

Dexmedetomidine in gastrointestinal endoscopic procedures

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Abstract

Gastrointestinal endoscopy is the gold standard in the examination and the treatment of the diseases of gastrointestinal system, but the disadvantage of being painful process. At this point the sedative and analgesic agents may be important. Dexmedetomidine is a new sedoanalgesic agent which is alternative to

benzodiazepines and opioids. It has analgesia, amnesia, sedative and anxiolytic properties. The use of dexmedetomidine as the sole anesthetic agent and as the adjuvant analgesic agent has been published but has not been approved because of the inconsistency of efficacy and safety. The author has been collected the published papers in the literature. This article is aimed to describe the use of dexmedetomidine in various gastrointestinal endoscopic procedures.

Key words: Complication; Safety; Dexmedetomidine; Gastrointestinal endoscopy; Sedation

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Core tip: Dexmedetomidine has analgesic, amnesic, sedative and anxiolytic properties. Use of dexmedetomidine as the sole anesthetic agent and as the adjuvant anesthetic agent in various gastrointestinal endoscopic (GIE) procedures has been published. A distinct advantage of dexmedetomidine is the maintenance of respiratory force and preserved airway patency. These properties of dexmedetomidine have verified to be beneficial in high-risk patients. This article is aimed to explain the clinical use of dexmedetomidine for GIE procedures of the published papers in the literature.

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INTRODUCTION

Dexmedetomidine is an alpha-2 adrenergic receptor agonist and has an eight times higher than clonidine for alpha-2 adrenergic receptors. It has sedative, anxiolytic and analgesic properties that produce cardiorespiratory

stability at the therapeutic doses. The use of dexmedetomidine may be expanded as an intravenous drug in the medical procedures^[1,2]. Dexmedetomidine is approved by the United States Food and Drug Administration for short-term sedation (< 24 h) in adult patients in the intensive care unit (ICU). It also has been used in combination with other sedoanalgesic drugs during painful procedures. Several reports in the literature have been confirmed about its effective use in various gastrointestinal endoscopic (GIE) procedures, although further controlled studies are needed to reinforce its use. This review is aimed to define the role of dexmedetomidine in GIE procedures.

PHARMACOLOGY OF DEXMEDETOMIDINE

The alpha-2 adrenergic receptors are principally postsynaptic receptors distributed in multiple areas^[3]. Sedative and anxiolytic properties are utilized throughout alpha-2 adrenergic receptors in the locus ceruleus of pons. The analgesic effects are employed across the stimulation of alpha-2 adrenergic receptors in the dorsal horn of spinal cord. Dexmedetomidine is an alpha-2 adrenergic receptor and has an eight times higher than clonidine for alpha-2 receptors^[4]. Its distribution half-life is 6 min in adults over a dose range of 0.2-0.7 mcg/kg per hour intravenous infusion^[5]. Dexmedetomidine is rapidly distributed and has an elimination half-life of 2 h. In addition, dexmedetomidine undergoes biotransformation by cytochrome P-450 and glucuronidation. Its clearance remains unaltered in severe renal impairment. However, the clearance decreased up to 32% in severe hepatic dysfunction. Its metabolites are excreted in urine (95%) and in feces (4%).

Moreover, the activation of postsynaptic alpha-2 receptors leads to sympatholysis and results in hypotension and bradycardia. These effects of dexmedetomidine on arterial blood pressure are biphasic with an initial transient rise with a reflex fall in heart rate. This is accompanied by the reduction of arterial blood pressure and heart rate due to inhibition of central sympathetic outflow and stimulation of presynaptic alpha-2 receptors cause decreased release of nor-adrenaline leading to further fall in the blood pressure^[6]. However, these hemodynamic profiles return to the baseline fifteen minutes later. Dexmedetomidine should be contraindicated in the patients with cardiovascular compromise, severe hypovolemia and atrioventricular nodal block.

Dexmedetomidine does not have any depressant effects on respiratory function even at higher doses with no impairment of ventilation or gas exchange^[7]. The ventilatory response to hypercapnia was not affected at a dose that created a negative response to strong stimulation. Dexmedetomidine converges on a natural sleep pathway, activating pathways that promote

endogenous non-rapid eye movement sleep to exert its sedative effect^[3]. Dexmedetomidine creates a reduction in cerebral metabolic demand of oxygen and cerebral blood flow with a slight reduction in intracranial pressure. Its neuroprotective effect is not well known^[8]. It seems to employ analgesic effects at the spinal cord level and at the supraspinal sites^[9]. However, the analgesic properties of dexmedetomidine are still controversial.

DEXMEDETOMIDINE IN GASTROINTESTINAL ENDOSCOPY

Generally, propofol alone or in combination with midazolam and/or fentanyl is one of the most widely used regimens for sedation during the GIE procedures^[10-12]. However, the combination use of sedatives and/or analgesics with propofol may produce some additional risks. Dexmedetomidine offers a sedation level that facilitates natural sleep and communication and also decreases analgesic requirements. The use of dexmedetomidine for sedation during GIE interventions remains to be established. Importantly, the use of dexmedetomidine for sedation in GIE procedures gives more respiratory safety and hemodynamic stability.

Hasanin and Sira^[13] evaluated the sedative, hemodynamic, respiratory and adverse effects of dexmedetomidine and propofol during GIE procedures in the pediatric patients. Eighty pediatric patients with ASA I, II aged 1-14 years were randomized into dexmedetomidine group or propofol group. Sedation was achieved with propofol 2 mg/kg bolus then infused at a rate of 100 mcg/kg per minute or dexmedetomidine 2.5 mcg/kg over 10 min then infused at a rate of 2 mcg/kg per hour to attain a Ramsay sedation scale (RSS) P5. The HR, MAP, RR and SpO₂ were continuously monitored and analyzed. Times of induction, procedure, recovery, and adverse effects were also reported. The HR values were significantly lower in the dexmedetomidine group at induction, after insertion of endoscope, and during the procedure. There were no significant differences in MAP, RR and SpO₂ values at all time points between the two groups. Induction and recovery times were significantly longer in the dexmedetomidine group. No cases in the dexmedetomidine group presented oxygen desaturation vs six patients (15%) in the propofol group ($P = 0.026$). This study confirmed that dexmedetomidine sedation in GIE procedures was safe and efficacy as well as also provided cardiorespiratory stability^[13].

Vetsa *et al*^[14] reported a retrospective study of dexmedetomidine used for GIE procedures in three years. They aimed to evaluate the procedure completion and adverse event rates. A total of 129 procedures with dexmedetomidine were analyzed. Of these, 29% had failed, and 69% had expected difficult sedation or prolonged procedure, and 70% required narcotics during the procedure. Dexmedetomidine was administered intravenously at a bolus of 1 mcg/kg in 5 min and was maintained at the variable rates. Additionally, midazolam

and meperidine or fentanyl was also administered. The result showed the procedure completion rate was 94%. Higher dexmedetomidine maintenance rate was observed in the successfully completed cases. The most common adverse event was hypotension (37%). The interventions for adverse events were required in 86%. All these adverse events were readily managed without significant morbidity. The authors concluded that the use of dexmedetomidine with standard sedative drugs for GIE procedures was related with excellent procedure completion rate in the difficult to sedate procedures. However, the prolonged recovery period and increased adverse events were also observed^[14].

