 ± 4.5	3.4 ± 4.3	2.8 ± 4.3	1.8 ± 3.5	1.6 ± 2.6	.180
Bradycardia (Y) (%)	0 (0)	2 (6.7)	3 (10)	3 (10)	4 (13.3)	.322
Atropine dose (mg)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	.26
Respiratory depression (Y) (%)	15 (50)	12 (40)	10 (33.3)	4 (13.3)*	3 (10)*	.001
$SpO_{2} < 90\%/apnea > 15 s (n)$	7/8	4/8	2/8	2/2	1/2	

Values are expressed as mean \pm SD, Median (/QR) or number of patients.

* P < .05 vs group NS.

T-LL- O

BCS = Bruggemann comfort scale, PONV = postoperative nausea and vomiting.

onset of the gastroscopy procedure was more likely to induce hypoxia and apnea. At the point, a dramatic increase in the plasma concentration of propofol can lead to a decrease in both respiratory frequency and tidal volume.^[24,25] A previous study conducted by Makoto et al^[25] concluded that incorporating a single low-dose of dexmedetomidine into propofol sedation reduced the need for airway support in children undergoing magnetic resonance imaging. In our study, the results revealed a gradual decrease in the incidence of respiratory depression as the dosage of dexmedetomidine increased. The mechanism by which dexmedetomidine decreases respiratory depression may be related to its dose-dependent propofolsparing effect. However, dexmedetomidine dosages of 0.8 and 1.0 µg/kg appeared to have a comparable effect on respiratory depression.

The findings of this study, specifically the higher score on the BCS in the group of patients who received dexmedetomidine compared to those who received a placebo, suggest a potential benefit of dexmedetomidine in enhancing patients' comfort level. Dexmedetomidine is known to induce a state of nonrapid eye movement sleep, thereby improving sleep quality, and may also have analgesic effects.^[12,13] These properties could help explain the observed improvement in postoperative comfort and reduction in discomfort when dexmedetomidine is used as an adjuvant to propofol sedation.

To minimize the adverse effects associated with the rapid infusion of dexmedetomidine, our study adopted an infusion rate over 10 minutes in the preparation room before the procedure. This approach did not increase the waiting time for endoscopists. However, we must acknowledge that this method inevitably increases the labor cost. Furthermore, our findings indicate that the recovery time was prolonged in the groups that received higher doses of dexmedetomidine (0.8 and 1.0 µg/kg) compared to the group that received a placebo. This is consistent with previous studies that have demonstrated the potential for dexmedetomidine to delay anesthesia recovery and hospital discharge.^[4,26,27] Nonetheless, the average difference in the increased recovery time in our study was approximately 2 minutes; it did not produce a significant clinical effect on patients, and dexmedetomidine did not prolong the time to leave the PACU in our study.

In conclusion, taking into account factors such as anesthesia effectiveness, potential side effects including hypotension, respiratory depression and bradycardia, and recovery time and comfort, it is suggested that a single dose of 0.6 to 0.8 µg/kg of dexmedetomidine should be used in combination with propofol for gastrointestinal endoscopy.

This study does have a few limitations. Firstly, the depth of anesthesia was determined by the anesthesiologist's subjective assessment, not by bispectral index, due to budget constraints. However, it's important to note that no patients reported intraoperative consciousness. Second, the study employed the up-and-down approach, which requires a smaller sample size. Therefore, future research should consider a larger sample and a longer observation period for more comprehensive results. Lastly, the average age of patients in this study was between 42 and 44 years. Consequently, the applicability of our findings to older patients may be limited.

6. Conclusion

In conclusion, a dosage of 0.6 to 0.8 μ g/kg of dexmedetomidine combined with propofol is recommended for gastrointestinal endoscopy. This combination reduces the EC50 and dosage of propofol, provides effective sedation, lessens respiratory depression, improves patient satisfaction, without increasing the risk of bradycardia or prolonging the recovery period. Additionally, the EC50 of propofol is found to be between 1.97 to 1.85 μ g/mL.

Acknowledgment

The authors would like to gratefully acknowledge the Gastroscopy Center at the Affiliated Hospital of North Sichuan Medical College for their support.

Author contributions

Data curation: Qin Ye. Methodology: Fang-Jun Wang. Project administration: Le Wu, Tian-Tian An. Software: Le Wu. Supervision: Hong-Chun Xu.

Writing – original draft: Hong-Chun Xu.

Writing – review & editing: Fang-Jun Wang.

References

- Goudra B, Gouda G, Mohinder P. Recent Developments in Drugs for GI endoscopy sedation. Dig Dis Sci. 2020;65:2781–8.
- [2] Varadarajulu S, Banerjee S, Barth BA, et al. ASGE Technology Committee. GI endoscopes. Gastrointest Endosc. 2011;74:1–6.e6.
- [3] Early DS, Lightdale JR, Vargo JJ, et al. ASGE Standards of Practice Committee. Guidelines for sedation and anesthesia in GI endoscopy. Gastrointest Endosc. 2018;87:327–37.
- [4] Nishizawa T, Suzuki H, Hosoe N, Ogata H, Kanai T, Yahagi N. Dexmedetomidine vs propofol for gastrointestinal endoscopy: a meta-analysis. United European Gastroenterol J. 2017;5:1037–45.
- [5] Schug SA, Zech D, Grond S. Adverse effects of systemic opioid analgesics. Drug Saf. 1992;7:200–13.

