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Research Article

The Effects of Different Loading Doses of Dexmedetomidine on the Bispectral Index-Guided Propofol Sedation in Patients Undergoing Advanced Upper Gastrointestinal Endoscopic Procedures: A Randomized Controlled Study

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ABSTRACT

Background: Propofol sedation is the most common method used in advanced upper gastrointestinal endoscopies, despite its short recovery time, narrow therapeutic window, and possible complications like desaturation and hypotension. Dexmedetomidine can replace or supplement propofol because it is a sedative and analgesic with little respiratory depression.
Methods: 44 patients were randomly allocated to 4 groups; each received a different loading dose of dexmedetomidine in combination with propofol. A targeted controlled infusion was guided by the bispectral index. Hemodynamics and recovery times were measured to reach the optimum regimen that produces significant propofol sparing while minimizing the side effects of both components & avoiding substantial delays in recovery.
Results: The 0.5 µg/kg dose of dexmedetomidine can co-produce adequate propofol-sparing sedation that is superior to 0.25 µg/kg of dexmedetomidine or using propofol alone, also with a lower rescue fentanyl dose, reduced overall propofol dosage, and higher endoscopist, anesthetist, and patient satisfaction scores without the higher incidence of dizziness and longer recovery time associated with the standard dose of 1 µg/kg.
Conclusion: The 0.5 µg/kg dose of dexmedetomidine can produce adequate propofol-sparing sedation that is superior to 0.25 µg/kg doses of dexmedetomidine or using propofol alone, also with a lower rescue fentanyl dose, reduced overall propofol dosage, and higher endoscopist, anesthetist, and patient satisfaction scores without the higher incidence of dizziness and longer recovery time associated with the standard dose of 1 µg/kg.

Introduction

Advanced upper gastrointestinal tract procedures, such as Endoscopic Retrograde Cholangiopancreatography (ERCP) and Endoscopic Ultrasound (EUS), are crucial diagnostic and therapeutic tools for diagnosing and managing various pancreatic and biliary pathologies, including benign and malignant conditions [1-4]. Propofol sedation has emerged as the most popular choice for advanced endoscopic procedures due to its shorter half-life, which

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translates into a significantly shorter recovery time compared to conventional sedation methods, such as benzodiazepines and opioids [5].

Propofol's narrow therapeutic window may cause fluctuations in the level of sedation, from moderate or deep sedation to near general anesthesia. Also, many complications are associated with propofol sedation, including desaturation, airway obstruction, restlessness, hypotension, bradycardia, gagging, regurgitation & vomiting, and lastly, delayed recovery [6].

Dexmedetomidine is a highly specific, potent, and selective α^2-adrenoceptor agonist and is an attractive agent for perioperative sedation, especially in remote areas outside the operating theaters, due to many unique properties in the form of analgesia, reduction of sympathetic tone, and attenuation of the neuroendocrine and hemodynamic responses to anesthesia and surgery with minimal respiratory depression [6].

The quest to replace propofol, coupled with dexmedetomidine's unique analgesic properties, led to interest in its use for sedation during advanced endoscopic procedures [6]. This study aims to investigate how different regimens of dexmedetomidine affect the recovery profile of BIS-guided propofol infusion during sedation in advanced upper endoscopic procedures, with the goal of determining the optimal dosing regimen for this combination, specifically the regimen that achieves significant propofol sparing while minimizing the side effects of both components and avoiding substantial delays in recovery.

Methods

The study was designed to be a randomized, prospective, double-blind comparative study. The study was conducted at the Theodor Bilharz Research Institute and Kasr Al-Ainy Hospital, Faculty of Medicine, Cairo University, after obtaining research ethics approval (PT 704), and patients provided informed consent. The study was registered at ClinicalTrials.gov, with the ID (NCT06409377).

Fifty-two adult patients were enrolled in this study. Randomization was performed using computer-generated numbers with Random Allocation Software in a 1:1:1:1 ratio, with 11 patients in each group. The patient's allocation and drug administration instructions were kept in consecutively numbered opaque envelopes. An investigator not participating in the study was responsible for study drug preparation and labeling.

Patients aged 18 to 65 years, both male and female, with an ASA classification of I-II and a BMI of less than 35 kg/m² were included in the study. Patients were excluded if they refused to participate, had an ASA III-IV classification, a BMI greater than 35 kg/m², or a high aspiration risk, such as gastric outlet obstruction, a known allergy to any used medications, or diabetes mellitus, or if they were patients receiving beta-blockers, calcium channel blockers, or inhaled beta-2 bronchodilators. Patients with pacemakers or a heart rate below 50 beats per minute, pregnant females, habitual drug abusers, and patients who required endotracheal intubation during the procedure were also excluded.