However, many anesthetic agents including dexmedetomidine reduce the lower esophageal sphincter pressure (LESP). The reduction of LESP and the gastroesophageal pressure gradient (GEPG) stimulates gastroesophageal reflux and can cause to aspiration pneumonia. Turan and coworkers compared the effects of dexmedetomidine and propofol on LESP and GEPG in the eleven healthy volunteers. The results demonstrated that no significant differences in LESP and GEPG were observed. They concluded that both dexmedetomidine and propofol had comparable effects on LESP and GEPG. Although both sedative drugs caused some decrease in LESP at high concentrations, it did not create gastroesophageal reflux during the sedation^[15].

ESOPHAGOGASTRODUODENOSCOPY

Esophagogastroduodenoscopy (EGD) is an endoscopic procedure for diagnosis and treatment of upper gastrointestinal tract problems. Generally, topical pharyngeal anesthesia is safe for the use as premedication for unsedated EGD procedure. Consequently, the unsedated EGD procedure is also well accepted^[16]. However, this procedure causes the patient discomfort and anxiety. The sedative drugs are used to relieve these symptoms and improve the endoscopic outcome.

Recently, a randomized, controlled study is conducted to evaluate the effect of dexmedetomidine and propofol on sedation for EGD procedure in outpatient cases. This study confirmed that dexmedetomidine and propofol offered an acceptable level of sedation without serious adverse effects during EGD procedure. The patients in the dexmedetomidine group demonstrated minimal respiratory-related adverse effects. More patients in the propofol group experienced a deeper level of sedation depth at the start of the procedure^[17].

Wu *et al*^[18] assessed the efficacy and safety of dexmedetomidine and midazolam for conscious sedation in patients with ASA physical status I - II who underwent elective EGD procedures. The results of the study demonstrated that patients in the dexmedetomidine group had significantly higher oxygen saturation and overall satisfaction than patients in the midazolam group. Additionally, the patients in the midazolam group experienced a significant decrease in the mean arterial blood pressure during sedation compared with

the baseline values. However, no clinically significant complications between the two groups were noted. The authors concluded that dexmedetomidine had a good safety property and was an effective sedation drug for EGD procedure^[18].

A randomized controlled study compared the efficacy and safety of dexmedetomidine and midazolam in EGD procedure. The result of the study confirmed that dexmedetomidine was suitable for endoscopic procedures of upper gastrointestinal tract. Furthermore, dexmedetomidine offered shorter recovery time and better patient's satisfaction^[19]. The study of Hashiguchi *et al*^[20] also demonstrated that dexmedetomidine for sedation during EGD procedure was as effective and safe as midazolam.

Recently, Samson *et al*^[21] evaluated and compared the sedation efficacy and hemodynamic effects of midazolam and propofol and dexmedetomidine in the patients underwent elective diagnostic EGD procedure. The 90 patients with ASA physical status I or II were randomized into three groups; Group I received midazolam infusion, Group II received propofol infusion and Group III received dexmedetomidine infusion. The study demonstrated that endoscopist satisfaction and recovery in the dexmedetomidine group was significantly better than in the midazolam and propofol groups. In addition, mean arterial blood pressure in the propofol group was significantly lesser than in the dexmedetomidine and midazolam groups^[21].

The safety and efficacy of dexmedetomidine for sedation in EGD procedure is confirmed. A prospective, randomized study investigated and compared the safety and efficacy of dexmedetomidine and midazolam for sedation in EGD procedure. A total of 50 adult patients with ASA physical status classification I and II were included. A brief questionnaire was performed to accumulate the demographic data, anxiety score, satisfaction and expected discomfort. Mean arterial blood pressure, heart rate, respiratory rate and oxygen saturation during and after the procedure were measured continuously and recorded every minute. Low levels of procedural discomfort and anxiety scores as well as high satisfaction levels were observed in these two groups. However, the endoscopist satisfaction was significant higher in the patients receiving dexmedetomidine. In addition, the adverse event rate in the midazolam group was higher than in the dexmedetomidine group. The study confirmed that dexmedetomidine was better than midazolam in term of retching, rate of adverse events and endoscopist satisfaction for sedation the patients for EGD procedures^[22].

Jiang *et al*^[23] studied the sedative effect and hemodynamic influence of dexmedetomidine on the patients undergoing EGD procedure. Forty patients were randomly assigned into two groups. In the control group (C), a single dose of 2.5 mg/kg propofol was infused. In the dexmedetomidine group (D), 0.8 mcg/kg of dexmedetomidine was infused slowly (longer than 10 min) before propofol application. The MAP, HR, SpO₂,

OAA/S, and Ramsay sedation score were recorded at four different time points, before infusion (T0), at beginning of operation (T1), when an endoscope entered the stomach (T2), after the operation was finished (T3). The total dosage of propofol, induction time and arousing time were also observed. The results showed the Ramsay sedation scores at T1, T2 and T3 of group D are statistically higher than group C and the T0 group. In addition, group D also showed the low HR and MAP of the three time points, shorter induction times and arousing times as well as less propofol dosage than group C. No patients showed signs of respiratory suppression. They suggested that the use of 0.8 mcg/kg of dexmedetomidine at periprocedural period of the EGD procedure could yield marked sedative effect, had antihypertensive effect and did not suppress respiration^[23].

Moreover, dexmedetomidine can use with the combination of other sedoanalgesic drugs. The case series of the combination use of dexmedetomidine and ketamine for EGD procedures were studied in 46 children aged 2-12 years. Dexmedetomidine 1 mcg/kg and ketamine 2 mg/kg were administered over 5 min. The alteration of mean arterial blood pressure, heart rate, and oxygen saturation was not significantly different from the baseline. In addition, no airway interventions were needed. The results of this case series showed that the combination of dexmedetomidine and ketamine not only promised to be clinically effective but also safe for EGD procedure in the pediatric patients^[24]. However, the combination dexmedetomidine and ketamine provided longer sedation times and deeper sedation level when compared to the combination etomidate and fentanyl^[25] (Table 1).

Generally, propofol has been used in combination with dexmedetomidine to offer sedation/anesthesia. The pharmacodynamic profile of this combination regimen in 24 children aged 3-10 years underwent EGD procedure was investigated^[26]. The plasma propofol concentration at which 50% of the patients presented minimal response to stimuli was evaluated. The result demonstrated that propofol in the combination with dexmedetomidine was no significant shift in the propofol concentration-response curve. The authors accomplished that a concurrent infusion of dexmedetomidine in a dose of 1 mcg/kg did not affect the propofol requirement^[26].

Sedation in the patients with obstructive sleep apnea (OSA) is very challenge. Dexmedetomidine offers sedation with minimal respiratory depression which is a desirable characteristic in the patients with OSA. An observational study assessed the safety and efficacy of dexmedetomidine/propofol anesthesia for the patients with OSA without endotracheal intubation during EGD procedure^[27]. Twenty patients with high probability of OSA undergoing EGD procedure were enrolled in the study. Dexmedetomidine 1 mcg/kg bolus was administered over 10 min followed by propofol boluses. After that, the anesthesia was maintained by

using continuous propofol infusion. The result showed transient hypoxemic events occurred in two patients during the EGD procedure. Additionally, transient hypotension was experienced in three patients during the procedure and three patients in the post-anesthesia care unit. After discharge, 16 patients complained of drowsiness, two patients informed dysphoric symptoms and one patient reported of dry mouth. The study concluded that the combination of dexmedetomidine and propofol could offer acceptable anesthesia for EGD procedure in the patients with OSA. This combination method provided a substitute to tracheal intubation in these high risk patients^[27].

