Safety of Gastroenterologist-Guided Sedation with Propofol for Upper Gastrointestinal Therapeutic Endoscopy in Elderly Patients Compared with Younger Patients

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Background/Aims: Propofol sedation for elderly patients during time-consuming endoscopic procedures is controversial. Therefore, we investigated the safety of using propofol in elderly patients during upper gastrointestinal therapeutic endoscopy. **Methods:** The medical records of 160 patients who underwent therapeutic endoscopic procedures under gastroenterologist-guided propofol sedation at a single institution were retrospectively reviewed. The subjects were divided into two groups: a younger group, patients <75 years old; and an elderly group, patients ≥75 years old. The two groups were compared with respect to the therapeutic regimen, circulatory dynamics, and presence/absence of discontinuation of propofol treatment. **Results:** Although the number of patients with liver dysfunction was higher in the elderly group, there were no other significant differences in the baseline characteristics, including the American Society of Anesthesiologists classification, between the elderly and younger groups. The average maintenance rate of continuous propofol infusion was lower in the elderly patients. No statistically significant differences were found in the occurrence of adverse events between the elderly and younger groups. None of the patients returned to a resedated state after the initial recovery from sedation. **Conclusions:** Gastroenterologist-guided propofol sedation in elderly patients can be safely achieved in the same manner as that in younger patients, even for time-consuming upper gastrointestinal therapeutic endoscopic procedures. **(Gut Liver 2015;9:38-42)**

INTRODUCTION

The use of sedation in gastrointestinal endoscopy has become increasingly common over the last decade.[1] During the last few years, propofol as a sedative agent for esophagogastroduodenoscopy (EGD) has gradually replaced benzodiazepines owing to its short-acting pharmacokinetic characteristics.[2] Moreover, the administration of propofol by nonanesthesiologists has been widely accepted to be effective and safe for gastrointestinal endoscopy and other interventional procedures.[3-6] Previous meta-analyses indicated that propofol sedation was not associated with an increased risk of complications compared with traditional sedative agents.[7,8] Propofol was also shown to decrease both time to sedation and recovery time, as well as to increase the quality of endoscopic examination, providing higher patient satisfaction for most endoscopic procedures. Most of the previous studies demonstrating the effectiveness and safety of propofol sedation were conducted in nonelderly patients. Although a few studies have reported the clinical use of propofol in elderly individuals,[9] these reports did not focus on the safety of propofol applied to elderly patients who underwent therapeutic endoscopy procedures that require long-time sedation, such as therapeutic endoscopic retrograde cholangiopancreatography (ERCP), intervention endoscopic ultrasound, or endoscopic submucosal dissection (ESD). To the best of our knowledge, there are as yet no reports on the safety of the clinical application of propofol in elderly patients during therapeutic endoscopy in Japan. Therefore, the aim of this case-series was to investigate the safety of propofol in elderly patients who underwent upper

gastrointestinal therapeutic endoscopy at a single institution in Japan.

MATERIALS AND METHODS

1. Patients

The records of 160 patients (181 procedures) who received endoscopic therapy for the treatment of cholangiopancreatic diseases and esophageal and gastric ESD at the Department of Gastroenterological Medicine of Akita Yuri Kumiai General Hospital (Yurihonjo, Akita, Japan) were analyzed. Patients who previously experienced hypersensitivity to 1% propofol (Diprivan®) or its constituents and pregnant women were excluded from the study. All study participants provided written informed consent.

2. Study design

The subjects were divided into two groups: younger group, patients <75 years old and elderly group, patients ≥75 years old. These two groups were compared regarding the following factors: (1) therapeutic regimen (procedure duration, details of propofol administration and presence/absence of delayed awakening after the operation); (2) circulatory dynamics (the fraction of patients who had a systolic blood pressure [SBP] of ≤80 mm Hg, a heart rate of ≤50 beats per minute [bpm] or an arterial oxygen saturation of ≤90%—these parameters were monitored 5 minutes after the initiation of sedation preoperatively and periodically perioperatively; and (3) presence/absence of the discontinuation of propofol treatment.

