Safety of Sedated Therapeutic Endoscopic Retrograde Cholangiopancreatography in Patients Older than 70 Years Old

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Objectives: The purpose of this study was to compare the safety and efficacy of midazolam sedated Endoscopic retrograde cholangiopancreatography (ERCP) with unsedated ERCP in patients 70 years of ages and older.

Methods: Seventy elderly patients 70 years of age or older who underwent ERCP were divided into two groups: midazolam sedated group (n=43) and unsedated group (n=27). Procedure time, success rate, complications related with ERCP procedure, satisfaction score were analyzed between two groups.

Results: Mean procedure time was 20.6 minutes for sedated group and 21.0 minutes for unsedated group (P=0.88). Success rate was 87.5% for sedated group and 100% for unsedated group (P=0.07). Incidence of complications from ERCP procedure showed no significant differences between the sedated and unsedated groups (P=0.10). There was no mortality in both groups related to the sedation or post-ERCP complication. Compared to the unsedated procedure, the sedated ERCP procedure was associated with higher patient satisfaction (P<0.001) and better repeat compliance (P=0.004).

Conclusion: There was no significant difference in success rate and complications at sedated and unsedated ERCP in patients 70 years of age and older. Unsedated ERCP showed 66.6% satisfaction score compared to sedated ERCP. **(Ewha Med J 2014;37(2):92-97)**

Introduction

The therapeutic procedure of endoscopic retrograde cholangiopancreatography (ERCP) of pancreaticobiliary disease is safe and effective [1]. Biliary and pancreatic diseases are frequently associated with complications in the elderly and are therefore attracting more attention owing to the increasing elderly population [2,3]. Several studies have been conducted on the safety and efficacy of therapeutic ERCP for elderly patients [4-6]. However, there is concern about the risk of cardiopulmonary complications and mortality in elderly patients who undergo ERCP, especially when they are sedated during the procedure [7,8]. Studies on the safety and efficacy of sedative ERCP in elderly patients have predominantly been conducted in Western populations [9,10]. Only a few prospective studies have been reported on elderly Asian patients [6,7]. The aim of our study was to evaluate the safety and efficacy of midazolam induced sedative ERCP in elderly patients and also conducted small study of unsedated ERCP in elderly. Seventy patients were enrolled and therapeutic ERCP was performed with or without sedation.

Methods

1. Subjects

Seventy patients older than 70 years were enrolled and divided into two groups. A single blind randomized allocation was

employed. The allocation sequence was concealed, and patients were assigned allocation on the day of ERCP procedure. ERCP procedures were performed by an experienced endoscopist at the Ewha Womans University Mokdong Hospital, Seoul, Korea. Written informed consent was obtained from each patient. Patients who refused the allocation were excluded from the study. All date from the study were stored on an encrypted server, and passwords were required to log in.

Overall, 70 patients were enrolled the study. Forty-three patients were allocated to midazolam induced sedated ERCP group, and 27 patients were allocated to unsedated ERCP group.

We analyzed underlying diseases and past medical history, including pancreatitis, previous cholecystectomy, and medications such as antiplatelet agents. ERCP findings, success rate, procedure duration, adverse events during ERCP (hypoxemia, electrocardiogram change, and hypotension), procedure-related complications (pancreatitis, bleeding, and perforation), and mortality within 1 month were evaluated.

2. ERCP procedure and monitoring

The subjects fasted for at least 8 hours before the ERCP. A standard ERCP was performed with the subjects in the lateral decubitus position, using an Olympus side-viewing video duodenoscope (Olympus TGF240; Olympus Optical Co, Tokyo, Japan). The patients were sedated by intravenous administration of 0.06 mg/kg of midazolam (Dormicum; Roche Korea, Seoul, Korea) before the procedure. To reduce duodenal motility and secretion, 10 mg of cimetropium bromide was administered intravenously. For pain control, 50 mg of meperidine was administered intramuscularly before the procedure. Monitoring included continuous assessment of peripheral oxygen saturation (SpO$_2$), heart rate, and blood pressure. Continuous oxygen administration was not used during sedation. When the SpO$_2$ was less than 90%, oxygen was provided and an antidote for midazolam, flumazenil (Anexate; Roche Korea) was injected.