Atkins *et al*^[28] presented a patient with previously undiagnosed extensive tracheomalacia who suffered airway obstruction during an elective EGD under anesthesia. In the second anesthesia, the authors used 1.5 mcg/kg of dexmedetomidine over 15 min then continuous infusion at a rate of 0.7 mcg/kg per hour and an *iv* bolus of 0.5 mg/kg of ketamine followed by infusion at a rate of 1 mcg/kg per minute. The patient was nonresponsive to the endoscope insertion and preserved normal airway tone with no episodes of any respiratory depression. This case demonstrated the potential advantages of the combination use of dexmedetomidine and ketamine for sedation the patients with achalasia underwent EGD procedure^[28].

Another case report of a nine-year-old, 45 kg child with Duchenne muscular dystrophy underwent EGD procedure by using dexmedetomidine was presented. The patient had a history of egg allergy, and the potential risk of malignant hyperthermia. The combination use of dexmedetomidine and ketamine was utilized for procedural sedation. In this case, a bolus dose of 1 mcg/kg of dexmedetomidine and a single dose of 1 mg/kg of ketamine was given and was maintained by dexmedetomidine continuous infusion at a rate of 0.5 mcg/kg per hour. This case report established that this combination regimen used for EGD procedure was successfully completed and the patient accepted the procedure^[29].

Additionally, intranasal dexmedetomidine can be used for the endoscopic procedure. Han *et al*^[30] compared the cardiorespiratory profiles between intranasal and intravenous dexmedetomidine administered 10 min before induction for the EGD procedure. A dose of 1.5-2 mg/kg of propofol was given for induction. The Mean arterial blood pressure, heart rate, respiratory rate, and oxygen saturation were monitored. The authors concluded that intranasal dexmedetomidine was an effective and safe method alternative to intravenous dexmedetomidine for EGD procedure^[30].

Cheung *et al*^[31] assessed the efficacy of intranasal dexmedetomidine combined with patient-controlled sedation (PCS) for EGD procedure. Intranasal dexmedetomidine 1.5 mcg/kg or intranasal saline was administered 1 h before the procedure. PCS with propofol and alfentanil was given for rescue sedation. The total requirement of PCS propofol and alfentanil

Table 1 The use of dexmedetomidine in a combination technique for gastrointestinal endoscopic procedures

Ref.	Type of endoscopy	No. of patients	DEX group	Non-DEX group	Summary of findings
Wu <i>et al</i> ^[17]	EGD	70	DEX 1 mcg/kg followed by 0.5 mcg/kg per hour infusion <i>iv</i> , FEN 1 mcg/kg <i>iv</i>	PRO 0.6 mg/kg and on demand bolus 10-20 mg <i>iv</i>	DEX showed minimal adverse effects on respiratory function. More patients in PRO created deeper sedation at start
Cheung <i>et al</i> ^[31]	EGD	50	DEX 1.5 mcg/kg <i>in</i> , PCS with PRO and Alfentanil	Normal saline <i>in</i> , PCS with PRO and Alfentanil	DEX <i>i.n.</i> with PCS PRO and alfentanil presented deeper sedation with significantly fewer use of additional sedative agents during EGD
¹ EL-Shmaa <i>et al</i> ^[25]	EGD	100	DEX 1 mcg/kg followed by 0.5-1 mcg/kg per hour infusion <i>iv</i> , KET 1 mg/kg and on demand bolus 0.5 mg/kg <i>iv</i>	ETO 0.15 mg/kg followed by 0.01-0.03 mg/kg per minute infusion <i>iv</i> , FEN 1 mcg/kg <i>iv</i>	ETO/FEN combination provides shorter sedation times and lighter sedation level compared to DEX/KET combination
Wu <i>et al</i> ^[18]	EGD	60	DEX 0.3 mcg/kg followed by 0.2-0.3 mcg/kg per hour infusion <i>iv</i> , FEN 1 mcg/kg <i>iv</i>	MDZ 0.05 mg/kg <i>iv</i> , FEN 1 mcg/kg <i>iv</i>	DEX had a good safety profile and was an effective sedation for EGD procedure
¹ Koksal <i>et al</i> ^[32]	EGD	80	DEX 0.5 mcg/kg followed by 0.2 mcg/kg per hour infusion <i>iv</i> , KET 1 mg/kg <i>iv</i>	REM 0.5 mcg/kg followed by 0.1 mcg/kg per minute infusion <i>iv</i> , KET 1 mg/kg <i>iv</i>	REM/KET combination provides faster, more sedoanalgesia and rapid recovery compared with DEX/KET combination
Hashiguchi <i>et al</i> ^[20]	EGD	40	Group D: DEX 6 mcg/kg followed by 0.6 mcg/kg per hour infusion <i>iv</i> , Butylscopolamine 20 mg <i>im</i> , Lidocaine viscous 5 mL gurgling	Group M: MDZ 0.05 mg/kg <i>iv</i> , Butylscopolamine 20 mg <i>im</i> , Lidocaine viscous 5 mL gurgling; Group L: Lidocaine viscous 5 mL gurgling	DEX is as safe and effective as MDZ. DEX significantly reduces blood pressure and heart rate
Saleh <i>et al</i> ^[36]	Esophageal dilatation	60	Group D: DEX 2 mcg/kg followed by 0.4 mcg/kg per hour infusion <i>iv</i> , MDZ 0.05 mg/kg <i>iv</i>	Group P: PRO 1 mg/kg followed by 5 mg/kg per hour infusion <i>iv</i> ; Group K: KET 2 mg/kg and on demand 0.5 mg/kg <i>iv</i> , Atropine 0.02 mg <i>iv</i>	DEX-MDZ combination and KET had more stable cardiorespiratory profiles, with adequate postprocedural analgesia
Ayazoglu <i>et al</i> ^[37]	Colonoscopy	121	DEX 0.2 mcg/kg <i>iv</i> , PRO 0.5-3 mg/kg per hour infusion <i>iv</i>	Group 1: SUF 0.1 mcg/kg <i>in</i> , PRO 0.5-3 mg/kg per hour infusion <i>iv</i> ; Group 2: MEP 0.4 mg/kg <i>iv</i> , PRO 1 mg/kg bolus followed by 0.5-3 mg/kg per hour infusion <i>iv</i> ; Group 3: MEP 0.4 mg/kg <i>iv</i> , MDZ 0.03 mg/kg <i>iv</i> , PRO 0.5-3 mg/kg per hour infusion <i>iv</i>	Sedation for colonoscopy can be safely and effectively utilized with low doses of PRO combined with DEX, in SUF, <i>iv</i> MEP and <i>iv</i> MEP with MDZ
Techanivate <i>et al</i> ^[36]	Colonoscopy	70	DEX 1 mcg/kg <i>iv</i> , FEN 0.5 mcg/kg <i>iv</i> , PRO 20 mg and on demand 20 mg <i>iv</i>	FEN 0.5 mcg/kg <i>iv</i> , PRO 1 mg/kg and on demand 20 mg <i>iv</i>	DEX for sedation in colonoscopy reduced hypotension incidence than PRO
Dere <i>et al</i> ^[34]	Colonoscopy	60	DEX 1 mcg/kg followed by 0.5 mcg/kg per hour infusion <i>iv</i> , FEN 1 mcg/kg <i>iv</i>	MDZ 0.05 mg/kg <i>iv</i> , FEN 1 mcg/kg <i>iv</i>	DEX provided more hemodynamic stability, higher sedation scores, higher satisfaction scores and lower pain scores
Abdalla <i>et al</i> ^[43]	ERCP	60	DEX 1 mcg/kg followed by 0.5 mcg/kg per hour infusion <i>iv</i> , PRO 5 mg/kg per hour and on demand bolus 0.5 mg/kg <i>iv</i>	KET 1 mg/kg followed by 0.5 mg/kg per hour infusion <i>iv</i> , PRO 5 mg/kg per hour and on demand bolus 0.5 mg/kg <i>iv</i>	DEX-PRO during ERCP showed better hemodynamic stability, less nausea/vomiting and shorter recovery time when compared with KET-PRO combination
¹ Ramkiran <i>et al</i> ^[54]	ERCP	72	DEX 1 mcg/kg followed by 0.5 mcg/kg per hour infusion <i>iv</i> , MDZ 0.05 mg/kg <i>iv</i> , Hyoscine 0.3 mg/kg <i>iv</i> , PRO 0.5-1.5 mg/kg and on demand bolus 20 mg <i>iv</i>	Group K: KET 0.25 mg/kg followed by 5 mcg/kg per minute infusion <i>iv</i> , MDZ 0.05 mg/kg <i>iv</i> , Hyoscine 0.3 mg/kg <i>iv</i> , PRO 0.5-1.5 mg/kg and on demand bolus 20 mg <i>iv</i> ; Group C: normal saline <i>iv</i> , MDZ 0.05 mg/kg <i>iv</i> , Hyoscine 0.3 mg/kg <i>iv</i> , PRO 0.5-1.5 mg/kg and on demand bolus 20 mg <i>iv</i>	Low dose KET with PRO boluses resulted in lesser PRO consumption, with earlier recovery and favorable hemodynamics compared with DEX in outpatient ERCP
Mukhopadhyay <i>et al</i> ^[46]	ERCP	45	DEX 1 mcg/kg followed by 0.5 mcg/kg per hour infusion <i>iv</i> , MDZ 0.5 mg/kg <i>iv</i> , Pentazocine 6 mg <i>iv</i> , KET 25 mg <i>iv</i> , PRO 0.75-1 mg/kg and on demand bolus 10-20 mg <i>iv</i>	Group 1: MDZ 1 mg/kg <i>iv</i> , PRO 0.75-1 mg/kg and on demand bolus 10-20 mg <i>iv</i> ; Group 2: MDZ 0.5 mg/kg <i>iv</i> , Pentazocine 6 mg <i>iv</i> , KET 25 mg <i>iv</i> , PRO 0.75-1 mg/kg and on demand bolus 10-20 mg <i>iv</i>	DEX increased efficacy and safety of sedate-analgesic cocktail. It reduces PRO requirement, more stable level of sedation and increases anesthetist satisfaction