3. Sedation and monitoring protocols

All of the patients initially received an intravenous infusion of lactated Ringer solution at 100 mL/hr, and they were then transported to the operating room. Vital signs were measured every 5 minutes using a serial pressure measurement apparatus and a percutaneous oxygen saturation measurement system. Patients were treated with oxygen via the nose at 2 L/min; thereafter as a pretreatment, lidocaine (4%) was sprayed into the pharyngeal mucosa and the anticonvulsant butylscopolamine bromide (20 mg, Buscopan®; Nippon Boehringer Ingelheime, Hyogo, Japan) or glucagon (1 mg, Glucagon G Novo®; Novo Nordisk Pharma, Tokyo, Japan) was administered intravenously. After confirming the absence of vital sign abnormalities, pentazocine (15 mg, Sosegon®; Maruishi Pharmaceutical Co., Ltd., Osaka, Japan) was administered as an intravenous slow bolus and then propofol (0.5 mg/kg/10 sec) as an intravenous bolus to initiate sedation. For the patients with the American Society of Anesthesiologists (ASA) score of III or IV, propofol was then administered as an intravenous bolus at 0.25 to 0.4 mg/kg/10 sec and an emergency cart was prepared for all patients in case of an adverse event. The level of sedation of each patient was determined using the Ramsay sedation score, and the operation was performed for patients with a score of 4 or greater. During the operation, propofol was intravenously administered at 2 to 5 mg/kg/hr to maintain the sedation depending on the condition of body movement and awakening. When a patient appeared to be in discomfort or exhibited restlessness following verbal stimulation, an additional 10 mg of propofol was administered as a bolus injection and the maintenance infusion rate was increased by 1 mg/kg/hr. When an adverse event was confirmed, the dose for maintenance sedation was decreased.

4. Management of adverse events

An SBP of ≤80 mm Hg, a heart rate of ≤50 bpm or an arterial oxygen saturation of ≤90% was recorded as adverse events. In cases with an SBP of ≤80 mm Hg, the administration rate of the lactated Ringer solution was increased to 300 mL/hr and the patient's legs were elevated if possible. For a heart rate of ≤50 bpm, the patient was observed for 10 seconds, and then after confirming no abnormalities in SBP and oxygen saturation rate, the administration rate of the lactated Ringer solution was increased to 300 mL/hr. When an arterial oxygen saturation of ≤90% was continuously observed for 10 seconds or longer, the oxygen treatment rate was increased until the oxygen saturation returned to ≥95%. When the adverse event was not resolved after performing the abovementioned procedures, the dose of propofol was decreased to 0.5 mg/kg/hr. If the adverse event was not resolved within 3 minutes, propofol treatment for maintenance sedation was discontinued temporarily. If the adverse event was resolved after the discontinuation, propofol treatment was resumed at the same dose as that before the discontinuation. After the operation was completed, propofol maintenance treatment was terminated, and the patient was observed for 15 minutes. When the Ramsay sedation score became level 3 or lower, the patient was defined as being awake. The patient was discharged from the operating room after confirming the absence of vital sign abnormalities. Oxygen treatment was continued after the discharge, and oxygen treatment was discontinued after lucidity was confirmed during the postoperative round.

5. Statistical analyses

The statistical significance of the differences between the two groups of patients, regarding their characteristics and the incidence of adverse events was assessed using the chi-square test. Differences in procedure duration and details of propofol administration were assessed by the t-test. p-values <0.05 were considered to indicate a statistically significant difference between the two groups. All statistical evaluations were carried out using SPSS software version 15.0 (SPSS Inc., Chicago, IL, USA).

Table 1. Details of the Patient Groups

	Younger group (<75 yr)	Elderly group (≥75 yr)	p-value
No. of patients (procedures)	85 (89)	75 (92)	
Gender, male/female	59/26	46/29	
Age, yr	65.25±7.49	80.75±4.29	
BMI, kg/m^2	23.24±3.94	22.98±3.27	0.583
Comorbidity			
Hypertension	43	41	0.882
Diabetes mellitus	13	13	1.000
Liver dysfunction	9	11	0.027
Chronic renal disease	3	7	0.133
ASA classification			
I/II	78	71	0.334
III	7	4	

BMI, body mass index; ASA, American Society of Anesthesiologists.