Hypoxemia was defined as a SpO$_2$ level of less than 90% for at least 10 seconds. Troponin T (TnT) elevation was defined as an increase in TnT level of at least 0.01 ng/mL. An electrocardiogram (ECG) change was defined as a new downward slope or horizontal elevation of the ST segment, an ECG decrease of 0.1 mV or more, or an ST segment elevation of 0.2 mV or more above baseline for at least 1 minute. Tachycardia was defined as heart rate in excess of 100 beats per minute (bpm),

bradycardia as heart rate of less than 50 bpm, and hypertension as systemic blood pressure greater than 200 mmHg. Hypotension was defined as systemic blood pressure less than 80 mmHg. Post-ERCP pancreatitis was defined as significant persistent (≥ 24 hours) abdominal pain associated with an elevation in amylase or lipase by at least 3 times above the upper limit of normal. After the procedure, vital signs and laboratory findings, including TnT levels, were noted. Morbidity and mortality were recorded for 30 days after the ERCP procedure.

3. Satisfaction score

A 10-point visual analogue scale was used to estimate the tolerance and satisfaction levels of patients on the day after the procedure. A score of 0 indicated a very poor satisfaction level, and a score of 10 indicated a very high one. Compliance with the procedure was assessed according to whether the patient would agree to a repetition of the same procedure, should the need arise.

4. Statistical analysis

The SAS ver. 9.1 (SAS Institute Inc., Cary, NC, USA) was used for statistical analysis. Data are expressed as the mean and standard deviation. Statistical analysis was performed using the Student t test. Logistic regression analysis was performed between complication and sedation and between complication and procedure time over 30 minutes. A two-tailed P value<0.05 was considered statistically significant.

Results

1. General characteristics and clinical presentations

The demographic and clinical characteristics of subjects in the two study groups were compared. There were no statistically significant differences in age, sex, weight, height, or smoking habits between two groups (Table 1).

The difference in the incidence of comorbid disease between groups was not significant. The most common comorbidity was hypertension, followed by diabetes mellitus, pulmonary diseases (such as asthma and chronic obstructive pulmonary disease), and cardiovascular diseases (such as coronary artery disease and congestive heart failure). There were no significant differences between previous history of pancreatitis, cholecystectomy, or medication between groups.

Table 1. Demographic and clinical data of study participants who underwent ERCP under sedation or without sedation

Variable	Sedated group (n=43)	Unsedated group (n=27)	Difference (P value)
Gender (male:female)	20:23	12:15	0.87
Mean age (yr)	77.5±5.0	77.4±4.8	0.99
Mean weight (kg)	54.8±7.6	57.6±10.3	0.19
Smoking status			0.63
Current smoking	2	0	
Smoked in past	14	6	
Never smoked	27	21	
Hypertension	23	14	0.90
Diabetes mellitus	9	8	0.43
Chronic renal disease	3	1	0.55
Pulmonary disease	7	4	0.87
Cardiovascular disease	8	2	0.16
Cerebral vascular accident	2	4	0.19
Previous pancreatitis	1	2	0.37
Previous ERCP	4	0	0.11
Cholecystectomy	11	5	0.49
Antiplatelet agent	15	6	0.25

ERCP, endoscopic retrograde cholangiopancreatography.

Table 2. Comparison between indications for ERCP in sedated group and unsedated group (P=0.87)

Variable	Sedated group (%)	Unsedated group (%)
Choledocholithiasis	34 (79.1)	22 (81.5)
Bile duct stenosis	1 (2.3)	1 (3.7)
Papillary tumor of pancreas	5 (11.6)	2 (7.4)
AUPBD	3 (7.0)	2 (7.4)

ERCP, endoscopic retrograde cholangiopancreatography; AUPBD, anomalous union of pancreaticobiliary duct.

The most common clinical presentation at admission in both groups was right upper-quadrant pain. The most common indication for ERCP was choledocholithiasis in both groups (Table 2).