Sethi <i>et al</i> ^[42]	ERCP	60	DEX 1 mcg/kg followed by 0.5 mcg/kg per hour infusion <i>iv</i> , FEN 1 mcg/kg <i>iv</i>	MDZ 0.04 mg/kg and on demand bolus 0.5 mg <i>iv</i> , FEN 1 mcg/kg <i>iv</i>	DEX could be a superior alternative drug to MDZ for conscious sedation in ERCP
¹ Mazanikov <i>et al</i> ^[53]	ERCP	50	DEX 1 mcg/kg followed by 0.7 mcg/kg per hour infusion <i>iv</i> , PCS with PRO and Alfentanil	Group P: Normal saline, PCS with PRO and Alfentanil	DEX alone was insufficient in alcoholics. PCS with PRO and Alfentanil could be recommended
¹ Nagaraj <i>et al</i> ^[51]	ERCP	70	DEX 1 mcg/kg followed by 0.5 mcg/kg per hour infusion <i>iv</i> , FEN 1 mcg/kg <i>iv</i>	PRO 0.5 mg/kg followed by 2 mg/kg per hour infusion <i>iv</i> , FEN 1 mcg/kg <i>iv</i>	PRO/FEN combination provided better overall conditions when compared to DEX/FEN combination

¹Negative result of dexmedetomidine. EGD: Esophagogastroduodenoscopy; ERCP: Endoscopic retrograde cholangiopancreatography; DEX: Dexmedetomidine; MDZ: Midazolam; PRO: Propofol; FEN: Fentanyl; MEP: Meperidine; REM: Remifentanyl; ETO: Etomidate; KET: Ketamine; SUF: Sufentanyl; PCS: Patient controlled sedation.

in the dexmedetomidine group was significantly lesser than in the saline group. There were no significant differences in recovery phase, adverse events and satisfaction between the two groups. The authors concluded that intranasal dexmedetomidine with propofol and alfentanil for PCS presented deeper sedation with significantly fewer use of supplementary sedative agents during the EGD procedure^[31].

Recently, Koksai *et al*^[32] compared the effects of adding dexmedetomidine to ketamine on the safety and efficacy of anesthesia for EGD procedures. They used a loading dose of 0.5 mcg/kg of dexmedetomidine, followed by a continuous infusion of 0.2 mcg/kg per minute and a bolus dose of 1 mg/kg of ketamine compared with a loading dose of 0.5 mcg/kg of remifentanyl, followed by a continuous infusion of 0.1 mcg/kg per minute and a bolus dose of 1 mg/kg of ketamine. Additionally, a bolus dose of 0.5-1 mg/kg of propofol was supplemented if inadequate sedation occurred. The authors concluded that a combination use of dexmedetomidine and ketamine offered lesser efficacy and relatively longer recovery phase than the combination of remifentanyl and ketamine^[32]. This negative result of a combination of dexmedetomidine and ketamine could be due to relatively small dose of dexmedetomidine (Table 1).

COLONOSCOPY

Colonoscopy is the gold standard in the examination and the treatment of the disease of lower gastrointestinal tract. The ideal sedative agent for this procedure should permit a rapid adjustment of the sedation level and should not have any side effects^[33]. Currently, several studies of the use of dexmedetomidine for colonoscopy are published. A previous study compared the effects of dexmedetomidine and midazolam on hemodynamic parameters, efficacy of sedation, satisfaction and recovery scores during colonoscopy. This study confirmed that dexmedetomidine offered more hemodynamic stability, lower pain scores as well as higher sedation and satisfaction scores in colonoscopic procedure^[34].

Sula *et al*^[35] evaluated the efficacy and side effects of dexmedetomidine and propofol. They prospectively studied 231 patients with ASA class I - III underwent colonoscopy. Sedation was accomplished with propofol

1.5 mg/kg and on demand bolus dose of 0.4-0.5 mg/kg (group P) and with dexmedetomidine 1 mcg/kg (group D). Arterial blood pressure, heart rate, respiratory rate, oxygen saturation values as well as the patients' satisfaction and the endoscopists' satisfaction were compared. A decline in the systolic blood pressure occurred in 29 patients (12.5%), 17 patients (58.6%) in the group D and 12 patients (41.4%) in group P. Eleven patients (4.7%) in group P and one patient in group D had a decline in oxygen saturation. All these adverse effects were not clinically significant, and without serious effects. No severe bradycardia was noted. The satisfaction scores in both groups were comparable. The authors suggested that both regimens were safe and effective for sedation during colonoscopic procedure. The use of propofol initiated more desaturation, while the use of dexmedetomidine caused more hypotension^[35].

