

Original article

Intravenous sedation for gastrointestinal endoscopy in very elderly patients of Thailand

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Background: The use of sedation for gastrointestinal endoscopy (GIE) procedures in elderly patients has been established as a safe and effective technique. However, it is still uncertain whether the situation is valid for Asians.

Objective: Evaluate the outcome of intravenous sedation (IVS) for GIE procedures in very elderly patients (≥ 86 years old) in Thailand and compare the clinical efficacy of IVS between very elderly and those younger (< 86 years old)

Methods: We undertook a retrospective review of the sedation service records of patients who underwent GIE procedures between 2007 and 2008 at Siriraj Hospital, Thailand. All sedations were administered by anesthetic personnel in the endoscopy room. The cohort was divided into three groups, < 65 years old (group 1), 65-85 years old (group 2), and ≥ 86 years old (group 3).

Results: Sedation was provided for 1,779 patients (965, 687, and 127 patients in group 1, 2, and 3, respectively) in 2,061 GIE procedures. Fentanyl, midazolam and propofol were the most common IVS drugs used in all three groups. Patients in group 3 required lower mean doses of these intravenous sedatives than those in group 1 or 2 ($p < 0.001$). Mean procedure time in group 3 was longer than in group 1 or 2 ($p = 0.010$). Adverse events in group 3 occurred more frequently when compared to group 1 or 2 ($p < 0.001$). Transient hypotension was the main complication across all aged groups.

Conclusion: IVS for GIE procedure in very elderly patients was associated with higher minor advance events but relatively safe and effective when carried out by trained anesthetic personnel with appropriate monitoring and dose adjustment.

Keywords: Clinical experience, gastrointestinal endoscopy, intravenous sedation, very elderly patient Thailand

The use of gastrointestinal endoscopy (GIE) is rising in geriatric patients. In Thailand, higher number of geriatric patients undergoing GIE is observed [1]. Elderly patients are likely to undergo GIE procedures because the procedures are better tolerated due to technological progress.

A significant factor to perform better tolerated endoscopies is the use of intravenous sedation (IVS).

Sedation in the elderly requires awareness of their increased response to sedative agents. Many physiologic processes contribute to the increase in sensitivity and sedation risk in geriatric patients [2]. When sedating the geriatric patient, the agent of choice should have a short half-life, with minimal active metabolites and limited side effects. Midazolam, fentanyl, and propofol are a common combination used for moderate to deep sedation. These sedatives have a reduced clearance in the elderly.

The use of sedation for GIE procedures in elderly patients has been established as a safe and effective technique. However, it is still uncertain whether the

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situation is valid for Asians. There is limited data on clinical efficacy of GIE in geriatric population in Asia. Lee et al. [3] examined geriatric population in Hong Kong undergoing upper endoscopy. However, their GIE procedures were done without sedation [3].

In this study, we evaluated the outcome of IVS for GIE procedure in very elderly patients (≥ 86 years old) and compared the clinical efficacy of IVS between very elderly and younger patients (< 86 years old) for GIE procedures performed in Thailand.

Methods

A retrospective study was performed on consecutive subjects who underwent GIE between January 2007 and June 2008 at Siriraj GI Endoscopy Center, Siriraj Hospital, Mahidol University in Bangkok. This study was approved by the Ethics Committee of Faculty of Medicine Siriraj Hospital, Mahidol University.

All patients were classified into three groups based on different age cut-offs as follows. In group 1, the patients were younger than 65 years of age. In group 2, the patients were 65 to 85 years of age. In group 3, the patients were 86 years of age or older. Inclusion criteria were age ≥ 86 , and procedures performed using IVS. Exclusion criteria were patients younger than 16 years, procedures performed in the intensive care units, procedures performed without sedation, or procedures performed under general anesthesia.

Endoscopy and IVS-related procedure

GIE procedures were performed by senior endoscopists or Gastroenterology fellows. All procedures were done using an Olympus video endoscope compatible with GIE procedure. After completion of the GIE procedure, all patients were observed in the recovery room for at least two hours prior to discharge or hospitalization. Patients were observed for both sedatives and/or procedural complications. Procedure related complication was defined according to the guidelines of the British Society of Gastroenterology [4].

