A comparison of efficacy and safety of sedation between dexmedetomidine-remifentanil and propofol-remifentanil during endoscopic submucosal dissection

Namo Kim

Department of Medicine

The Graduate School, Yonsei University

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Directed by Professor Kyeong Tae Min

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Namo Kim

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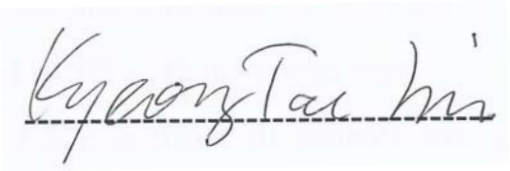
This certifies that the Master's Thesis

of Namo Kim is approved.



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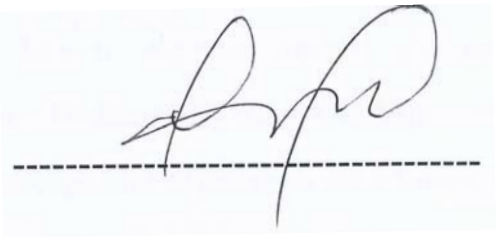

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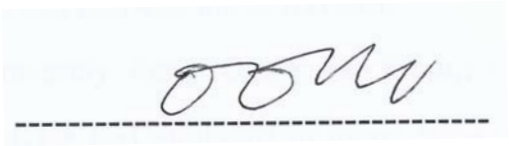

Sang Kil Lee

The Graduate School

Yonsei University

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ABSTRACT

A comparison of efficacy and safety of sedation between dexmedetomidine-remifentanil and propofol-remifentanil during endoscopic submucosal dissection

Namo Kim

Department of Medicine

The Graduate School, Yonsei University

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Introduction: Endoscopic submucosal dissection (ESD) requires adequate sedation and pain control, for which the short acting drugs such as propofol and remifentanil are recommended. Dexmedetomidine has sedative and analgesic effects and suppresses gastrointestinal motility, which might be critical during ESD. We compared the efficacy and safety of sedation between dexmedetomidine-remifentanil and propofol-remifentanil for use during ESD.

Method: Fifty-nine patients scheduled for ESD were randomly

allocated into a dexmedetomidine-remifentanil (DR) group or a propofol-remifentanil (PR) group. To control patient anxiety, dexmedetomidine or propofol was infused to maintain a score of 4–5 on the Modified Observer's Assessment of Alertness/Sedation scale. Remifentanil was infused continuously at a rate of 6 μg/h/kg in both groups. The ease of advancing the scope into the throat, gastric motility grading, and satisfaction of the endoscopist and patient were assessed. Hemodynamic variables and hypoxemic events were compared to evaluate patient safety.

Results: Demographic data were comparable between the groups. The hemodynamic variables and pulse oximetry values were stable during the procedure in both groups despite a lower heart rate in the DR group. No desaturation events occurred in either group. Although advancing the scope into the throat was easier in the PR group ("very easy" 24.1% vs. 56.7%, P = 0.01), gastric motility was more suppressed in the DR group ("no + mild" 96.6% vs. 73.3%, P = 0.013). The endoscopists felt that the procedure was more favorable in the DR group ("very good + good" 100% vs. 86.7%, P = 0.042), whereas patient satisfaction scores were comparable between the groups.

Conclusions: The efficacy and safety of dexmedetomidine and remifentanil were comparable to propofol and remifentanil during ESD. However, endoscopists favored dexmedetomidine perhaps due to lower gastric motility.

Key words: dexmedetomidine, efficacy, safety, peristalsis, endoscopic submucosal dissection

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Namo Kim

Department of Medicine

The Graduate School, Yonsei University

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I. INTRODUCTION

Endoscopic submucosal dissection (ESD) is associated with greater and longer patient discomfort and pain than conventional endoscopic procedures. It is essential to address this issue with ESD[1]. Propofol has been widely used for endoscopic procedures[2], as it is safe and effective[3], and is associated with shorter recovery time and better sedation and amnesia level without an

increased risk for cardiopulmonary complications[4] than other traditional sedatives. However, in addition to the dose-dependent respiratory depression of propofol, aspiration pneumonia occurs with an incidence of 2.3% following ESD[5]. Moreover, it is difficult to control sedation depth with propofol[6]; however, its use in combination with other analgesics can offset these complications by reducing the dose of propofol[7].