Another study of the hemodynamic parameters of dexmedetomidine for sedation in colonoscopy was presented. Seventy patients with ASA physical status I - III were randomized into two groups. In group P, the patients were received 0.5 mcg/kg of fentanyl over 5 min, and maintained by 1 mg/kg of propofol. In group D, the patients were received 1 mcg/kg of dexmedetomidine with 0.5 mcg/kg of fentanyl over 5 min, followed by 20 mg of propofol. The 20 mg propofol was titrated as required to achieve the target bispectral index (BIS) and sedation score. The results showed that the incidence of hypotension in group P was significantly higher than in group D. Heart rate in group P was greater than group D at 10th minute and from 25th minute throughout the period of colonoscopy. There were no significant differences in the induction time, incidence of bradycardia, patient satisfaction and postprocedural complications between the two groups. Additionally, the patients in group D recovered from sedation more quickly than in group P^[36].

Several sedation regimens are administered during colonoscopy. To date, the propofol-based sedation regimens are commonly used. The safety, efficacy and patient satisfaction of propofol combined with dexmedetomidine for conscious sedation in the colonoscopy were evaluated by Ayazoğlu *et al*^[37]. The patients in the dexmedetomidine combination with propofol group accomplished a greater degree of sedation and a rapid

recovery activity when compared with the meperidine, sufentanil and midazolam in combination with propofol groups. The authors recommended that sedation for colonoscopy could be effectively and safely done with propofol combined with dexmedetomidine and other sedoanalgesic drugs^[37].

However, the sole use of dexmedetomidine has inadequate utility for sedation during outpatient colonoscopy. For example, the study of Jalowiecki *et al*^[38] showed that dexmedetomidine sedation for colonoscopic procedure was incomplete because of its adverse effects including prolonged recovery and hemodynamic instability. The authors evaluated the capability of dexmedetomidine sedation for 64 patients underwent outpatient colonoscopic procedures. In group D, patients received 1 mcg/kg of dexmedetomidine over 15 min and maintained by an infusion of 0.2 mcg/kg per hour. Group P received 1 mg/kg of meperidine and 0.05 mg/kg of midazolam. Group F, patients received 0.1-0.2 mg of fentanyl *iv* on demand. The study was terminated because of adverse effects in group D. There was a significantly greater reduction in heart rate and arterial blood pressure in group D. In group D, additional fentanyl was needed in 47% of patients compared with 42.8% and 79.2% of patients in group P and F, respectively. Nausea/vomiting, vertigo and ventricular arrhythmia were noted only in group D. In addition, group D had the longest time to home readiness^[38]. This limited utility of dexmedetomidine for sedation during outpatient colonoscopy might be due to a relatively low dose during the procedure and inadequate analgesia (Table 2).

ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

Endoscopic retrograde cholangiopancreatography (ERCP) is a routinely carried out diagnostic and/or therapeutic procedure of many pancreatic and biliary diseases. It is a distressing procedure in awaked patients. These patients require sedation/anesthesia mainly to minimize their anxiety and analgesics to lessen pain and discomfort thereby enhancing patient's cooperation throughout the procedure^[39].

Kilic *et al*^[40] presented the use of dexmedetomidine for sedation during ERCP procedure. The efficacy, hemodynamic parameters and adverse effects were compared between dexmedetomidine and midazolam^[40]. Fifty patients aged 18-80 years were randomized into two groups. Group M, patients received a bolus infusion of 0.04 mg/kg of midazolam, and followed by a supplementary dose of 0.5 mg midazolam. Group D, patients received a bolus infusion of 1 mcg/kg per hour of dexmedetomidine over 10 min, and maintained by a continuous infusion of 0.2-0.7 mcg/kg per hour. All patients were sedated to target a Ramsay scale of 3-4. Heart rate in group D was significantly lesser than group M. In addition, the dexmedetomidine group also

showed higher endoscopist satisfaction scores^[40].

Furthermore, Ceylan *et al*^[41] evaluated the effects of propofol and dexmedetomidine hemodynamics, adverse effects, cognitive functions, and satisfaction during ERCP procedure. The fifty patients with ASA physical status class I and II were randomized into the two groups. Group P received propofol 75 mcg/kg per hour *iv* over 10 min, and followed by an infusion of 12.5-100.0 mcg/kg per minute. Group D received dexmedetomidine 1 mcg/kg per hour over 10 min, and maintained by an infusion of 0.2-0.7 mcg/kg per hour. All patients were sedated to attain a RSS of 3-4. The mental status examination before and after the procedure as well as pain was evaluated. The blood pressure and heart rate values in group D were significantly lesser than in group P. However, there were no significant differences in patient and endoscopist satisfaction among the two groups^[41].

Dexmedetomidine has been tried for various endoscopic procedures, and the evidence occurs to recommend its use for ERCP procedure. A randomized controlled study was planned to evaluate the hemodynamic and the recovery profiles of dexmedetomidine and midazolam. It was also to assess the grade of comfort and the procedural performance. All patients received 1 mcg/kg of fentanyl at the start of ERCP. Group M received a bolus dose of 0.04 mg/kg of midazolam and supplementary 0.5 mg doses. Group D received a bolus dose of 1 mcg/kg of dexmedetomidine at over 10 min and maintained by a continuous infusion of 0.5 mcg/kg per hour. The targeted depth of sedation was a RSS score 3-4. The heart rate, blood pressure, respiratory rate, oxygen saturation, the time to accomplish the targeted depth of sedation and pain score were evaluated and compared during and after the ERCP procedure. Heart rate and pain scores in group D were significantly lower than in group M. There were no significant differences in mean blood pressure and respiratory rate. The modified Aldrete score of 9-10 at 5 min during recovery was achieved in 27 (90%) patients in group D in contrast to 5 (17%) patients in group M ($P < 0.05$). Dexmedetomidine also showed higher patient and endoscopist satisfaction scores ($P < 0.05$)^[42].

The efficacy of dexmedetomidine for anesthesia in ERCP procedure was evaluated by Abdalla *et al*^[43]. Sixty patients with ASA physical status class II or III underwent ERCP procedures were randomly assigned into two groups. Group D, patients received a bolus dose of dexmedetomidine 1 mcg/kg and maintained by 0.5 mcg/kg per hour. Group K, patients received a loading dose of ketamine 1 mg/kg and followed by 0.5 mg/kg per hour. Propofol was used for induction of anesthesia and atracurium was utilized for endotracheal intubation. After that, anesthesia was maintained by continuous infusion of propofol. The combination of dexmedetomidine and propofol during ERCP procedure showed better hemodynamic stability, less nausea and vomiting, as well as shorter recovery time when compared with the combination of ketamine and

Table 2 The use of dexmedetomidine in a single agent technique for gastrointestinal endoscopic procedures