All patients underwent routine preoperative preparations. Upon arrival in the endoscopy room, routine monitoring, including ECG, pulse oximetry, and non-invasive blood pressure measurements, was performed on all patients. Baseline readings of mean blood pressure (MAP), heart rate (HR), and oxygen saturation (SpO_2) were recorded and repeated every 5 minutes until the procedure concluded.

Two intravenous (IV) lines were placed in each patient's upper limb. One was dedicated to propofol and IV Ringer administration. The other one was dedicated to the administration of dexmedetomidine. Throughout the procedure, the IV Ringer was kept at a rate of 4-6 ml/kg/h. All patients received oxygen 2-4 L/min through a nasal cannula with an end-tidal CO_2 sampling line connected to the monitor to observe end-tidal CO_2 levels throughout the procedure.

After positioning the patient for the procedure, four BIS electrode sensors were applied to the patient's forehead, which had been cleaned using the frontal-temporal method for monitoring the level of sedation, and the electrodes were pressed for 5 seconds. BIS values were recorded using the COVIDIEN BIS™ Complete 4-Channel Monitoring System (Medtronic, USA), and a baseline BIS reading was obtained.

Sedation technique

The recruited patients were randomized into four equal groups, named $D_{1.0}$, $D_{0.5}$, $D_{0.25}$, and control, which corresponded to the loading doses of dexmedetomidine of 1 µg/kg, 0.5 µg/kg, 0.25 µg/kg, and placebo saline infusion, respectively, administered over 10 minutes. In groups $D_{1.0}$, $D_{0.5}$, $D_{0.25}$, and control, dexmedetomidine (Precedex®; United Pharmaceutical Group Company, USA) 200, 100, 50, and 0 µg was diluted to 50 ml with normal saline & labeled study drug loading dose, respectively, by an investigator not participating in the study. The loading doses were infused via a Fresenius Kabi Injectomat Agilia syringe pump at a rate equivalent to the patient's body weight (kg) × 1.5 mL/hr.

After finishing the loading dose, the mouth gag was inserted, and all patients, except those in the control group, received a continuous infusion of dexmedetomidine. 0.5 µg/kg/hr. Prepared by adding dexmedetomidine 200 µg diluted to 50 ml with normal saline, while patients in the control group received 50 ml of normal saline as a placebo. After the loading dose of dexmedetomidine was administered, a propofol IV infusion (10 mg/mL) was initiated using a TCI Fresenius Kabi Injectomat Agilia syringe pump, based on the

Marsh pharmacokinetic model, with an initial target effector site concentration (Ce) of 0.5 µg/mL. The Ce was increased by 0.5 µg/ml in a stepwise pattern until the targeted BIS reading was reached (60 - 70%). After reaching the target Ce for 15 seconds, the endoscopist started the procedure.

During the procedure, when the BIS reading exceeded 70 or there were excessive patient movements, a rescue bolus of 10-20 mg propofol was given, and the target effect site concentration of propofol was increased by 0.5 µg/ml until the BIS reading returned to the target range, and the patient was settled. On the contrary, when the patient was over-sedated and the BIS reading dropped below 60, the Ce was lowered by 0.5 µg/ml, and when the BIS reading dropped below 50, the propofol TCI infusion was stopped until the BIS reading exceeded 55. It was restarted at a lower Ce by 0.5 µg/ml.

Hemodynamic changes were managed as follows: for any decrease in HR < 45 beats/min, IV atropine 0.01 mg/kg was given. Hypotension (a reduction of patients' MAP by more than 20% of patients' baseline) was managed by increasing the rate of IV fluids, and increments of 5 mg ephedrine were given to maintain MAP ≥ 65 mmHg. Hypertension and tachycardia (an increase in the patient's MAP and heart rate greater than 20% of the patient's baseline) with a high BIS value (>70%) were managed by a propofol 10-20 mg bolus until the BIS value lay within the targeted range (60–70%). If the BIS reading was within the desired range of 60-70, then hypertension and/or tachycardia were considered to be caused by pain, and a rescue bolus of 10 µg fentanyl was given as rescue analgesia until they returned to within 20% of baseline. All adverse events, such as bradycardia, apnea (absence of spontaneous breath for at least 20 seconds), hypoxia (SpO2<90%), cough, and restlessness observed during the procedure were recorded. In case of airway obstruction or apnea, a jaw thrust was applied, and ventilation with a bag valve mask using 100% FiO_2 was used if necessary. Before the end of the procedure, IV paracetamol 1 g and diclofenac sodium 75 mg were given. At the end of the procedure, the propofol and dexmedetomidine infusions were stopped. The patient's oropharynx was suctioned, and the patient was supine, and the head of the trolley was tilted upwards (15 degrees). Then, the patient was transferred to the recovery room. During the recovery period, patients were monitored every five minutes until they achieved a modified Aldrete score (MAS) of 9 or higher. The time taken to reach this score was recorded for all groups, along with the time required to achieve a BIS reading of >90 or the preoperative baseline reading. During the first 24 hours postoperatively, ondansetron (4-8 mg) was administered to patients experiencing postoperative nausea and vomiting. Paracetamol (1 g every 6 hours) and diclofenac (75 mg every 12 hours) were administered intravenously for the first 24 hours postoperatively.