Dexmedetomidine, a selective α_2-adrenoceptor agonist with sedative and analgesic effects, has been successfully used during colonoscopy[8] and ESD[9]. Dexmedetomidine suppresses gastrointestinal motility and inhibits gastric emptying in healthy volunteers[10] whereas propofol does not[11]. Suppressing gastric motility may be crucial for successful ESD.

In this study, we compared the procedural efficacy and patient safety of the use of dexmedetomidine-remifentanil versus propofol-remifentanil during ESD.

II. MATERIALS AND METHODS

1. Patient and sedation protocol

This study was approved by the Institutional Review Board of Severance Hospital, Yonsei University Health System (ref: 4-2012-0621) and was

registered at http://ClinicalTrials.gov (ref: NCT01920113). Written informed consent was obtained from all patients before the procedure. Sixty patients aged > 20 years belonging to American Society of Anesthesiology classification I–III and scheduled for ESD were enrolled in this prospective, randomized, and endoscopist-blind study from September 2012 to January 2013. Patients with end-organ diseases (i.e., heart failure, respiratory failure, hepatic failure, or renal failure), known drug allergies, or a history of drug abuse were excluded.

The patients were randomly assigned to the dexmedetomidine-remifentanil group (DR group, n = 30) or the propofol-remifentanil (PR group, n = 30) group using a random number table provided by www.random.org. Among the 60 patients, data for 59 patients (29 patients in the DR group and 30 patients in the PR group) were analyzed because surgical removal was considered in one patient.

Both the endoscopists and patients were blinded to the sedation protocol. None of the patients were pre-medicated. The level of sedation in both groups was targeted to a score of 4–5 on the Modified Observer's Assessment of Alertness/Sedation scale (MOAA/S, Table 1) for minimal sedation during the entire procedure. For the DR group, a bolus dose of 0.5 μg/kg dexmedetomidine (Precedex®, Abbott, Istanbul, Turkey) was injected

intravenously for 5 min before starting the procedure. Thereafter, a continuous infusion dose of 0.3–0.7 μg/h/kg was given. For the PR group, a bolus injection of 0.5 mg/kg propofol was followed by continuous infusion at a rate of 30 μg/min/kg (Pofol®, Dongkook Pharm. Co. Ltd., Seoul, Korea) using an infusion pump (Syringe Pump TE-331, Terumo, Tokyo, Japan). In both groups, remifentanil (Ultiva®, GlaxoSmithKline, Co. Ltd., Genval, Belgium) was infused continuously at the rate of 6 μg/h/kg beginning 5 min before commencing the procedure.

We monitored the MOAA/S scale score continuously. If the score was 6 or the patient wanted deeper sedation, a bolus of 10 mg propofol was administered. If the patient complained of pain during the procedure, 0.1 μg/kg remifentanil bolus was administered, and its infusion rate was increased by 0.5 μg/h/kg.

TABLE 1. Modified Observer's Assessment of Alertness/Sedation (MOAA/S)

Alertness/Sedation level	Description
6	Agitated
5	Respond readily to name spoken in normal tone (alert)
4	Lethargic response to name spoken in normal tone
3	Responds only after name is called loudly, repeatedly, or both
2	Responds only after mild prodding or shaking
1	Does not respond to mild prodding or shaking
0	Does not respond to deep stimulus (asleep)

Hartman's solution was administered at a rate of 3–5 mL/kg/h, and 2 L/min oxygen was given through a nasal cannula.

Oxygen saturation (SpO_2), systolic and diastolic blood pressure (SBP and DBP), electrocardiogram (ECG), and heart rate (HR) were monitored continuously and recorded at 5-min intervals.