Table 2. Details of the Management of Propofol Sedation during the Endoscopic Procedures

	Younger group (<75 yr)	Elderly group (≥75 yr)	p-value
No. of procedures	89	92	
Procedure time, min	76.89±51.71	70.61±41.79	0.369
Initial bolus infusion, mg/10 sec	29.8±16.1	27.5±12.6	
Maintenance rate, mg/kg/hr	4.76±3.26	4.02±1.31	0.048
Additional no. of bolus infusions	2.44±2.33	2.24±2.44	0.624
No. of changes of maintenance rate	1.40±1.46	1.08±1.56	0.146
Total infusion dose, mg	323.08±257.79	256.47±197.83	0.053

RESULTS

1. Details of the patients

The details of the 160 patients categorized into either the younger or elderly patient group are shown in Table 1. No statistically significant differences in body mass index, comorbidities or ASA classification were found between the two groups.

2. Details of the management of sedation with propofol during the endoscopic procedures

The average durations of the endoscopic procedures in the two groups were not statistically significantly different. No evidence of significant differences in the details of the management of sedation with propofol during the endoscopic therapy was found (Table 2).

Table 3. Circulatory Dynamics during the Procedures

	Younger group (<75 yr)	Elderly group (≥75 yr)	p-value
No. of procedures	89	92	
Hypotension (SBP <80 mm Hg)	4	11	0.104
Desaturation (BOS <90%)	15	11	0.400
Bradycardia (pulse rate <40 bpm)	1	1	1.000

SBP, systolic blood pressure; BOS, blood oxygen saturation; bpm, beats per minute.

3. Adverse events and complications

Regarding details of the circulatory dynamics, the fraction of patients with an SBP of ≤80 mm Hg, a heart rate of ≤50 bpm or an arterial oxygen saturation of ≤90% at 5 minutes after the initial propofol treatment preoperatively and perioperatively with propofol maintenance treatment are shown in Table 3. There were no statistically significant differences in any of the categories. Although temporary discontinuation of propofol maintenance treatment was recorded in seven cases in the younger group and in 10 cases in the elderly group, propofol administration was resumed and the therapy was completed in all cases. No cases revealed delayed awakening, resedation after discharge from the operating room or other complications.

DISCUSSION

To the best of our knowledge, this retrospective study is the first to investigate the clinical feasibility of continuous propofol infusion for sedation in elderly patients during upper gastrointestinal therapeutic endoscopy, esophageal ESD, gastric ESD, and therapeutic ERCP. The results indicate that propofol can be used safely without any adverse effects in both elderly patients and younger patients. Our study demonstrates that the induction and maintenance of continuous propofol infusion can be safely performed resulting in faster recovery even in elderly patients categorized as ASA classification I/II.

Recently, propofol has been increasingly used in many countries because of the greater satisfaction of both endoscopists and patients than in the case of using conventional sedation. Furthermore, balanced propofol sedation with conventional sedation (midazolam and meperidine) in patients undergoing therapeutic endoscopic procedures was shown to provide a significantly higher level of endoscopist satisfaction and better patient cooperation than conventional sedation alone.[10] Propofol is a phenolic derivative with satisfactory sedative, hypnotic, antiemetic, and amnesic properties. This sedative-hypnotic drug is also highly lipophilic, and therefore can rapidly cross the blood-brain barrier resulting in an early onset of action and a shorter

recovery profile.[11] The combination of propofol and midazolam has synergistic effects and may have advantages over the use of propofol as a single agent.[12] Recovery time after propofol sedation from EGD or colonoscopy was quantified by detailed tests in other studies and it ranged from 14 to 19 minutes.[13,14] The stability of awareness after recovery from propofol sedation was shown in a previous study by evaluating patients' psychomotor and driving skills.[15] For nontherapeutic endoscopy, the doses of propofol used are relatively low and hence it was reported to be safe and the clinical recovery to be rapid.[16-18] Although a study comparing satisfaction, recovery scores, and safety profiles during ERCP revealed no difference in the procedure completion rate and adverse profiles between continuous infusion of propofol and conventional sedation (meperidine and midazolam), the infusion of propofol does provide a better recovery profile.[19] Moreover, patients treated with continuous propofol administration experienced a quicker recovery time than those treated with midazolam.[20,21]