The following data were recorded:

- The recovery time is the time from stopping the sedation until meeting the discharge criteria (Modified Aldrete Score ≥ 9).
- BIS recovery time refers to the duration required to achieve BIS readings greater than 90 or to return to the baseline reading.
- The total propofol consumption overall & hourly consumption during the procedure.
- The sedation onset time is the time from starting the test drug until reaching the target BIS value.
- The success rate of endoscopy insertion without patient gagging is high.
- The intraoperative adverse events, such as hemodynamic instability, hypoxia, apnea, patient movement, or gagging, can occur.
- Postoperative adverse events, e.g., nausea, vomiting, dizziness, shivering
- Number of patients requiring intraoperative rescue fentanyl boluses & the total amount of fentanyl consumed.
- The endoscopist's satisfaction was evaluated based on the adequacy of working conditions during the procedure, using a 10-point numerical scale where 1 represents the worst conditions and 10 represents the best conditions.
- The anesthetist's satisfaction was evaluated through the smoothness of the sedation technique and how easy it was to follow it using a 10-point numerical scale, where 1 is the worst condition and 10 is the best condition (10-point numeric scale).
- The patient's satisfaction (10-point numeric scale), where 1 is the worst experience and 10 is the best one ever (10-point numeric scale). We asked the patients if they would have it again, should they need to.

The primary outcome was the recovery time of each group, defined as the time from the end of infusions until a modified Aldrete score (MAS) of 9 or higher was achieved. Secondary outcomes were total propofol consumption, intraoperative adverse events (e.g., hemodynamic instability, hypoxia, and airway obstruction), time to attain an adequate sedation level to start endoscopy, and postoperative adverse events (e.g., nausea, vomiting, and dizziness), endoscopist satisfaction, patient satisfaction, and anesthetist satisfaction.

Sample size

Based on a previously published study [7], patients who received propofol attained a modified Aldrete score (MAS) > 9 after 7.5 ± 3.29 minutes. Patients who received dexmedetomidine 1 µg/kg loading and

maintenance of 0.5 µg/kg attained a MAS after 16.6 ± 3.18 minutes. Assuming a 25% reduction in recovery time with a lower dose of dexmedetomidine loading, the effect size was calculated to be 1.49, and a sample size of 11 patients was required in each group to achieve 90% power (a total of 44 patients). A total of 52 patients (13 patients in each group) will be enrolled to compensate for possible dropouts.

Statistical Analysis

Statistical analysis was conducted using the Statistical Package for the Social Sciences version 25 (IBM Inc., Chicago, IL, USA). To determine the appropriate statistical testing method, we performed a Shapiro-Wilk normality test and created histograms for quantitative variables. Parametric variables were expressed as means and standard deviations (SD) and compared among the four groups using an F-test. A post hoc Tukey test was then conducted to compare each pair of groups. Non-parametric variables were expressed as median and interquartile range (IQR) and analyzed using Kruskal-Wallis's test. The Whitney (U) test was used to compare each pair of groups. Categorical variables were expressed as frequency and percentage and analyzed using the Chi-square test. A two-tailed P value ≤ 0.05 was considered statistically significant.

Results

In this study, 52 patients were assessed for eligibility; 4 patients did not meet the criteria, and 4 patients refused to participate in the study. The remaining 44 patients were randomly allocated into one of four groups. All of them were followed up on, and the data collected were statistically analyzed. (Figure 1).

The patients were recruited according to the previously mentioned inclusion and exclusion criteria. There was no statistical significance in the comparison of demographic data (Table 1).