The MOAA/S scale score was recorded as follows: just before the procedure (baseline, T0); 1 min after induction of sedation (1 min after a 5 min loading of dexmedetomidine in the DR group and 1 min after the propofol bolus injection in the PR group, T1); as the endoscope was passed into the esophagus (T2); as the tumor margin was marked by argon plasma coagulation (T3); 5 min after normal saline containing epinephrine (0.01 mg/mL) injection was given in the gastric submucosa (T4); at dissection of the gastric tumor region from the gastric submucosa (T5); once bleeding control was performed at the gastric bed after dissection (T6); and at the end of the procedure (T7).

Butylscopolamine (20 mg) was administered to suppress gastric motility during the procedure at the request of the endoscopist.

The discharge Aldrete score (Table 2) was recorded to document the patient's general status at the end of the procedure.

All patients were observed in the post-anesthetic care unit (PACU) until their discharge Aldrete score reached 10.

TABLE 2. Modified Aldrete scoring system

Discharge criteria	**Score**
Activity: Able to move voluntarily or on command	
Four extremities	2
Two extremities	1
Zero extremities	0
Respiration	
Able to deep breathe and cough freely	2
Dyspnea, shallow or limited breathing	1
Apneic	0
Circulation	
Blood pressure ± 20 mmHg of preanaesthetic level	2
Blood pressure ± 20 - 50 mmHg preanaesthesia level	1
Blood pressure ± 50 mmHg of preanaesthesia level	0
Consciousness	
Fully awake	2
Arousable on calling	1
Not responding	0
O_2 saturation	
Able to maintain O_2 saturation > 92% on room air	2
Needs O_2 inhalation to maintain O_2 saturation >90%	1
O_2 saturation < 90% even with O_2 supplementation	0

From Aldrete JA. The post anaesthesia recovery score revisited. J Clin Anesth 1995;7:89 – 91

2. Methods

가. Assessment of procedural performance

The ease of advancing the scope through the throat (four grades: very easy, easy, slight difficulty, and difficult), gastric motility[12] (no, mild, moderate, and vigorous) (Table 3), and procedural satisfaction (very good, good, fair, and bad) were evaluated by the endoscopist. Patients were also asked about their satisfaction with the procedure (very good, good, bearable, and unbearable) before discharge from the PACU. The total amount of butylscopolamine used was recorded.

TABLE 3. Evaluation of gastric peristalsis

Motility grading of gastric peristalsis
Grade 1: No peristalsis
No or very weak gating movement of the pyloric ring is observed, but the movement does not show strong contraction → No peristalsis
Grade 2: Mild peristalsis
A circular peristaltic wave is formed in the antrum but disappears without reaching the pyloric ring, or circular contraction temporarily occurs immediately before the pyloric ring → Peristaltic wave does not reach the pyloric ring
Grade 3 : Moderate peristalsis
A pronounced peristaltic wave is formed and reaches the pyloric ring → Peristaltic wave reached the pyloric ring, which opens and closes, showing star-like contraction as a result of the peristaltic wave
Grade 4 : Vigorous peristalsis
Peristaltic wave is deep and pronounced and proceeds, strangulating the antrum → Peristaltic wave reaches the pyloric ring, and the pyloric ring is totally covered by the wave, the area exhibiting star-like contraction protrudes toward the opening of the pyloric ring, and the mucosa is pushed out from the central part of the opening

This classification was cited from Hiki et al[12] classification method.

나. Assessment of patient safety

Hemodynamic variables of SBP and DBP, HR, and SpO_2 were compared when measuring the MOAA/S score.

All respiratory (apnea and desaturation) and hemodynamic (hypertension, hypotension, tachycardia, or bradycardia; defined as a change in baseline value of more than 20%) adverse events were recorded. Apnea was defined as not breathing spontaneously for at least 20 s. Desaturation was defined as $SpO_2 < 90\%$. We managed adverse respiratory events with a jaw thrust, mask ventilation, or by increasing oxygen flow. Ephedrine, nicardipine, atropine, or esmolol were administered for adverse hemodynamic events. The total amount of sedative drug, remifentanil, and sedation were recorded.