Sedation should be generally safe; however, complications may occur for various reasons, including the type, dose and mode of administration of the sedative, as well as the patient's age, underlying chronic disorders, and so forth. Prolonged hypoxemia (an oxygen saturation of <90% for ≥15 seconds) and apnea (lack of respiratory activity for ≥15 seconds) are not uncommon during moderate sedation for endoscopy. It was demonstrated that hypoxemia usually develops within 5 minutes of sedative administration or endoscope intubation and that only one-third of all apnea/abnormal ventilation events cause hypoxemia.[22] A study using a large number of patients reported that adverse events occurred in a small proportion of patients (4.5%) and the six major complications, namely, hypotension, desaturation, bradycardia, hypertension, arrhythmia, and aspiration developed in 0.1% of the patients.[23]

On the other hand, a prospective study indicated that the administration of propofol as a sedative agent in gastrointestinal endoscopy results in a significant reduction in mean arterial pressure compared with its preadministration level. However, severe hypotension (an SBP of <60 mm Hg) was found in only 0.5% of the patients. Oxygen saturation decreased from an average of 96.5% to 94.4%, although a critical decrease (<90%) was documented in only 2.4% of patients.[24] The authors hence concluded that propofol is safer and more effective than midazolam for maintaining an adequate level of sedation during endoscopy, and also demonstrates a shorter recovery time.

Although gastrointestinal endoscopy with sedation in elderly patients is increasingly being performed, data on the outcomes and side effects of sedation are limited. The results of our study indicate that propofol can be safely used in both elderly and younger patients. Moreover, no severe adverse events, such as desaturation or hypotension, occurred upon the administration of continuous propofol infusion by a gastroenterologist. However, a recent study concluded that deep sedation by continuous propofol infusion with opioid administration, performed by anesthesiologists, might be a risk factor for pneumonia.[25] It is well known that administration of propofol with an analgesic drug, such as fentanyl, is difficult to control by both gastroenterologists and endoscopists. The gag reflex is a protective mechanism to prevent aspiration. The deep sedation protocol using propofol infusion with an opioid may actually increase the risk of aspiration pneumonia, especially in elderly patients. In our study, no patients underwent time-consuming endoscopic procedures under sedation with propofol and an opioid. Fortunately, our data (n=160) did not include patients with pulmonary disease, and the average time of the procedure in our cases was approximately 70 minutes. In addition, the frequency of patients categorized as ASA classification I/II was similar between the two groups in our study. The reason for the low incidence of severe complications in these studies was probably due to the exclusion of patients categorized as ASA classification III, after careful assessment of their cardiopulmonary function.

Age-related pharmacokinetic changes and their comorbidities complicate drug therapy. Consequently, lipophilic drugs may have a prolonged half-life in the elderly. Combined with reduced hepatic and renal clearance mechanisms because of hypertension and coronary heart disease, this prolonged half-life can prolong the recovery of elderly patients after sedation.[26] Thus, sedation should be modified by the administration of fewer agents at a slower rate and lower cumulative dose in elderly people. Our data actually showed that the average maintenance rate (mg/kg/hr) of continuous propofol infusion was lower in elderly patients. That is, we may be administering propofol at lower maintenance rates unconsciously in elderly patients. This is likely to be the key to manage gastroenterologist-guided propofol sedation in elderly patients.

Medication used for endoscopic sedation should be determined effectively and safely, taking into account the type and duration of the procedure, as well as the patient's condition including their age and ASA classification. We conclude that lengthy gastroenterologist-guided propofol sedation can be safely managed in the elderly population with less comorbidity, by careful monitoring of the patients. The best methods for sedation during digestive endoscopy are still controversial. Nevertheless, sedation with propofol for complicated and time-consuming therapeutic endoscopic procedures in elderly patients should be monitored by anesthesiologists. Since our study was conducted in a single center, considering the clinical features of the elderly patients, further large-scale studies should be performed to confirm these results.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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