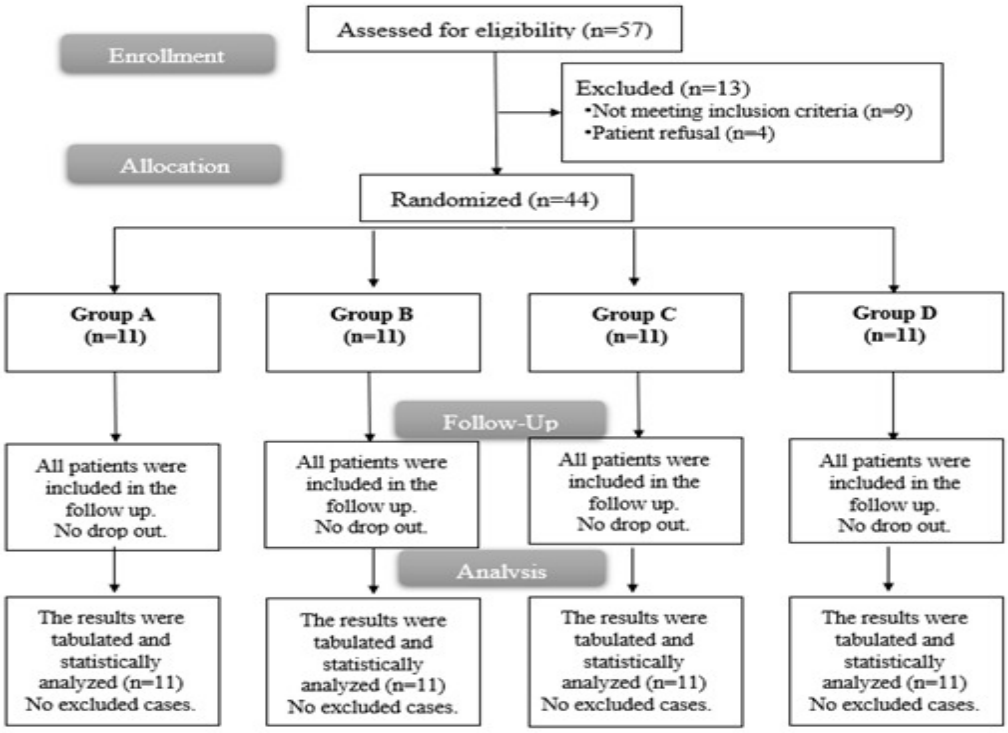

Figure 1- CONSORT flow diagram of the participants

Table 1- Demographic data of the four groups.

		Control (n=11)	$D_{0.25}$ (n=11)	$D_{0.5}$ (n = 11)	D_1 (n=11)	P value
Age (years)	Mean ± SD	51.9 ± 9.13	52.8 ± 10.55	49 ± 8.6	51.2 ± 11.42	0.831
Sex	Male	6 (54.55%)	6 (54.55%)	5 (45.45%)	4 (36.36%)	0.801
	Female	5 (45.45%)	5 (45.45%)	6 (54.55%)	7 (63.64%)	
ASA	I	3 (27.27%)	7 (63.64%)	7 (63.64%)	3 (27.27%)	0.118
	II	8 (72.73%)	4 (36.36%)	4 (36.36%)	8 (72.73%)	
BMI (kg/m^2)	Mean ± SD	28.3 ± 1.74	26.2 ± 3.93	26.2 ± 8.5	27.5 ± 3.39	0.709

BMI: Body Mass Index. ASA: American Society of Anesthesiologists. Data is presented as: Mean ± SD or number (percentage) %. The P value is obtained by comparing the four groups. P value ≤ 0.05 is statistically insignificant.

The four study groups were matched regarding procedure type, successful completion of the procedure, and its duration with no statistically significant difference (Table 2), the procedure (ERCP) was terminated in two patients in the control group due to failure of cannulation because of distorted biliary anatomy. On the other hand, successful endoscope insertion on the first attempt was significantly lower in control compared to $D_{1.0}$. (P value<0.001), $D_{0.5}$ (P value = 0.005), and $D_{0.25}$ (P value=0.024). Within DEX groups, there was no statistically significant difference between the three groups. However, failure of the first attempt was often due to patient gagging or movement. The recovery times of MAS and BIS and the sedation onset time of the studied groups varied statistically significantly among the four groups, with a P value < 0.001, as indicated in (Table 3). The sedation onset time of group $D_{1.0}$ required a significantly shorter time than groups $D_{0.5}$, $D_{0.25,}$ and control, with a P value < 0.05. On the contrary, the difference in sedation onset time between the DEX groups was statistically insignificant. The BIS recovery time (> 90) and recovery time (MAS ≥ 9) were significantly longer in $D_{1.0}$ compared to the other groups, with a P value < 0.05. This was followed by recovery times in D0.5, which were significantly longer than in the control, but not in $D_{0.25}$. No other statistically meaningful difference was found regarding recovery times. (Table 3) The rate of propofol consumption was not statistically significantly different between $D_{0.5}$ and $D_{1.0}$. However, both groups showed statistically significant (P value < 0.05) reductions in comparison to $D_{0.25}$ and the control group, whose rate of propofol consumption was significantly higher than that of $D_{0.25}$ (P value < 0.05) (Table 4). Total propofol consumption was significantly the highest in the control group compared to the other groups (P value < 0.05). It was insignificantly different between the DEX groups. Analysis of the intraoperative adverse events revealed that the events of hemodynamic instability and hypoxia were of no statistically significant difference among the four groups. However, events such as bradycardia, apnea, and patient movement, as well as gagging, showed a statistically significant difference between groups (P value < 0.05) (Table 5). Regarding postoperative adverse events such as nausea, vomiting, and shivering, they weren't present in any patients. On the other hand, dizziness was more noticeable only in Group $D_{1.0}$ (Table 6). Concerning the need for rescue analgesia, the need for intraoperative rescue fentanyl was significantly different among the four groups (P value=0.004), being highest in Control (45.45%) and $D_{0.25}$ (9.09%), respectively, while none of the D0.5 and D1 groups required intraoperative rescue analgesia. Endoscopist satisfaction score and anesthetist satisfaction score were significantly higher in $D_{1.0}$ than in the control group, with a P value of 0.031 and <0.001, respectively. Patient satisfaction was significantly lower in the control than in $D_{1.0}$, $D_{0.5,}$ and $D_{0.25,}$ with a P value <0.001 (Table 7).