다. Statistical Analysis

Continuous variables are presented as means ± standard deviations and dichotomous variables are given as numbers (percentages). Continuous variables were compared using an unpaired Student's *t*-test. Dichotomous variables were compared using the chi-squared or Fisher exact tests, as appropriate. Repeated measured variables such as the MOAA/S scale score,

SpO_2, SBP, DBP, and HR were analyzed using a linear mixed model with patient indicator as a random effect and group, time, and group × time as fixed effects. When the interaction of group, time, or group × time of the variables was significant, a post-hoc analysis with Bonferroni correction was used for multiple comparisons. All statistical tests were two-tailed. P-values < 0.05 were considered significant. All statistical analyses were performed using SPSS software ver. 19.0 (SPSS Inc., Chicago, IL, USA).

Calculation of sample size was adopted by the previous study[13] which compared the efficacy and safety of dexmedetomidine with propofol TCI during endoscopic esophageal intervention. In which, 32 patients per group (α=0.05, 1-β=0.8 and 20% drop out) were calculated. Therefore, we intended to enroll 30 patients per group with a 10% of drop out rate.

III. RESULTS

No significant differences were observed in patient demographic data such as age, sex ratio, height, weight, snoring history, ASA classification, or sedation duration (Table 4).

Tumor characteristics, including histology, macroscopic appearance, location and size measured by the endoscopist were similar between the groups (Table 5).

TABLE 4. Patient characteristics

	DR group (n=29)	PR group (n=30)	p-value
Age (years)	62.1 ± 10.3	62.9 ± 12.3	0.763
Male [n (%)]	19 (65.5)	22 (73.3)	0.514
Height (cm)	162.2 ± 7.7	164.8 ± 5.8	0.274
Weight (kg)	62.8 ± 8.5	65.1 ± 10.2	0.276
ASA classification [n (%)]			0.390
I	19 (65.5)	15 (50.0)	
II	9 (31.0)	12 (40.0)	
III	1 (3.4)	3 (10.0)	
Snoring history (%)	9 (31.0)	7 (23.3)	0.506

Values are presented as mean ± SD or number (percentage). DR group indicates dexmedetomidine-remifentanil group; PR group, propofol-remifentanil group; ASA classification, American Society of Anesthesiology classification.

TABLE 5. Tumor characteristics

		DR group (n=29)	PR group (n=30)	p-value
Number of site		36	32	
Histology [n (%)]	Adenoma	19 (52.8)	17 (53.1)	0.995
	Carcinoma	16 (44.4)	14 (43.8)	
	Others	1 (2.8)	1 (3.1)	
Macroscopic appearance	Elevated	32 (88.9)	27 (84.4)	0.584
[n (%)]	Flat or depressed	4 (11.1)	5 (15.6)	
Location	Upper body	3 (8.3)	3 (9.4)	0.945
[n (%)]	Middle body	8 (22.2)	8 (25)	
	Lower body	25 (69.4)	21 (65.6)	
Size (mm)		15.7 ± 7.0	14.0 ± 6.7	0.344

Values are presented as mean ± SD or number (percentage).

Sedation duration was similar in the groups (P = 0.477). Dexmedetomidine in the DR group and propofol in the PR group were infused at rates of 0.47 ± 0.3 μg/h/kg and 23.8 ± 16.5 μg/min/kg, respectively. The infusion rates of remifentanil were 5.74 ± 1.44 μg/h/kg and 6.34 ± 4.02 μg/h/kg in the DR and PR groups, respectively (P = 0.451). Additional propofol requirements were 16.9 ± 10.3 mg in 8 patients of DR group and 13.3 ± 5.8 mg in 3 patients of PR group (P = 0.081) (Table 6).

TABLE 6. Drugs used for ESD

	DR group (n=29)	PR group (n=30)	p-value
Sedation duration (min)	42.8 ± 26.7	37.6 ± 18.5	0.477
Dexmedetomidine infusion rate (μg/hr/kg)	0.47 ± 0.3		
Propofol infusion rate (μg/min/kg)		23.8 ± 16.5	
Remifentanil infusion rate (μg/hr/kg)	5.74 ± 1.44	6.34 ± 4.02	0.451
Additional propofol required			
Patients [n (%)]	8 (27.6)	3 (10)	0.083
Dose (mg)	16.9 ± 10.3	13.3 ± 5.8	0.596

Values are presented as mean ± SD or number (percentage).