- [6] Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg. 2000;90:699–705.
- [7] Mittal NP, Goyal M. Dexmedetomidine: a potential agent for use in procedural dental sedation. Indian J Dentistry. 2014;5:21–7.
- [8] Amri P, Nahrini S, Hajian-Tilaki K, et al. Analgesic effect and hemodynamic changes due to dexmedetomidine versus fentanyl during elective colonoscopy: a double-blind randomized clinical trial. Anesth Pain Med. 2018;8:e81077. In Press.
- [9] Le Guen M, Liu N, Tounou F, et al. Dexmedetomidine reduces propofol and remifentanil requirements during bispectral index-guided closedloop anesthesia: a double-blind, placebo-controlled trial. Anesth Analg. 2014;118:946–55.
- [10] Edokpolo LU, Mastriano DJ, Serafin J, Weedon JC, Siddiqui MT, Dimaculangan DP. Discharge readiness after propofol with or without dexmedetomidine for colonoscopy. Anesthesiology. 2019;131:279–86.
- [11] Mahmoud M, Mason KP. Dexmedetomidine: review, update, and future considerations of paediatric perioperative and periprocedural applications and limitations. Br J Anaesth. 2015;115:171–82.
- [12] Lee S. Dexmedetomidine: present and future directions. Korean J Anesthesiol. 2019;72:323–30.
- [13] Chen H, Deng F, Tang S, Liu W, Yang H, Song J. Effect of different doses of dexmedetomidine on the median effective concentration of propofol during gastrointestinal endoscopy: a randomized controlled trial. Br J Clin Pharmacol. 2023;89:1799–808.
- [14] Li S, Yu F, Zhu H, Yang Y, Yang L, Lian J. The median effective concentration (EC50) of propolo with different doses of fentanyl during colonoscopy in elderly patients. BMC Anesthesiol. 2015;16:24.
- [15] Marsh B, White M, Morton N, Kenny GN. Pharmacokinetic model driven infusion of propofol in children. Br J Anaesth. 1991;67:41–8.
- [16] Aldrete JA. The post-anesthesia recovery score revisited. J Clin Anesth. 1995;7:89–91.
- [17] Jarzyna D, Jungquist CR, Pasero C, et al. American society for pain management nursing guidelines on monitoring for opioid-induced

sedation and respiratory depression. Pain Manag Nurs. 2011;12:118-45.e10.

- [18] Wang J-f, Li B, Yang Y-g, Fan X-h, Li J-b, Deng X-m. Target-controlled infusion of propofol in training anesthesiology residents in colonoscopy sedation: a prospective randomized crossover Trial. Med Sci Monit. 2016;22:206–10.
- [19] Chan WH, Chang SL, Lin CS, Chen MJ, Fan SZ. Target-controlled infusion of propofol versus intermittent bolus of a sedative cocktail regimen in deep sedation for gastrointestinal endoscopy: comparison of cardiovascular and respiratory parameters. J Dig Dis. 2014;15:18–26.
- [20] Zhou X, Li BX, Chen LM, et al. Etomidate plus propofol versus propofol alone for sedation during gastroscopy: a randomized prospective clinical trial. Surg Endosc. 2016;30:5108–16.
- [21] Sottas CE, Anderson BJ. Dexmedetomidine: the new all-in-one drug in paediatric anaesthesia? Curr Opin Anaesthesiol. 2017;30:441–51.
- [22] Jang YE, Kim YC, Yoon HK, et al. A randomized controlled trial of the effect of preoperative dexmedetomidine on the half maximal effective concentration of propofol for successful i-gel insertion without muscle relaxants. J Anesth. 2015;29:338–45.
- [23] Riphaus A, Wehrmann T, Kronshage T, et al. Clinical value of the Integrated Pulmonary Index® during sedation for interventional upper GI-endoscopy: a randomized, prospective tri-center study. Dig Liver Dis. 2017;49:45–9.
- [24] Marik P. Propofol: therapeutic indications and side-effects. CPD. 2004;10:3639-49.
- [25] Nagoshi M, Reddy S, Bell M, et al. Low-dose dexmedetomidine as an adjuvant to propofol infusion for children in MRI: a double-cohort study. Paediatr Anaesth. 2018;28:639–46.
- [26] Makary L, Vornik V, Finn R, et al. Prolonged recovery associated with dexmedetomidine when used as a sole sedative agent in office-based oral and maxillofacial surgery procedures. J Oral Maxillofac Surg. 2010;68:386–91.
- [27] Ma H, Wachtendorf LJ, Santer P, et al. The effect of intraoperative dexmedetomidine administration on length of stay in the post-anesthesia care unit in ambulatory surgery: a hospital registry study. J Clin Anesth. 2021;72:110284.