Table 2- Procedure data in the four groups.

		Control (n=11)	$D_{0.25}$ (n=11)	$D_{0.5}$ (n = 11)	D_1 (n=11)	P value
Procedure	ERCP	8 (72.73%)	7 (63.64%)	9 (81.82%)	6 (54.55%)	0.211
	EUS	1 (9.09%)	4 (36.36%)	0 (0%)	2 (18.18%)	
	ERCP+EUS	2 (18.18%)	0 (0%)	2 (18.18%)	3 (27.27%)	
Successful procedure	Yes	9 (81.82%)	11 (100%)	11 (100%)	11 (100%)	0.099
	No	2 (18.18%)	0 (0%)	0 (0%)	0 (0%)	
Successful endoscope insertion on the first attempt	Yes	4 (36.36%) [a, b, c]	9 (81.82%)	10 (90.91%)	11 (100%)	<0.001*
	No	7 (63.64%)	2 (18.18%)	1 (9.09%)	0 (0%)	
Duration (min)	Mean ± SD	43.4 ± 17.04	48.6 ± 20.79	42.6 ± 18.44	36.4 ± 10.36	0.425

Data are presented as Mean ± SD or N (%). P values are obtained by comparing the four groups. [a] p < 0.05 vs. $D_{1.0}$; [b] p < 0.05 vs. $D_{0.5}$; [c] p < 0.05 vs. group $D_{0.25}$; [d] p < 0.05 vs. Control. *****: Significant as P value < 0.05.

Table 3- Sedation onset time, recovery time of (MAS and BIS), and sedation onset time in the four groups

		Control (n=11)	$D_{0.25}$ (n=11)	$D_{0.5}$ (n=11)	D_1 (n=11)	P value
Sedation onset time (min)	Mean ± SD	2.7 ± 0.9 [a]	2.3 ± 0.4 [a]	2.4 ± 1.07 [a]	1.3 ± 0.47	<0.001*
BIS recovery time (> 90) (min)	Mean ± SD	3.8 ± 0.6 [a, b]	4.9 ± 0.7 [a]	6.4 ± 2.06 [a]	9.4 ± 1.91	<0.001*
Recovery time (MAS ≥ 9) (min)	Mean ± SD	1.4 ± 0.49 [a, b]	2.1 ± 0.64 [a]	3.2 ± 1.5 [a]	5.2 ± 1.83	<0.001*

Data are presented as Mean ± SD. The P value is obtained by comparing the four groups: [a] p < 0.05 vs. $D_{1.0}$; [b] p < 0.05 vs. $D_{0.5}$; [c] p < 0.05 vs. $D_{0.25}$; [d] p < 0.05 vs. Control. *****: Significant as P value < 0.05.

Table 4- Detailed propofol dosage in the four groups.

		Control (n=11)	$D_{0.25}$ (n=11)	$D_{0.5}$ (n=11)	D_1 (n=11)	P value
Rate of Propofol Consumption (mg/kg/hr)	Mean ± SD	9.7 ± 1.69 [a,b,c]	8.2 ± 2.7 [a,b]	5.5 ± 1.54	4.9 ± 1.28	<0.001*
Total propofol consumption (mg)	Mean ± SD	566.4 ± 222.36 [a,b,c]	354.5 ± 86.43	360.2 ± 124.5	336.5 ± 112.9	<0.001*

Data are presented as Mean ± SD. The P value is obtained by comparing the four groups: a p < 0.05 vs. D1.0; b p < 0.05 vs. D0.5; c p < 0.05 vs. $D_{0.25}$; [d] p < 0.05 vs. Control. *****: Significant as P value < 0.05.

Table 5- Intraoperative adverse events in the four groups.