Although the endoscope was more easily advanced through the throat in the PR group than in the DR group (P = 0.01), low-grade gastric motility (no or mild) was more frequent in the DR group (96.6% vs. 73.3%, P = 0.013). The butylscopolamine was administered in 10 patients of PR group compared with 4 patients of DR group (P = 0.078).

While the endoscopists were satisfied with the procedural performance and judged the procedures as favorable (P = 0.042) in all patients in the DR group and in 86.7% of patients in the PR group, patient satisfaction was comparable between the two groups (Table 7).

The Aldrete score at the end of the procedure was not different between the groups (9.5 ± 0.6 in the DR group and 9.4 ± 0.6 in the PR group, P = 0.924) and all patients left the PACU within 30 min (21.2 ± 6.8 min in the DR group and 20.4 ± 5.8 min in the PR group, P = 0.636).

No differences in the MOAA/S scale score, SBP, DBP, or SpO_2 were observed, except HR was different between the groups (Figure 1). No cases of oxygen desaturation or any adverse hemodynamic events were observed during the ESD procedures in either group.

TABLE 7. Efficacy of procedural performance

	DR group (n=29)	PR group (n=30)	p-value
Advancing scope into throat			0.010
Very easy [n (%)]	7 (24.1)	17 (56.7)	
Easy [n (%)]	14 (48.3)	12 (40)	
Slight difficult [n (%)]	1 (3.4)	1 (3.3)	
Difficult [n (%)]	7 (24.1)	0 (0)	
Gastric motility			0.101
No [n (%)]	21 (72.4)	16 (53.3)	
Mild [n (%)]	7 (24.1)	6 (20)	
Moderate [n (%)]	1 (3.4)	7(23.3)	
Vigorous [n (%)]	0 (0)	1 (3.3)	
Low : no + mild [n (%)]	28 (96.6)	22 (73.3)	0.013
High : moderate + vigorous [n (%)]	1 (3.4)	8 (26.7)	
Butylscopolamine use			
Frequency [n (%)]	4 (13.8)	10 (33.3)	0.078
Endoscopist's general satisfaction			0.216
Very good [n (%)]	21 (72.4)	17 (56.7)	
Good [n (%)]	8 (27.6)	9 (30)	
Fair [n (%)]	0 (0)	2 (6.7)	

Bad [n (%)]	0 (0)	2 (6.7)	
Favorable : very good + good [n (%)]	29 (100)	26 (86.7)	0.042
Unfavorable : fair + bad [n (%)]	0 (0)	4 (13.3)	
Patients' satisfaction of sedation			0.616
Very good [n (%)]	4 (13.8)	7 (23.3)	
Good [n (%)]	21 (72.4)	20 (66.7)	
Bearable [n (%)]	4 (13.8)	3 (10)	
Unbearable [n (%)]	0 (0)	0 (0)	
Aldrete score at the end of procedure	9.5 ± 0.6	9.4 ± 0.6	0.924
PACU discharge duration (min)	21.2 ± 6.8	20.4 ± 5.8	0.636

Values are presented as mean ± SD or number (percentage). The gastric motility and endoscopist's satisfaction were reclassified as low (no + mild) or high (moderate + vigorous) and favorable (very good + good) or unfavorable (fair + bad), respectively.