For all patients who underwent IVS, appropriate monitoring was used. Cardiovascular monitoring included continuous electrocardiogram, heart rate, oxygen saturation measurements, and five-minute interval non-invasive blood pressure measurements from blood pressure cuff device. Ventilation monitoring included continuous respiratory rate measurements and interval observation of patterns of respiration, chest

movement, and signs and symptoms of airway obstruction. Level of consciousness was also periodically assessed. End-tidal carbon dioxide (CO_2) monitoring with capnography was not used during sedation.

The sedative agents used depended on the patient's medical condition and the familiarity of the anesthesiologist with the particular case. All patients were given supplemental oxygenation via nasal canula and sedated by well-trained anesthetic personnel directly supervised by a staff anesthesiologist in the endoscopy room.

All patients were sedated in either a moderate (conscious) or deep sedation level, according to the guideline of the American Society of Anesthesiologists (ASA) [5] and the American Society of Gastrointestinal Endoscopy [6-8].

Sedation complications were recorded. Complications were defined as follows: hypertension or hypotension (increase or decrease in blood pressure by 20% from baseline and above or below normal for age), tachycardia or bradycardia (increase or decrease in heart rate by 20% from baseline and above or below normal for age), any cardiac arrhythmias; hypoxia (oxygen desaturation $< 90\%$), and airway obstruction. A significant sedation related adverse event was defined as prolonged desaturation or apnea with duration more than 30 seconds.

Statistical analysis

Results were expressed as means standard deviation (SD), median or percentage when appropriate. Comparisons between the three different groups were done with one-way ANOVA F-test for numeric variables and Chi-square test for categorical variables. The statistical software package SPSS for Window Version 11 (SPSS Inc, Chicago, USA) was used to analyze the data. A significance level of 5% was used throughout the study.

Results

During the study period, 1,779 patients (784 men, 995 women) underwent 2,061 GIE procedures under IVS technique, where 965 patients (403 men, 562 women), 687 patients (339 men, 348 women), and 127 patients (50 men, 77 women) were assigned to group 1, group 2, and group 3, respectively. **Table 1** shows the characteristics and indications of procedures for group 1 (age < 65 years), group 2 (age 65-85 years), and group 3 (age ≥ 86 years).

Table 1. Characteristics of patients and indications of procedures

	Group 1 (Age <65)	Group 2 (Age 65-85)	Group 3 (Age ≥86)	P-value
Number of patients	965	687	127	
Age (year) (mean SD)	49.7±10.9	73.0±5.4	89.2±3.2	
Gender (%):				
Male	403 (41.8)	339 (49.3)	50 (39.4)	0.004*
Female	562 (58.2)	348 (50.7)	77 (60.6)	0.004*
Weight (kg) (mean SD)	57.8±11.3	55.9±11.3	51.2±10.7	0.891
ASA physical status (%):				
I	452 (46.8)	4 (0.6)	0	<0.001*
II	426 (44.1)	480 (69.9)	51 (40.2)	
III	87 (9.0)	202 (29.4)	71 (55.9)	
IV	0	1 (0.1)	5 (3.9)	
Duration of procedure (minute) (mean SD)	33.0±18.9	34.3±17.7	40.3±21.3	0.010*
Indications (%):				
Colon cancer	156 (16.2)	144 (21.0)	8 (6.3)	<0.001*
Lower gastrointestinal hemorrhage	78 (8.1)	55 (8.0)	16 (12.6)	0.204
Abdominal pain	78 (8.1)	19 (2.8)	2 (1.6)	<0.001*
Bowel habit change	57 (5.9)	30 (4.4)	6 (4.7)	0.370
Pancreatic tumor	51 (5.3)	31 (4.5)	1 (0.8)	0.076
Anemia	40 (4.1)	40 (5.8)	8 (6.3)	0.231
Common bile duct stone	39 (4.0)	34 (4.9)	5 (3.9)	0.653
Colon polyp	38 (3.9)	42 (6.1)	7 (5.5)	0.123
Chronic diarrhea	38 (3.9)	19 (2.8)	2 (1.6)	0.222
Check up	37 (3.8)	17 (2.5)	4 (3.1)	0.308
Others	353 (36.6)	256 (37.3)	69 (54.3)	<0.001*

ASA: American Society of Anesthesiologists, *statistically significant

The type of procedure and pre-sedation problems are summarized in **Table 2**.