Ref.	Type of endoscopy	No. of patients	DEX group	Non-DEX group	Summary of findings
Samson <i>et al</i> ^[21]	EGD	90	DEX 1 mcg/kg followed by 0.5 mcg/kg per hour infusion <i>iv</i>	MDZ 0.04 mg/kg followed by an additional dose of 0.5 mg <i>iv</i>	Endoscopist satisfaction and recovery in DEX group was significantly better than in MDZ and PRO groups
Jiang <i>et al</i> ^[23]	EGD	40	DEX 0.8 mcg/kg <i>iv</i>	PRO 2.5 mg/kg <i>iv</i>	DEX could yield marked sedative effect, had antihypertensive effect and did not suppress respiration
Demiraran <i>et al</i> ^[22]	EGD	50	DEX 1 mcg/kg followed by 0.2 mcg/kg per hour infusion <i>iv</i>	MDZ 0.07 mg/kg (total dose 5 mg) <i>iv</i>	DEX was superior to MDZ with regard to retching, rate of adverse events and endoscopist satisfaction for EGD sedation
Sula <i>et al</i> ^[35]	Colonoscopy	231	DEX 1 mcg/kg <i>iv</i>	PRO 1.5 mg/kg and on demand bolus 0.4-0.5 mg/kg <i>iv</i>	Both regimens were effective and safe for sedation. PRO caused more desaturation, while DEX caused more hypotension
¹ Jalowiecki <i>et al</i> ^[38]	Colonoscopy	64	Group D: DEX 1 mcg/kg followed by 0.2 mcg/kg per hour infusion <i>iv</i>	Group P: 1 mg/kg of MEP with 0.05 mg/kg of MDZ <i>iv</i> , Group F: 0.1-0.2 mg of FEN <i>iv</i> on demand	There was a significantly greater decrease in heart rate and blood pressure in group D. Time to home readiness was the longest in group D
¹ Eldesuky Ali Hassan <i>et al</i> ^[48]	ERCP	50	Group D: DEX 1 mcg/kg followed by 0.5 mcg/kg per hour infusion <i>iv</i>	Group K: ketofol 1 mg/kg <i>iv</i> bolus followed by 50 mcg/kg per minute infusion <i>iv</i>	Time to achieve sedation score and total dose of rescue sedation were not significantly different. Patient and endoscopist satisfaction in group K was significantly higher than in group D
Kilic <i>et al</i> ^[40]	ERCP	50	Group D: DEX 1 mcg/kg followed by 0.2-0.7 mcg/kg per hour infusion <i>iv</i>	Group M: MDZ 0.04 mg/kg followed by an additional dose of 0.5 mg <i>iv</i>	DEX showed higher endoscopist satisfaction. Coughing, nausea and vomiting were observed in three patients in group M, but no patients in group D
Ceylan <i>et al</i> ^[41]	ERCP	50	Group D: DEX 1 mcg/kg followed by 0.2-0.7 mcg/kg per hour infusion <i>iv</i>	Group P: PRO 75 mcg/kg per hour followed by 12.5-100.0 mcg/kg per minute infusion <i>iv</i>	Blood pressure and heart rate values in group D were significantly lower than in group P. There were no significant differences in patient and endoscopist satisfaction
¹ Muller <i>et al</i> ^[52]	ERCP	26	Group D: DEX 1 mcg/kg followed by 0.2-0.5 mcg/kg per hour infusion <i>iv</i>	Group P: PRO (target plasma concentration 2-4 mcg/mL) with FEN 1 mcg/kg <i>iv</i>	DEX alone was not as effective as PRO combined with FEN. DEX was associated with greater hemodynamic instability and a prolonged recovery period
Eberl <i>et al</i> ^[55]	Esophageal intervention	64	DEX 1 mcg/kg (0.5 mcg/kg in age > 65) followed by 0.7-1 mcg/kg per hour infusion <i>iv</i>	PRO Target Controlled Infusion (OAAS scale ≤ 4)	DEX was a new representative for endoscopic sedation. The acceptance level after PRO was relatively high compared with DEX
Takimoto <i>et al</i> ^[58]	ESD	90	Group D: DEX 3 mcg/kg followed by 0.4 mcg/kg per hour infusion <i>iv</i>	Group P: PRO 5 mg bolus and 3 mg/kg per hour infusion <i>iv</i> , Group M: MDZ 0.1 mg/kg <i>iv</i>	DEX was effective and safe for patients with gastric tumors who underwent ESD

¹Negative result of dexmedetomidine. EGD: Esophagogastroduodenoscopy; ERCP: Endoscopic retrograde cholangiopancreatography; DEX: Dexmedetomidine; MDZ: Midazolam; PRO: Propofol; FEN: Fentanyl; MEP: Meperidine; REM: Remifentanyl; ETO: Etomidate; KET: Ketamine; SUF: Sufentanil; PCS: Patient controlled sedation.

propofol^[43].

Moreover, Han-wei *et al*^[44] observed the safety and feasibility of dexmedetomidine and fentanyl for conscious sedation in the ERCP procedure. Sixty patients of ASA class I - II who planned to receive ERCP were allocated into dexmedetomidine group and propofol group. The patients in the two groups were treated with anisodamine 10.0 mg and fentanyl 1.0 mcg/kg before ERCP. The patients in dexmedetomidine group were treated with dexmedetomidine 0.5 mcg/kg by injection

within 15 min, then the dexmedetomidine was infused continuously at the rate of 0.5-1.0 mcg/kg per hour to the end of operation. Patients in the propofol group were treated with propofol 1.0 mg/kg in 2 min, and followed by continuous infusion of 4.0-6.0 mg/kg per hour to the end of operation. Arterial blood pressure, heart rate and oxygen saturation were noted at the time points of before anesthesia (T0), before inserting endoscope (T1), while inserting endoscope (T2), 20 min after inserting endoscope (T3) and 10 min after the

end of examination (T4). The intubation process and cooperation of patients were scored; and the patients' satisfaction for examination was evaluated next day. In dexmedetomidine group, heart rate of patients at the time points of T1, T2, T3 and T4 was significantly lower than that at the time point of T0; but there was no significant difference in the systolic and diastolic blood pressure among the time points of T0, T1, T2, T3 and T4. There was no significant difference in the oxygen saturation all time points in the two groups. The heart rate at the time points of T1, T2, T3 and T4 in the propofol group was significantly higher than that in the dexmedetomidine group. The score of intubation process and cooperation of patients in the dexmedetomidine group was significantly higher than that in the propofol group. However, patient satisfaction in both groups was not significantly different. The authors concluded that dexmedetomidine and fentanyl for conscious sedation in ERCP procedure was safe and feasible, which could meet the test needed of sedation, and could obtain better cooperation of the patients^[44].

Generally, the combination regimens are commonly used for invasive procedures. Dexmedetomidine may employ a synergistic effect in the combination with sedoanalgesic drugs. Lee and coworkers evaluated the efficacy and adverse effects of midazolam-meperidine-dexmedetomidine (MMD) and midazolam-meperidine (MM) for ERCP procedure in 110 patients. Lower additional and total doses of midazolam were needed in group MMD. Oxygen desaturation and pain scores in group MMD were significantly lesser than in group MM. In addition, the satisfaction scores in group MMD were significantly greater than group MM. The authors recommended that the combination of dexmedetomidine, midazolam and meperidine regimen presented superior sedative efficacy and a greater safety profile during ERCP procedure compared with the combination of midazolam and meperidine regimen^[45]. Recently, Mukhopadhyay *et al*^[46] assess the safety and efficacy of dexmedetomidine as an add-on for deep sedation in prolonged ERCP procedure. The authors concluded that the addition of dexmedetomidine in sedoanalgesic cocktail increased the safety and efficacy of deep sedation^[46].