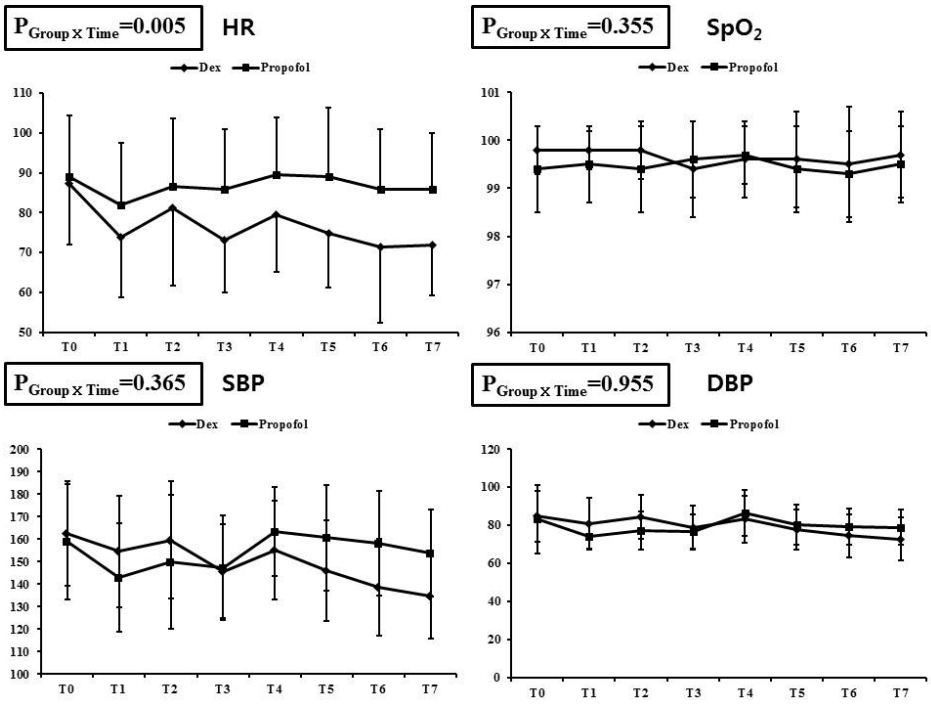

FIGURE 1. Changes of hemodynamic variables and SpO_2 during ESD. HR, heart rate; SpO_2, oxygen saturation; SBP, systolic blood pressure; DBP, diastolic blood pressure.

T0, just before the procedure; T1, 1 min after induction of sedation (1 min after a 5 min loading of dexmedetomidine in the DR group and 1 min after the propofol bolus injection in the PR group); T2, as the endoscope was passed into the esophagus; T3, as the endoscope marked the tumor region; T4, 5 min after epinephrine (0.01 mg/mL) injection was given in the gastric submucosa; T5, at dissection of the gastric tumor region from the gastric submucosa; T6, once bleeding control was reached at the gastric bed; T7, and at the end of the procedure.

Repeated measured variables such as MOAA/S scale, SpO_2, SBP, DBP and HR were analyzed using a linear mixed model with patient indicator as a random effect and group, time, and group-by-time as fixed effects. When the interaction of group, time, group-by-time of the variables was statistically significant, post-hoc analysis with Bonferroni correction was used for multiple comparisons.

IV. DISCUSSION

We found that minimal sedation using dexmedetomidine-remifentanil was safe for patients, and that endoscopists were satisfied with the procedural efficacy perhaps due to lower gastric motility.

This study has some clinical implications regarding the sedating protocol for ESD. First, our results suggest the importance of analgesics and optimal sedation level to avoid patient anxiety. ESD was safely performed under MOAA/S sedation levels of 4–5 if adequate analgesic was provided. As shown in Figure 1, no patient needed management due to hemodynamic instability or adverse respiratory events despite the decreased HR in the DR group. We believe that continuous infusion of remifentanil enabled patients to tolerate this procedure well in an orientated and anxiety-free state. The analgesic requirement for a painful procedure was evident in a previous colonoscopy trial, which was terminated early before enrolling the planned number of patients because of the higher rate of supplemental fentanyl required and adverse hemodynamic events in the group of patients administered dexmedetomidine alone[14]. In fact, the sedation level for endoscopic procedures is controversial. International sedation guidelines for gastrointestinal endoscopic procedures[15, 16] recommend sedating patients to improve procedural performance. However,