Propofol, fentanyl, and midazolam were the most common sedative agents used in all three groups. The mean dose and dose range of the sedative agents used in each group is shown in **Table 3**. We note that patients in group 3 used significantly lower mean dose of propofol, fentanyl, and midazolam, compared to those in group 1 or 2.

Comparisons of the mean sedative doses in the different groups by ASA physical status are shown in **Table 4**. We note that patients in group 3 with ASA physical status I and II required lower mean doses of propofol, fentanyl, and midazolam compared to those in group 1 or 2 with the same ASA classification. This was similarly observed for patients in group 3 with ASA classification III and IV who required lower mean sedative doses than those in group 1 or 2 with same ASA classification.

Most sedative agents were used in combination with two or three other agents in all age groups. The most common combinations in each group were propofol, midazolam and fentanyl, midazolam and fentanyl, and propofol and pethidine. However, the combination of propofol, midazolam and fentanyl was the most common sedative combination used in group 3.

Comparisons of the observed sedation and procedure related complications are summarized in **Table 5**. We note more respiratory and cardiovascular related adverse events observed in group 3 than in group 1 or 2. Upper airway obstruction accounted for the majority of respiratory complications in group 3. These were managed conservatively with chin lift and/or placement of nasal airways without endotracheal intubation. Significant respiratory adverse events occurred with prolonged desaturation and/or apnea. The main cause of cardiovascular

complication in group 3 was hypotension. These were treated with fluid resuscitation. All of the sedation related adverse events in all three groups were

managed under the care of an anesthesiologist. No procedures were aborted as a result of insufficient sedation or complications of IVS.

Table 2. Type of procedure and pre-sedation problem in group 1 (age <65 years), group 2 (age 65-85 years), and group 3 (age ≥86 years)

	Group 1	Group 2	Group 3	P-value
<i>Type of procedure (number, %)</i>				
EGD	61 (6.3)	23 (3.3)	19 (15.0)	<0.001*
Colonoscopy	475 (49.2)	333 (48.5)	43 (33.9)	0.005*
EGD and colonoscopy	178 (18.4)	88 (12.8)	16 (12.6)	0.005*
PEG	40 (4.1)	97 (14.1)	26 (20.5)	<0.001*
ERCP	105 (10.9)	66 (9.6)	14 (11.0)	0.685
EUS	106 (11.0)	80 (11.7)	8 (6.3)	0.205
Proctoscopy	0	0	1 (0.8)	<0.001*
<i>Pre-sedation problem</i>				
Hypertension	175 (18.1)	313 (45.6)	36 (28.3)	0.001*
Hematologic disease	97 (10.1)	114 (16.6)	35 (27.6)	<0.001*
Diabetes mellitus	95 (9.8)	169 (24.6)	15 (11.8)	<0.001*
Cardiovascular disease	64 (6.6)	129 (18.8)	30 (23.6)	<0.001*
Respiratory disease	49 (5.1)	68 (9.9)	12 (9.4)	0.001*
Electrolyte imbalance	43 (4.5)	49 (7.1)	29 (22.8)	<0.001*
Renal disease	34 (3.5)	61 (8.9)	17 (13.4)	<0.001*
Liver disease	28 (2.9)	13 (1.9)	4 (3.1)	0.420
Dyslipidemia	14 (1.4)	54 (7.9)	8 (6.3)	<0.001*
Brain disease	13 (1.3)	39 (5.7)	18 (14.2)	<0.001*
Others	28 (2.9)	43 (6.3)	3 (2.4)	0.002*

EGD: esophagogastroduodenoscopy, PEG: percutaneous endoscopic gastrostomy, ERCP: endoscopic retrograde cholangiopancreatography, EUS: endoscopic ultrasonography, *statistically significant