2. ERCP results

The mean dosage of midazolam used for sedation in sedated group was 3.5±0.8 mg. The duration of the ERCP procedure ranged from 5 to 67 minutes, and the mean duration of the procedure did not differ between groups (20.6±9.3 minutes vs.

Table 3. Comparison between ERCP results of sedated group and unsedated group

Variable	Sedated group (%)	Unsedated group (%)	Difference (P value)
Success rate	38 (88.4)	27 (100)	0.07
ERCP time (min)*	20.6±9.3	21.0±11.7	0.88
ERCP results			0.87
CBD stone	38 (88.4)	22 (81.5)	
Bile duct dilation[†]	2 (4.6)	4 (14.8)	
Biliary malignancy	1 (2.3)	0	
IPMN	2 (4.7)	1 (3.7)	
Diverticulum	22 (51.2)	17 (63.0)	0.34
EST	32 (74.4)	25 (92.6)	0.06

ERCP, endoscopic retrograde cholangiopancreatography; CBD, common bile duct; IPMN, intraductal papillary mucinous neoplasm; EST, endoscopic sphincterotomy.
*ERCP time expressed as mean±SD values. [†]Bile duct dilation without apparent cause.

21.1±11.7 minutes; P=0.88) (Table 3). The success rate was 88.4% for sedated group and 100% for unsedated group, but this difference was not significant (P=0.07). Failure was seen on three patients with cannulation failure due to large diverticulum, two patients with clearance failure due to multiple and large stones. The most common ERCP finding in both groups was a common bile duct stones (88.4% vs. 81.5%).

3. ERCP complications

There were no significant cardiopulmonary events, including ECG changes, hypoxemia, and hypotension in both groups during the ERCP procedure (P=0.62) (Table 4).

No significant differences between number of complications that occurred after ERCP were seen (P=0.10). These consisted of 4 cases of transient pancreatitis, 2 cases of perforation and 1 case of bleeding in sedated group, and 1 case of pancreatitis after ERCP in unsedated group.

Two cases of perforation were seen; 70 year-old male patient after ampullectomy of ampulla of vater adenoma with severe dysplasia and 87 year-old male patient after removal fail of impacted CBD stone. ERCP time of two cases of perforation were 38 minutes and 30 minutes, respectively. One case of bleeding was seen in 76 year-old male patient after advanced EST for removal of CBD stone. In bleeding case, ERCP time was 15 minutes.

Minor complications consisted of ECG changes without TnT

Table 4. Comparison between the number of complications in sedated group and unsedated group

Variable	Sedate group (%)	Unsedated group (%)	Difference (P value)
During ERCP			0.62
Hypoxemia	2 (4.7)	0	
ECG change	1 (2.3)	1 (3.7)	
Hypotension	0	1 (3.7)	
No complication	40 (93.0)	25 (92.6)	
After ERCP			0.10
Pancreatitis	4 (9.3)	1 (3.7)	
Bleeding	1 (2.3)	0	
Perforation	2 (4.7)	0	
No complication	36 (88.7)	26 (96.3)	

ERCP, endoscopic retrograde cholangiopancreatography; ECG, electrocardiogram.

Table 5. Comparison between participant satisfaction level by visual analogue score and compliance of sedated group and unsedated group

Variable	Sedated group	Unsedated group	Difference (P value)
Satisfaction score*	7.9±1.8	5.6±2.7	<0.001
Repeat compliance (%)	90.7	63.0	0.004

*Score on a scale of 1 to 10 points (1, very poor satisfaction; 10, very high satisfaction). mean±SD

elevation in 3 patients and transient pleural effusions in 2 patients. There were 2 cases of TnT level elevation without ECG change (1 for sedated group, 1 for unsedated group) and there were no significant differences between two groups (P=0.65). Minor complications were clinically insignificant. No mortalities occurred within a month of the procedure in both groups. The logistic regression analysis showed no significance between complication and sedation (P=0.14) and between complication and procedure time over 30 minutes (P=0.78).