Ketofol, a combination of ketamine and propofol, is significant interest as an agent for procedural sedation. This combination regimen has several advantages in the terms of hemodynamic stability, lack of respiratory depression, post-operative analgesia and recovery^[47]. Recently, a double-blind randomized study is carried out to evaluate two techniques of moderate sedation for patients undergoing ERCP procedure, using either dexmedetomidine or ketofol as regards hemodynamic, sedation, respiratory effect, pain, recovery time, patient and endoscopist satisfaction as well as the complications. Fifty patients were randomly assigned in the two groups; dexmedetomidine received 1 mcg/kg *iv* bolus over 10 min followed by 0.5 mcg/kg per hour or ketofol received 1 mg/kg *iv* bolus and maintained by 50

mcg/kg per minute. Mean arterial pressure and heart rate in the dexmedetomidine group were significantly lesser than in the ketofol group. Additionally, time to achieve RSS score and total dose of rescue sedation in both groups were not significantly different. However, patient and endoscopist satisfaction in the ketofol group was significantly higher than in the dexmedetomidine group^[48] (Table 2). The advantage of ketofol in this study may be due to design of the study. The depth of sedation level was targeted to attain a RSS score of 4. The combination use of ketamine and propofol offered better outcome variables than the use of dexmedetomidine alone.

Several case studies also have been reported the efficacy of dexmedetomidine for procedural sedation in the difficult patients. For example, Srivastava *et al*^[49] reported a 65-year-old female presented with anorexia, vomiting and yellowish discoloration of skin for 3 mo. The patient was diagnosed as extrahepatic cholangiocarcinoma with extrahepatic biliary obstruction type 3 and was advised surgical resection of tumor. The patient had history of dyspnea on mild exertion (New York Heart Association III), left bundle branch block, and cardiomegaly. The transthoracic echocardiography demonstrated dilated left ventricle, global hypokinesia, ejection fraction 25%, moderate pulmonary artery hypertension. However, the patient refused for surgery owing to increased cardiac risk. The patient was advised endoscopic placement of stents to drain the biliary system for symptomatic relief. Monitored anesthesia care with light sedation was required for this procedure. She was induced with 1 mcg/kg of dexmedetomidine over 20 min and then continuous infusion was titrated between 0.2 and 0.5 mcg/kg per hour to keep blood pressure and HR within 10% of baseline. Mean HR during procedure was 74 ± 10 beats/min, and mean blood pressure was 80 ± 15 mmHg. The total procedure time was 40 min. The patient was oxygenated throughout the procedure until recovery from sedation by face mask. The SpO₂ was never below 98%. The recovery time was 30 min^[49].

Ko *et al*^[50] presented a 10-year-old boy, 29 kg with obstructive jaundice and a distal common bile duct stone. Five days before, ERCP sedation performed by a gastroenterologist was failed. Non-invasive blood pressure, electrocardiography, SpO₂, BIS values and Observer's Assessment of Alertness/Sedation scores were monitored. In this second sedation, a dose of 0.5 mg/kg of ketamine and 0.5 mcg/kg of fentanyl were given before the procedure. Additionally, a bolus dose of 0.7 mcg/kg of dexmedetomidine was given over 10 min followed by a continuous infusion of 0.5 mcg/kg per hour. The oxygen saturation decreased to 85% for a second. However, oxygen saturation recovered to 100% when the scope was inserted. Oxygen supplementation was administered and a child breathed spontaneously. This procedure was successfully completed with minimal decreases in blood pressure and heart rate. After the procedure, dexmedetomidine infusion was stopped.

The patient did not report of postprocedural nausea and vomiting and did not present emergence agitation or delirium^[50].

However, the negative results of the use of dexmedetomidine for ERCP procedure have been occurred (Table 2). For example, the study of Nagaraj *et al*^[51] compared the combination of dexmedetomidine and fentanyl with the combination of propofol and fentanyl for procedural sedation in ERCP procedure. In the dexmedetomidine group, patients received fentanyl 1 mcg/kg and a bolus dose of dexmedetomidine 1 mcg/kg over 10 min followed by a maintenance dose of 0.5 mcg/kg per hour intravenously. In the propofol group, the patients received fentanyl 1 mcg/kg and a loading dose of propofol infused at 0.5 mg/kg over 10 min followed by a maintenance dose of 2 mg/kg per hour intravenously. The study showed that the combination of propofol and fentanyl achieved better overall conditions for ERCP compared to the combination of dexmedetomidine and fentanyl^[51].

Generally, deep sedation is utilized for invasive GIE procedures including ERCP. A combination of two or more sedative drugs produces a synergistic effect and is commonly used for deep sedation technique. Another negative result of the use of dexmedetomidine alone was published by Muller *et al*^[52]. They conducted a randomized, double blind, study to test the hypothesis that dexmedetomidine was as effective as propofol combined with fentanyl for sedation during an ERCP procedure. Twenty-six patients with ASA physical status class I to III were randomly assigned to receive either propofol combined with fentanyl 1 mcg/kg, or dexmedetomidine 1 mcg/kg in 10 min, followed by 0.2 to 0.5 mcg/kg per minute. Supplementary sedative drugs were added if an inadequate sedation was not attained. Heart rate, blood pressure, respiratory rate and oxygen saturation were continuously monitored. The result of the study proved that dexmedetomidine alone was not as effective as a combination of propofol and fentanyl for sedation during ERCP procedure. Moreover, dexmedetomidine was related with lesser hemodynamic stability and prolonged recovery period^[52].

Similarly, the use of dexmedetomidine alone for sedation in the alcoholic patients is also inadequate (Table 1). This outcome was confirmed by the study of Mazanikov *et al*^[53]. They assessed the suitability of dexmedetomidine for sedation of the alcoholic patients during ERCP procedure. Fifty patients with chronic alcoholism underwent elective ERCP procedure were randomly assigned to receive dexmedetomidine (group D) (a bolus dose of 1 mcg/kg in 10 min, followed by continuous intravenous infusion 0.7 mcg/kg per hour) or normal saline (group P). Additionally, PCS with propofol and alfentanil was used by patients as a rescue method. Sedation was considered as successful if no intervention of an anesthesiologist was needed. Consumption of sedatives was registered, and sedation levels and vital signs were monitored. The result of the study indicated that the use of dexmedetomidine

alone was insufficient in all alcoholic patients. The mean consumption of propofol was 159 ± 72 mg in group P, and 116 ± 61 mg in group D ($P = 0.028$). Sedation was successful in 19 of 25 (76%) patients in group D and all patients in group P ($P = 0.022$). The incidence of sedation-related adverse events in both groups was comparable. However, dexmedetomidine was associated with delayed recovery. They suggested that PCS with propofol and alfentanil but not dexmedetomidine could be recommended for sedation of the alcoholic patients during ERCP procedure^[53]. Additionally, a negative result of the use of dexmedetomidine was also reported by Ramkiran *et al*^[54]. The report showed that the use of dexmedetomidine presented in greater propofol consumption, with delayed recovery and unfavorable hemodynamic profiles when compared with a combination of low dose ketamine and propofol in outpatient ERCP procedure^[54].

ESOPHAGEAL INTERVENTION

Early neoplastic lesions in esophagus could be treated by endoscopic intervention has evolved as a valid. These esophageal interventions are minimal invasive treatment options alternative to the surgical operations. The safety and effectiveness of dexmedetomidine sedation for endoscopic esophageal interventions was observed in the study of Eberl *et al*^[55]. The 64 patients were randomly allocated to the propofol and the dexmedetomidine groups. The effectiveness of sedation was the primary outcome of the study. Respiratory and hemodynamic complications were the secondary outcome variables. The authors suggested that dexmedetomidine was a new representative for endoscopic sedation. However, the sedation efficacy in the propofol group was relatively high compared with the dexmedetomidine group^[55].