Table 3. Mean dose of common sedative agents categorized by age problem

	Group 1 (age <65) number (%) mg/kg/hr (SD, range)	Group 2 (age 65-85) number (%) mg/kg/hr (SD, range)	Group 3 (age ≥ 86) number (%) mg/kg/hr (SD, range)	P-value
Propofol	684 (70.9) 7.3 (4.2), 0.4-30.0	493 (71.8) 5.3 (3.3), 0.7-22.4	104 (81.9) 2.7 (1.8), 0.7-12.8	<0.001*
Fentanyl	602 (62.4) 0.003 (0.003), 0.000-0.019	476 (69.3) 0.002 (0.002), 0.000-0.013	117 (92.1) 0.001 (0.001), 0.000-0.005	<0.001*
Pethidine	289 (29.9) 1.8 (1.1), 0.2-11.0	176 (25.6) 1.6 (1.0), 0.4-8.0	7 (5.5) 0.9 (0.4), 0.6-1.7	0.325
Midazolam	669 (69.3) 0.10 (0.09), 0.00-0.85	483 (70.3) 0.06 (0.05), 0.02-0.36	101 (79.5) 0.04 (0.02), 0.00-0.12	<0.001*
Ketamine	0	4 (0.6) 1.2 (0.2), 0.9-1.5	0	

*statistically significant

Table 4. Mean dose of common sedative agents categorized by ASA physical status (mg/kg/hr, SD, range) problem in group 1 (age <65 years), group 2 (age 65-85 years), and group 3 (age ≥86 years)

	ASA I-II			P-value	ASA III-IV			P-value
	Group 1	Group 2	Group 3		Group 1	Group 2	Group 3	
PRO	7.5 (4.2) 0.4-30.0	5.8 (3.3) 1.1-22.4	2.9 (2.2) 0.97-12.77	<0.001*	5.0 (3.3) 1.2-18.1	4.0 (3.1) 0.7-20.4	2.6 (1.4) 0.65-9.27	0.032*
FEN	0.003 (0.003) 0.000-0.019	0.002 (0.002) 0.000-0.013	0.001 (0.001) 0.000-0.005	<0.001*	0.002 (0.001) 0.000-0.006	0.002 (0.001) 0.000-0.008	0.001 (0.001) 0.000-0.003	0.002*
PET	1.9 (1.1) 0.2-11.0	1.7 (1.1) 0.4-8.0	0.9 (0.4) 0.6-1.7	0.468	1.3 (0.6) 0.5-2.2	1.3 (0.6) 0.6-2.7	0.63 -	0.397
MID	0.10 (0.09) 0.00-0.85	0.07 (0.05) 0.02-0.36	0.05 (0.03) 0.01-0.12	<0.001*	0.06 (0.03) 0.01-0.12	0.06 (0.04) 0.02-0.30	0.04 (0.02) 0.00-0.09	0.022*
KET	0	0	0		0	1.2 (0.2) 0.9-1.5	0	

ASA: American Society of Anesthesiologists. PRO: propofol, FEN: fentanyl, PET: pethidine, MID: midazolam, KET: ketamine, *statistically significant

Table 5. Comparison of sedation and procedure related complications (number, %) in group 1 (age <65 years), group 2 (age 65-85 years), and group 3 (age ≥86 years)

Adverse events	Group 1	Group 2	Group 3	P-value
Overall	315 (32.6)	297 (43.2)	62 (48.8)	<0.001*
Respiratory	6 (0.6)	5 (0.7)	4 (3.1)	0.013*
Hypoxia (SpO ₂ <90%)	3 (0.3)	2 (0.3)	1 (0.8)	0.661
Upper airway obstruction	3 (0.3)	3 (0.4)	3 (2.4)	0.009*
Cardiovascular	304 (31.5)	289 (42.1)	56 (44.1)	<0.001*
Hypotension	261 (27.0)	256 (37.3)	54 (42.5)	<0.001*
Hypertension	10 (1.0)	7 (1.0)	0.517	
Bradycardia	21 (2.2)	16 (2.3)	1 (0.8)	0.539
Tachycardia	8 (0.8)	7 (1.0)	0.513	
Arrhythmia	4 (0.4)	3 (0.4)	1 (0.8)	0.838
Procedure related	5 (0.5)	3 (0.4)	2 (1.6)	0.278
Colonic perforation	2 (0.2)	1 (0.1)	1 (0.8)	0.368
Hemorrhage	1 (0.1)	1 (0.1)	0.897	
Pancreatitis	1 (0.1)	1 (0.1)	0.897	
Pain	1 (0.1)	0	1 (0.8)	0.051

SpO₂: oxygen desaturation, *statistically significant

Discussion

This study demonstrated that IVS for GIE even among the very elderly (≥86 years old) in the developing country is safe. Across all age groups, including those with advanced age, procedures were completed with similar procedural complications. Our observation confirms previous studies done in Western geriatric populations [9-11].