the adequate level of sedation for patients has not been well defined (conscious sedation vs. deep sedation). Takimoto et al.[9] compared the efficacy and safety of conscious sedation for ESD targeting a Ramsay sedation score (RSS) of 2–3 among propofol, dexmedetomidine, and midazolam. They found that dexmedetomidine provided comparable hemodynamic stability and improved oxygen saturation as well as no major surgical complications compared to propofol or midazolam, whereas two patients who received propofol or midazolam developed gastric perforation. An RSS of 2–3 represent a level of sedation that is similar to, but slightly more extending than, the MOAA/S of 4–5 used in the present study (MOAA/S 4 = responding to normal verbal tone; RSS 3 = responding to commands). Sasaki et al.[14] reported hypoxemia in 15.9–17.8% of patients and hypotension in 19.3–34.4% of patients, suggesting a deeper sedation level and a higher rate of complications. In the present study, minimal sedation, regardless of the group, allowed the patients to achieve an Aldrete score of 9.5 at the end of the procedure and to leave the PACU within 30 min. This may also be an economic benefit of minimizing sedation.

Second, regarding procedural performance, endoscopists felt that the endoscope could be more easily advanced into the throat (in 7 of 29 patients in the DR group vs. 17 of 30 patients in the PR group, P = 0.01). The underlying causes of this difference are unclear but might be explained, in part, by the

different effect of propofol and dexmedetomidine on the pharyngeal function. Kiriyama et al.[17] assessed the effects of a bolus of 0.5 mg/kg propofol injected before ESD compared to no bolus of propofol, found that the propofol bolus decreased pharyngeal muscle tone and obtunded the scope-stimulated pharyngeal reflex in 77% of patients compared to 21% of patients with no bolus. Therefore, in the present study, the intact pharyngeal function in the DR group may have made it more difficult for the endoscopists to advance the scope into the throat, because our sedation protocols included a bolus 0.5 mg/kg propofol or dexmedetomidine known to preserve the pharyngeal tone.

Inhibiting gastric motility is crucial to successfully perform ESD, and this is the first report of endoscopist-evaluated gastric motility during ESD, in relation to two different sedation protocols (Table 6). The endoscopists graded gastric motility as low (no and mild among four grades) in 96.6% of the DR group and in 73.3% of the PR group (P = 0.013). This result was also noted as less of a requirement for butylscopolamine to suppress gastric motility. The effects of dexmedetomidine on gastric motility seemed to differ according to subject and dosage. In a previous study, infusion with a 1.0 μg/kg loading dose for 20 min followed by infusion of 0.7 μg/h/kg inhibited gastric emptying in healthy volunteers, as measured by paracetamol absorption compared to 0.1 mg/kg morphine or placebo[10]. In contrast, Memis et al.[18] found no difference in gastric

emptying time between propofol (2 mg/h/kg) and dexmedetomidine (0.2 μg/h/kg) for 5 h in critically ill patients. This discrepancy may have resulted from the different doses of drugs and measuring methods (direct visualization vs. indirect paracetamol absorption test) used the two studies. Dexmedetomidine itself does not alter gastric motility in rats but markedly enhances the inhibitory effect of morphine on gastric motility[19]. We are uncertain of the interactive effect of dexmedetomidine and remifentanil on gastric motility. As another evaluation of performance efficacy, the endoscopists were able to perform 94.4% of the complete resections of 36 *en bloc* resections (DR group) and 100% of the complete resections of 32 *en bloc* resections (PR group), suggesting that both sedation protocols were effective and safe for ESD.

Our study had some limitations. We analyzed a small number of patients, which limited the statistical power of our results. Gastric motility did not differ between the two groups (P = 0.101) when measured using the four grades (no, mild, moderate, and vigorous); however, there was a significant difference when just two grades of low (no/mild) and high (moderate/vigorous) were applied (P = 0.013). This same issue was also observed with the statistical analysis of endoscopist satisfaction. We did not find any statistical difference when the ratings were based on four grades (very good, good, fair, and bad).