		Control (n=11)	$D_{0.25}$ (n=11)	$D_{0.5}$ (n=11)	D_1 (n=11)	P value
Hypotensive episodes	Yes	0 (0%)	2 (18.18%)	3 (27.27%)	4 (36.36%)	0.080
	No	11 (100%)	9 (81.82%)	8 (72.73%)	7 (63.64%)	
Bradycardia	Yes	1 (9.09%)	0 (0%)	1 (9.09%)	6 (54.55%)	0.004*
	No	10 (90.91%)	11 (100%)	10 (90.91%)	5 (45.45%)	
Hypoxia	Yes	0 (0%)	0 (0%)	0 (0%)	2 (18.18%)	0.099
	No	11 (100%)	11 (100%)	11 (100%)	9 (81.82%)	
Apnea	Yes	0 (0%)	0 (0%)	0 (0%)	5 (45.45%)	0.001*
	No	11 (100%)	11 (100%)	11 (100%)	6 (54.55%)	
Patient movement gagging	Yes	8 (72.73%)	4 (36.36%)	3 (27.27%)	0 (0%)	0.004*
	No	3 (27.27%)	7 (63.64%)	8 (72.73%)	11 (100%)	

Data are presented as N & %. The P value is obtained by comparing the four groups. *: Significant at $p < 0.05$.

Table 6- Postoperative adverse events in the four groups.

		Control (n=11)	$D_{0.25}$ (n=11)	$D_{0.5}$ (n=11)	D_1 (n=11)	P value
Nausea	Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	----
	No	11 (100%)	11 (100%)	11 (100%)	11 (100%)	
Vomiting	Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	----
	No	11 (100%)	11 (100%)	11 (100%)	11 (100%)	
Dizziness	Yes	0 (0%)	0 (0%)	0 (0%)	8 (72.73%)	< 0.001
	No	11 (100%)	11 (100%)	11 (100%)	3 (27.27%)	
Shivering	Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	----
	No	11 (100%)	11 (100%)	11 (100%)	11 (100%)	

Data is presented as N & %, and the P value is obtained by comparing the four groups, *****: Significant as P value < 0.05.

Table 7- Satisfaction scores in the four groups.

		Control (n=11)	$D_{0.25}$ (n=11)	$D_{0.5}$ (n=11)	D_1 (n=11)	P value
Endoscopist satisfaction score	Mean ± SD	8.2 ± 0.6[a]	8.4 ± 0.67	8.6 ± 0.67	8.9 ± 0.3	0.031*
Anesthetist satisfaction score	Mean ± SD	7.7 ± 0.47[a]	8.2 ± 0.87	8.2 ± 0.6	8.6 ± 0.5	<0.001*
Patient satisfaction	Mean ± SD	7.8 ± 0.87[a]	8.7 ± 0.47	9.2 ± 0.6	8.6 ± 0.5	<0.001*

Data were presented as Mean ± SD, and the P value was obtained by comparing the four groups. [a] $p < 0.05$ vs. $D_{1.0}$. *****: Significant as P value < 0.05.

Discussion

Endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasonography (EUS) are the gold standards for diagnosing and managing pancreatic and biliary diseases. While these procedures are highly diagnostic and therapeutic, they are complex, lengthy, and carry significant risks such as aspiration, hypoxemia, and hypotension. Patients undergoing these procedures often have comorbidities, making them high-risk candidates for complications. Therefore, optimizing anesthetic techniques is successful outcomes while prioritizing patient safety [8].

The current study evaluated the effects of different dexmedetomidine dosages on sedation quality, recovery profiles, procedural success, and associated side effects. The findings indicate a dose-dependent effect of dexmedetomidine on sedation onset, recovery time, and procedural conditions.

Recovery times, as assessed by the Modified Aldrete Score (MAS ≥ 9) and Bispectral Index (BIS > 90) were significantly prolonged in the dexmedetomidine-treated groups ($D_{1.0}$, $D_{0.5}$, and $D_{0.25}$) compared to the control group. Notably, the shortest sedation onset was observed in group $D_{1.0}$. Furthermore, $D_{1.0}$ exhibited the highest rate of successful endoscopic insertion, suggesting that deeper sedation improves procedural conditions by minimizing patient movement and suppressing airway reflexes.

Although $D_{0.5}$ showed significantly shorter recovery times than $D_{1.0}$, the difference was clinically negligible (2-3 minutes). $D_{0.5}$ also demonstrated a favorable intraoperative profile, with fewer side effects and improved postoperative recovery, allowing for quicker case turnover, which suggests that it may offer a balanced approach between procedural efficiency and patient safety.

In agreement with our study, Xu et al. [8] and Chen et al. [9] reported prolonged recovery times with higher doses of dexmedetomidine. They attributed the prolonged recovery times of higher doses of dexmedetomidine to its long elimination half-life (approximately 2 hours).

Our data also showed a significant decrease in propofol consumption with increasing doses of dexmedetomidine. The control group required the highest amounts of propofol, while groups $D_{0.5}$ and $D_{1.0}$ showed similar, lower consumption levels. This suggests that beyond a

certain threshold ($D_{0.5}$), higher dexmedetomidine doses do not further reduce propofol requirements. The significant differences between the control group, $D_{0.25}$, and the higher-dose groups, $D_{0.5}$ and $D_{1.0}$, indicate that lower adjunct doses may lead to increased propofol consumption, potentially due to inadequate sedation or anesthetic effects. Similar to our findings, Xu et al. [8] and Chen et al. [9] reported that dexmedetomidine pretreatment significantly reduced propofol requirements and resulted in a significant decrease in the median effective concentration (EC50) of propofol compared to the control group. However, no significant differences were observed between groups with lower dexmedetomidine dosage and the control group, nor were any significant differences found among groups with higher dexmedetomidine dosage.