In our cohort, the very elderly patients were sicker with more co-morbid conditions. More very elderly patients had ASA physical status III or IV. In addition, these very elderly patients usually had cardiovascular diseases and renal diseases. All these factors make sedation in this group a challenge. Assessment of patients with advanced age should be thoroughly done prior to sedation for endoscopy. When endoscopy is

performed in the elderly more frequently, awareness of the different physiologic processes in the elderly must be emphasized. Elderly have increased response to sedatives with greater risks for hypoxia, respiratory depression, and apnea [2].

More colonoscopy than esophagogastroduodenoscopy (EGD) was performed under sedation in our very elderly group. This is similar to the extremely elderly cohort described by Clarke et al. [9]. However, the most common indication for colonoscopy is slightly different. In our very elderly cohort, the most common indication was lower gastrointestinal hemorrhage, a more urgent indication. In the study by Clarke et al. [9], the most common indication was surveillance for colorectal cancer, a more elective indication.

In this study, more very elderly patients underwent EGD under sedation compared with younger patient groups. A possible explanation is that very elderly patients or accompanying relatives may be more likely to request sedation. Alternatively, very elderly patients may be less tolerant to unsedated endoscopy and more likely to offer sedation to very elderly patients. The impact of unsedated endoscopy on the practice of GIE procedures for geriatric patients is complex, and large randomized controlled trials are lacking.

Sedative drugs used for IVS in geriatric patients should have a short half-life, with minimally active metabolites and limited side-effects [2]. Our sedation practice reflects that fentanyl, midazolam, and/or propofol are often used in combination in very elderly patients. Fentanyl has a short half-life and rapid onset of action, may have an advantage over pethidine in geriatric patients. Propofol has a narrower margin of safety. However, it has been shown to be safe when used in elderly patients [10, 12, 13]. Propofol is widely employed for anesthesia outside the operating room.

The modification in sedation practice required in geriatric patients is administration of fewer agents at a slower rate and with a lower cumulative dose [4]. Compared to younger patients, elderly patients may require dose reduction of midazolam and/or propofol. Heuss et al. [14] has shown that the elderly required the propofol dose equaling 35-40% of the dose administered to younger adults. The dose requirements of the different sedatives were also lower in our study. The mean doses of fentanyl, midazolam, and propofol used for very elderly patients is approximately 33 to 40% lower than the mean doses used in patients less than 65 years of age.

The present study used only standard monitoring, including an assessment of blood pressure, pulse rate, respiratory rate and pulse oximetry. We detected a relatively high overall adverse event rate, 48.8% of procedures, in very elderly patients. A majority of the complications were transient hypotensions (42.5%) which were treatable with saline resuscitation. Respiratory complications occurred in 3.1% in very elderly patients which is similar to that reported by Heuss et al. [14].

The procedural related complication rate in very elderly patients was 1.6%, similar to the rates in the younger age groups. This rate is similar to the rate of 1.4% reported by Clarke et al. [9]. The rate of colonic perforation in the very elderly patient group was 0.8%, similar to the study by Lagares-Garcia et al. [11].

The success of GIE under IVS in our cohort may be attributable to two main factors. These are anesthesia service involved with sedation in all age groups and the use of appropriate non-invasive monitoring.

In conclusion, sedation in those with advanced age especially in the very elderly group is challenging. Very elderly patients have multiple co-morbid conditions, required lower dosages of sedatives, and are more prone to sedation related complications. IVS for GIE procedures in very elderly patients can be done safely with low serious sedation related complications.

The authors have no conflict of interest to declare.

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