To date, esophageal strictures after accidental ingestion of a corrosive substance are still clinical problems and the esophageal dilatation sessions are frequently required. The use of dexmedetomidine for these esophageal interventions in children is perceived. The combination of dexmedetomidine and the sedoanalgesic agents was used to evaluate the safety, efficacy, recovery profiles and hemodynamic parameters with those of the combination of propofol and ketamine in pediatric patients underwent endoscopic esophageal balloon dilatation^[56]. The study verified that the combination of dexmedetomidine, ketamine and midazolam had relatively more hemodynamic and respiratory stabilities, with adequate postprocedural analgesia. However, the use of ketamine alone had quicker onset and rapid recovery of sedation than the combination of dexmedetomidine and midazolam^[56].

ENDOSCOPIC SUBMUCOSAL DISSECTION

Endoscopic submucosal dissection (ESD) is an endos-

copic treatment of early gastric cancer. It has been extensively accepted. However, ESD is correlated with a longer procedure time and a higher risk of patient distress than the conventional endoscopic procedures. An acceptable and safe sedation is necessary. A combination of benzodiazepines and analgesics are usually utilized for sedation, but a new sedative agent such as dexmedetomidine is estimated to be a useful agent^[57].

Takimoto and coworkers conducted a randomized study of dexmedetomidine sedation in 90 patients with gastric tumors underwent the ESD procedure. All patients were sedated either with dexmedetomidine (a bolus of 3.0 mcg/kg per hour in 5 min followed by a continuous infusion of 0.4 mcg/kg per hour), propofol, or midazolam. The resection of gastric tumor was completed in 88 (98%) patients. No patients in the dexmedetomidine group demonstrated a significant decrease of the oxygen saturation level. This study proved that sedation with dexmedetomidine was safe and effective for patients with gastric tumors who underwent ESD procedure^[58].

Ishibashi *et al*^[59] assessed the efficacy and safety of sedation with dexmedetomidine in the intubated spontaneously breathing patients after ESD procedure for pharyngeal or esophageal cancer. The 55 patients with ASA class I or II who underwent ESD under general anesthesia and who were remained intubated until the next day in the ICU receiving sedation with dexmedetomidine. A continuous infusion of dexmedetomidine at 0.4-0.7 mcg/kg per hour was administered during procedure and continued in the ICU until extubation. Hemodynamic and respiratory parameters as well as the Richmond Agitation Sedation Scale (RASS) scores were noted. The 39 patients in group G were remained well sedated (RASS < 1). The 16 patients were poorly sedated (RASS ≥ 1 at any time-point) were in group P. Hemodynamic and respiratory variables in the ICU were not significantly different between the two groups. The requirements of rescue sedatives and analgesics in group P were significantly higher than in group G. The authors concluded that sedation with dexmedetomidine in the intubated spontaneously breathing patients after ESD was safe and effective. The higher plasma concentration of dexmedetomidine at the time of entrance into the ICU was associated with better sedation and less analgesic requirements^[59].

The combination of dexmedetomidine and propofol for the ESD procedure is also safe and effective. Forty patients with ASA physical status class I or II underwent ESD were randomized into two groups. Group A was given propofol alone. Group B was given intravenously dexmedetomidine followed by propofol. The study demonstrated that the use dexmedetomidine combined with propofol and propofol alone were no significant differences in the respiratory rate, oxygen saturation, operative time and anesthetic effect. This study confirmed that anesthetic effect of dexmedetomidine combined with propofol for patients underwent ESD procedure was satisfactory and safe^[60].

The ESD procedure of colorectal tumor is withstanding. However, this is a technical difficulty procedure. Takimoto *et al*^[61] examined the efficacy and safety of dexmedetomidine sedation for ESD procedure. The 210 patients underwent the colorectal ESD were categorized into group A (continuous infusion of dexmedetomidine at 0.2 mcg/kg per hour) and group B (no administration of dexmedetomidine). A reduced blood pressure and heart rate or a decrease of oxygen saturation was not observed. The endoscopic treatment was succeeded in 100% and 82% of the patients in group A and B, respectively. The authors suggested that the use of dexmedetomidine reduced the requirement for a rescue medication and eased an endoscopic treatment. Consequently, a combination use of dexmedetomidine might establish as an effective and safe technique for the colorectal ESD^[61].

Moreover, dexmedetomidine suppresses gastric motility. The use of dexmedetomidine during ESD procedure should be useful. The study of Kim *et al*^[62] evaluated the safety and efficacy of the combination of dexmedetomidine and remifentanyl with the combination of propofol and remifentanyl for ESD procedure. Although, the efficacy and safety of these two groups were comparable, the endoscopists favored dexmedetomidine because of its action^[62].

The patients with severe chronic obstructive pulmonary disease (COPD) have validated an increased risk for oxygen desaturation following the general anesthesia. The use of dexmedetomidine sedation is one of the appropriate methods for management of the COPD patients^[63]. Iizuka *et al*^[63] reported an anesthetic management of a 74-year-old man with severe COPD and gastric cancer underwent ESD procedure. They used dexmedetomidine under monitored anesthesia care and the patient spontaneously breathed during the procedure. The ESD procedure took 5.5 h with satisfactory analgesia, and no airway management was needed. The patient accepted the procedure and recovered well with no adverse events. Finally, the patient was discharged on the fifth postprocedural day^[63].

SMALL BOWEL ENTEROSCOPY

Currently, small bowel enteroscopy is the standard method for diagnosis and treatment of small bowel abnormalities. It is a long and invasive endoscopic procedure. Anesthesia/sedation is regularly used for this endoscopy procedure^[64]. The safety and efficacy of dexmedetomidine used in this procedure were investigated by the study of Sun *et al*^[65]. Thirty patients with ASA physical status class I or II, planned for single balloon enteroscopy were randomly assigned into two groups: Group D (intravenous perfusion of dexmedetomidine 0.6 mcg/kg), and group C (normal saline of equal volume with dexmedetomidine). Group D and group C respectively received dexmedetomidine and normal saline before induction by *iv* infusion in

10 min. Then general anesthesia was induced with propofol, fentanyl and vecuronium. The maintenance of anesthesia was used by propofol in both groups. The study summarized that the use of dexmedetomidine 0.6 mcg/kg for 10 min before induction presented more stable during the period of induction. It also reduced the doses of propofol in the period of induction and operation. Dexmedetomidine could make the patient hemodynamics more stable and the recovery more rapid and complete^[65].

To date, there is a wide variability of the efficacy of the use of dexmedetomidine in various GIE procedures. Several reports have been demonstrated the positive results. However, some studies did not confirm the benefits of dexmedetomidine for GIE procedures. The author also summarizes these in the two tables. Table 2 shows the use of dexmedetomidine in a single agent technique for GIE procedures including the positive and negative results. In addition, Table 1 lists the use of dexmedetomidine in a combination technique for GIE procedures including the positive and negative results.

CONCLUSION

Several sedative and analgesic drugs are commonly used in the GIE procedures. Their safety profile is dependent on their pharmacokinetic and pharmacodynamic profiles, the patient medical condition and the experience of the physician using them. Dexmedetomidine has analgesic, amnesic, sedative and anxiolytic properties. The use of dexmedetomidine as the sole anesthetic agent and as the adjuvant anesthetic agent in various GIE procedures has been published. A distinct advantage of dexmedetomidine is the maintenance of respiratory force and preserved airway patency even in the existence of rising sedation. These properties of dexmedetomidine have verified to be beneficial in high-risk patients such as the patients with OSA and COPD patients as well as the patients with extensive tracheomalacia. However, it can produce bradycardia and hypotension. Additionally, the negative results of dexmedetomidine for some GIE procedures have been happened. Therefore, further clinical investigations should to be done.

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