In addition, Ramkiran et al. [10] found that propofol consumption was significantly higher in the control group compared to the DEX group. Furthermore, Gu et al. [11] reported that DEX reduced the propofol requirements for loss of consciousness. Additionally, Mukhopadhyay et al. found that dexmedetomidine can reduce the need for propofol and maintain a more stable level of sedation during ERCP procedures [12]. However, it was demonstrated that dexmedetomidine infusion alone was not as effective as propofol in terms of sedation quality, as propofol is a potent depressant of the airway reflexes. Furthermore, dexmedetomidine administration was associated with significantly lower blood pressure and heart rate, as well as a prolonged recovery time [13-14].

Perioperative adverse events varied across the groups. Although an increased incidence of hypotension was observed with higher doses of dexmedetomidine, this difference did not reach statistical significance. Conversely, the incidence of bradycardia demonstrated a statistically significant decrease with increasing dexmedetomidine doses, indicating a dose-related trend that may be clinically significant in patients with cardiovascular risk factors. Similarly, hypoxia and apnea were more common with higher dexmedetomidine doses, necessitating careful monitoring. Conversely, gag reflex and patient movement were less pronounced in higher-dose groups, supporting their effectiveness in achieving deeper sedation.

In contrast, gag reflexes and movements were less obvious in groups with higher doses of dexmedetomidine. This pattern suggests that higher doses effectively suppress the patient's movement and reflexes and provide a better depth of anesthesia, potentially improving procedural conditions but also increasing the risk of over-sedation.

Dizziness was reported exclusively in group $D_{1.0}$; this side effect would be annoying to patients and affect turnover in the recovery room, potentially delaying their discharge. Nausea, vomiting, and shivering were absent in all groups, suggesting that the intervention did not contribute to these common postoperative side effects and that pre-medication with an antiemetic had a favorable outcome. These findings imply that higher doses of dexmedetomidine ($D_{1.0}$) provide deeper sedation and better procedural conditions but come with a higher risk of bradycardia, apnea, and postoperative dizziness, while lower doses ($D_{0.25}$, $D_{0.5}$) maintain better hemodynamic stability and lower respiratory risks but may be associated with increased patient movement and gag reflex presence.

The findings emphasize the need to balance dose selection based on patient risk factors, procedural requirements, and the necessity for close monitoring with higher-dose sedation. Contrary to our findings, Xu et al. [8] found that apnea was significantly different among the four groups. Incidences of respiratory depression were higher in groups with lower dosages of dexmedetomidine; this may be attributed to the fact that, unlike our study, they used only a bolus dose of dexmedetomidine with no maintenance dose that may have contributed to the deeper sedation and the resultant apnea found in our study.

Our hemodynamic findings align with those of Ramkiran et al. [10], who found that hemodynamic instability was statistically indistinguishable among the three groups (DEX, Ketamine, and Control), with patients in the dexmedetomidine group showing a statistically significant lower heart rate.

Consistent with our findings, Xu et al. [8] found that heart rate was significantly decreased in the dexmedetomidine group compared to the NS group. On the contrary, MAP showed a significant reduction in group NS compared to group $D_{1.0.}$ Similarly, Chen et al. [9] found that the average percent change from baseline in Group $DEX_{1.0}$ was significantly higher than that in Group Control and Group DEX0.5. Additionally, the co-administration of dexmedetomidine with propofol (Groups $DEX_{0.5}$ and $DEX1_{.0}$) resulted in a significantly larger reduction in heart rate from baseline compared to propofol alone (Group Control). This difference may be attributed to the different populations, sample sizes, and doses in both studies, and again due to the lack of a maintenance dose of dexmedetomidine, which led to higher propofol consumption and consequently lower MAP. Additionally, Chen et al. [9] found that postoperative nausea and vomiting were almost absent in all patients. In a prospective randomized comparative study conducted by Zhao et al. [15], they found that the body movement was significantly different between the propofol-dexmedetomidine (PD) and propofol-remifentanil (PR) groups, which was more obvious in the PD group. This may be attributed to the usage of a lower bolus dose of 0.5 μg/kg and just for 5 minutes; also, the superior analgesic effect of remifentanil was a factor. Nausea and vomiting weren't present in any patients. In