4. Satisfaction score

The satisfaction score was greater in sedated group than unsedated group (7.9±1.8 vs. 5.6±2.8; P<0.001), as was the compliance for a repeat procedure (90.7% vs. 63.0%; P=0.004) (Table 5). Unsedated ERCP showed relatively 66.6% satisfaction score if sedated ERCP satisfaction score was 100%.

Discussion

ERCP is an effective endoscopic procedure for the treatment of biliary and pancreatic diseases [1]. There is concern about using ERCP for elderly patients because of possible cardiopulmonary complications [11]. Despite this concern, the demand for ERCP in elderly patients is increasing because of the increasing incidence of biliary tract disease [2,11]. As the population ages, the use of therapeutic endoscopic procedures for treatment of the elderly will increase [2,12]. Even when biliary drainage is successful in elderly patients, they still exhibit a high incidence of severe cholangitis and additional medical complications (such as hypotension, altered sensorium, and renal failure), and the mortality rate is 9.6% [13]. Transient myocardial ischemia and various cardiac arrhythmias frequently occur in elderly patients during ERCP [14,15].

Sedation is a critical issue for elderly patients. Most studies on sedation have compared its effects in elderly and younger patients by using retrospective experimental designs [3,11]. Few prospective studies have been performed to examine the risk of sedation in the elderly in terms of their tolerance of ERCP procedures [16-18]. Sedation regimens for ERCP are midazolam alone or midazolam plus opioids, propofol alone or balanced propofol sedation (propofol in combination with midazolam and meperidine) [19]. The midazolam sedation used had been previously shown to result in a good level of satisfaction, few paradoxical responses, and a short discharge time without any side effects [20].

Arterial hypoxemia, arrhythmias, and myocardial ischemia have been associated with ERCP in elderly patients [10,11]. Patients undergoing ERCP may develop true myocardial ischemia with reduced myocardial blood flow [18]. Elevated cardio-specific troponin levels have been presented as biochemical evidence of ERCP-related myocardial injury [11]. Troponin levels in patients over 65 years of age become elevated if the duration of ERCP exceeds 30 minutes [11]. In the present study, the mean procedure time was approximately 20 minutes, and the TnT level after ERCP did not differ significantly in both sedated and unsedated groups. And the linear regression analysis showed no significance between major complication and procedure time over 30 minutes. Changes in ECG and TnT levels after ERCP in this study were transient and not clinically significant.

Elderly patients who undergo ERCP may be at risk of cardio-

pulmonary complications because of preexisting cardiovascular disease, combinations of benzodiazepine and opioid sedation, or prolonged procedures [11,21]. Several studies have recently been conducted on ERCP in elderly Asian patients. Sugiyama et al. [22] showed that ERCP and sphincterotomy are safe treatments for choledocholithiasis in people aged above 90 years. Between 2% and 9% of elderly patients require ventilatory support after endoscopic sphincterotomy for bile duct stones [22]. The most common complications of ERCP in elderly Asian patients were cholangitis, pancreatitis, and biliary perforation [22]. The complication rate associated with therapeutic ERCP in elderly patients was 2.6% according to a prospective study, and short-term complications after endoscopic sphincterotomy were not related to age [23].

Of the previously reported prospective studies, only 3 addressed sedation and age [16–18,20]. Moreover, most prospective studies were conducted on Western patients. The prospective studies for Asian patients concerned propofol sedation [6,7] or endoscopic sphincterotomy for elderly patients [23].

In the present study, in addition to a higher satisfaction score in the sedated group (P<0.001), procedure tolerance or repeat compliance was also higher in the sedated group (P=0.004). The complications were not significant in both groups, and there was no mortality in this study. A limitation of our study is the restricted study population, which may be responsible for the differences in certain observations of this study compared to those of other studies. For instance, there was a relatively low incidence of malignancies and mortality in our subject population.

In conclusion, sedated ERCP is a safe and effective procedure for elderly patients aged 70 years and above. Moreover, patients who underwent sedated ERCP were more satisfied and had better compliance than those treated with nonsedative ERCP.

Acknowledgments

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