However, when satisfaction was divided into favorable (very good/good) and unfavorable (fair/bad), endoscopists were in favor of the DR group treatment (favorable, 100% in DR group vs. 86.7% in PR group, P = 0.042). Although we intended this to be a prospective endoscopist-blinded study, we are unsure whether each endoscopist was aware of the type of sedative drugs because of the difference in the pharmacologic properties between dexmedetomidine and propofol even though we covered the patient's venous access site with a drape. Therefore, we could not conclusively eliminate any bias of personal preference when they answered the questionnaires. Finally, our study design did not include a psychometric test for patients or comprehensive questionnaires to assess patient and endoscopist satisfaction as suggested by Vargo[20].

In conclusion, use of dexmedetomidine and remifentanil targeting minimal sedation resulted in safe and effective ESD procedures, perhaps by suppressing gastric motility. However, further studies with a greater number of subjects may be required.

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ABSTRACT (IN KOREAN)

내시경적 점막하절제술을 시행받는 환자에서 덱스메데토미딘-레미펜타닐(dexmedetomidine-remifentanil)과 프로포폴-레미펜타닐(propofol-remifentanil)의 진정효과 및 안전성 비교

<지도교수 민경태>

연세대학교 대학원 의학과

김 남 오

내시경적 점막하절제술은 충분한 진정과 진통이 필요한 시술인데, 이를 위해 프로포폴과 레미펜타닐의 사용이 많이 추천되고 있다. 덱스메데토미딘은 진정작용과 진통작용을 모두 가지고 있는 약제로 위장관 운동 억제 작용이 있으며, 이는 내시경적 점막하 절제술을 시행하는데 있어서 매우 중요한 요소가 될 수 있다. 본 연구에서는 내시경적 점막하절제술 동안 덱스메데토미딘-레미펜타닐과 프로포폴-레미펜타닐 약제의 유효성과 안전성을 비교하였다.

내시경적 점막하절제술이 예정되어 있던 총 59명의 환자가 무작위로 덱스메데토미딘-레미펜타닐 군과 프로포폴-레미펜타닐 군으로 나뉘었다.

환자의 진정작용을 위하여 덱스메데토미딘 혹은 프로포폴을 투여하

여 Modified Observer's Assessment of Alertness/Sedation 척도의 4-5 레벨을 유지하였다. 두 군 모두 진통작용을 위하여 레미펜타닐이 6 μg/hr/kg 의 용량으로 연속적으로 투여되었다. 내시경 기구를 환자의 식도로 삽입 시 수월한 정도, 위 연동운동 정도, 시술자와 환자의 만족도 등이 조사되었다. 혈역학적 변수들과 저산소증 발생 여부를 조사하여 환자의 안정성을 평가하였다.

조사한 두 군간의 환자의 특성 및 종양의 특성 차이는 없었다. 심박수가 덱스메데토미딘-레미펜타닐 군에서 낮았던 것 이외에 혈역학적 변수나 산소포화도는 두 군간에 차이를 보이지 않았다. 저산소증은 두 군에서 발생하지 않았다. 내시경 기구를 환자의 식도로 넘길 때 덱스메데토미딘-레미펜타닐 군보다 프로포폴-레미펜타닐 군이 보다 수월하였으며(내시경 집도 의사를 대상으로 한 설문조사 결과 "매우 수월" 7 vs. 17, P=0.01), 위 연동운동은 덱스메데토미딘-레미펜타닐 군에서 더 억제되었다(내시경 집도 의사를 대상으로 한 설문조사 결과 "연동운동 적음" 28 vs. 22, P=0.013). 보다 많은 내시경 집도의사들이 덱스메데토미딘-레미펜타닐 군에서 시술이 용이하다고 느꼈다(내시경 집도 의사를 대상으로 한 설문조사 결과 "시술에 호의적" 29 vs. 26, P=0.042). 두 군간 환자 만족도는 차이가 없었다.

결론적으로 본 연구를 통하여 내시경적 점막하절제술의 시행시 덱스메데토미딘-레미펜타닐의 사용과 프로포폴-레미펜타닐의 사용은 유효성과 안정성에서 차이를 보이지 않았다. 그러나 위 연동운동 억제효과로 인하여 덱스메데토미딘이 보다 선호된 것으로 생각해볼 수 있다.

핵심되는 말: 덱스메데토미딘, 유효성, 안전성, 위 연동운동, 내시경적 점막하절제술