a study conducted by Hasanin and Sira [16], the authors evaluated the sedative, hemodynamic, respiratory, and adverse effects of dexmedetomidine and propofol during gastrointestinal endoscopy procedures in pediatric patients. The heart rate (HR) values were significantly lower in the dexmedetomidine group ($D_{1.0}$) during induction, endoscope insertion, and the entire procedure. Notably, there were no significant differences in mean arterial pressure (MAP), respiratory rate (RR), and oxygen saturation (SpO_2) values at any time point between the two groups. Furthermore, the induction and recovery times were significantly longer in the dexmedetomidine group. Moreover, none of the patients in the dexmedetomidine group experienced oxygen desaturation, unlike six patients (15%) in the propofol group. This study concluded that dexmedetomidine sedation during gastrointestinal endoscopy procedures was safe, effective, and provided cardiorespiratory stability. However, it's important to consider that the differences observed may be attributed to the varying age groups and dexmedetomidine doses used in the two studies. This study highlights the dose-dependent effects of dexmedetomidine on BIS readings, showing that higher doses lead to deeper and longer sedation, which could be useful for procedures where prolonged immobilization is needed. Intermediate dosing may offer a balance between adequate sedation and reduced side effects, making it a potential choice for shorter procedures requiring quick sedation, while lower doses may be more suitable for procedures requiring minimal sedation. The choice of dosage should be tailored based on the desired level of sedation, procedure duration, and patient safety considerations. Supporting our findings, Wang et al. [17] reported that BIS values in groups with higher dexmedetomidine loading doses were significantly lower compared with those receiving lower doses or control groups from 10 minutes after the start of the dexmedetomidine infusion. Also, Jia Lin et al. [7] reported that the lowest BIS value during the procedure was lower with the higher dexmedetomidine doses. In agreement with our findings, Sim et al. [18] reported that the BIS of group $D_{1.0}$ was lower than that of group $D_{0.5}$ 10 minutes after loading of dexmedetomidine.

On the contrary, Gu et al. [11] found that the BIS value at LOC was higher when dexmedetomidine was added to propofol compared to propofol alone. However, it's important to note that hypnotic drugs and their combinations can influence BIS values. One possible explanation is that the BIS value depends on the propofol dose, and it tends to be higher with smaller doses. Another reason is that propofol primarily produces a delta-to-beta frequency band in EEG, which differs from the delta and alpha range activity induced by dexmedetomidine. Propofol's action site differs from dexmedetomidine, which may also influence BIS values. Additionally, the BIS value has a 24 to 122 second time delay, which may affect measurement precision. This reason precisely better explains the difference in our results, as the measurement was only taken at the point of LOC with no follow-up readings.

In the current study, perioperative rescue fentanyl usage was significantly higher in groups D0.25 and control, suggesting superior analgesic effects of higher dexmedetomidine doses. Luo X et al. [19] conducted a prospective, randomized, double-blind study, similar to our findings, on a total of 60 patients undergoing elective gastric ESD under general anesthesia. They found that the incidence of postoperative moderate to severe pain was significantly higher in the control group compared to the dexmedetomidine group. Additionally, VAS pain scores, the dosage of opioids in the PACU, and the total dosage of opioids within 24 hours postoperatively were significantly decreased in the dexmedetomidine group.

In the present study, satisfaction scores were highest among endoscopists and anesthetists in group $D_{1.0}$, while patient satisfaction scores were significantly the lowest in the control group. On the contrary, Zhao et al. [12] found that endoscopists experienced significantly higher satisfaction in the propofol-remifentanil (PR) group compared to the propofol-dexmedetomidine (PD) group. This was attributed to faster induction times, reduced body movement, and quicker patient recovery times. However, patient satisfaction remained unaltered between the two groups.

Chen et al. [9] found that the satisfaction of both gastroenterologists and patients was not significantly different between the control group, the group receiving dexmedetomidine 0.5, and the group receiving dexmedetomidine 1.0. This discrepancy may be due to the varying populations in both studies.

Vetsa et al. [20] conducted a retrospective study over three years to evaluate the use of dexmedetomidine for gastrointestinal endoscopic procedures. Their primary objective was to assess the procedure completion rate and adverse event rates in patients who had previously failed sedation, were anticipated to have challenging sedation, had prolonged procedures, or were on narcotics at the time of the procedure. Dexmedetomidine was administered intravenously as a bolus of 1 µg/kg over 5 minutes, followed by variable maintenance rates. After the bolus, midazolam and meperidine or fentanyl were also administered.

The study revealed a remarkable procedure completion rate of 94%. Patients who completed the procedure had higher dexmedetomidine maintenance rates. This study's limitations include being a single-center study, which may yield different findings than those in other settings; a small sample size that may produce insignificant results; and a lack of comparison with other anesthetic drugs and procedures. Additionally, we did not include patients with ASA classifications higher than II.

Conclusion

The combination of dexmedetomidine with standard sedative drugs for gastrointestinal endoscopic procedures resulted in an excellent procedure completion rate in challenging sedation scenarios. However, they also noted that the prolonged recovery period and increased incidence of adverse events, such as hypotension, bradycardia, hypoxia, nausea, and vomiting, were observed.

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