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BRIEF ARTICLE

Safety and effectiveness of propofol sedation during and after outpatient colonoscopy

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Abstract

AIM: To study the safety and effectiveness of propofol sedation for outpatient colonoscopy.

METHODS: Propofol was given by bolus injection with an age-adjusted standard protocol consisting of 60 mg for patients < 70 years old, 40 mg for patients age 70-89 years, and 20 mg for those ⩾ 90 years, and additional injections of 20 mg propofol were given up to a maximum of 200 mg. The principal parameters were the occurrence of adverse events within 24 h after colonoscopy and overall satisfaction for this procedure. Secondary parameters included successful procedure, respiratory depression, and other complications.

RESULTS: Consecutive patients were entered prospectively and all 2101 entered successfully completed outpatient colonoscopy. The mean dose of propofol used was 96.4 mg (range 40-200 mg). Younger patients required higher doses of propofol than older patients (20-40 years *vs* ⩾ 61 years: 115.3 ± 32 mg *vs* 89.7 ± 21 mg, $P < 0.001$). Transient supplemental oxygen supply was needed by five patients (0.2%); no other complications occurred. The questionnaires were completed by 1820 (87%) of 2101 patients and most rated their overall satisfaction as excellent (80%) or good (17%). The majority (65%) of patients drove home or to their office after their colonoscopy. Most (99%) were willing to repeat the same procedure. No incidents occurred within 24 h after colonoscopy.

CONCLUSION: Propofol sedation using a dose < 200 mg proved both safe and practical for outpatient colonoscopy.

Key words: Colonoscopy; Propofol; Colorectal cancer

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INTRODUCTION

Colorectal cancer is one of the main causes of death

from cancer in western countries and in Japan. There is no clear strategy for reducing the incidence of colorectal cancer, therefore, reduction in mortality relies on removal of premalignant lesions and detection of cancer at an early stage by colonoscopy[1,2]. In the face of increasing demands for gastroenterological services, the success of colonoscopic screening in the outpatient setting depends on patient acceptability[3]. CO_2 insufflation and the water method for unsedated colonoscopy have been shown to be more acceptable than unsedated conventional colonoscopy[4,5]. We previously demonstrated that use of a small-caliber pediatric colonoscope resulted in completed colonoscopies in patients who had an unsuccessful procedure using a standard colonoscope[6]. The use of variable stiffness colonoscopes significantly reduced procedure-related pain and the dose of propofol required for sedation during colonoscopy[7].

Recently, the feasibility and safety of endoscopist-directed propofol administration was confirmed in a study of 646 080 cases from 28 centers[8]. Endoscopist-directed propofol sedation refers to administration of propofol by a non-anesthesia specialist under the direct supervision of the endoscopist performing the endoscopic procedure. Propofol sedation for colonoscopy was shown to be superior to other sedation methods in that propofol was associated with a low incidence of cardiopulmonary complications and was superior to benzodiazepines with regard to rapidity of both induction of sedation and recovery[9-11].

These results have been confirmed by meta-analysis[12]. We have previously reported that propofol sedation was both safe and practical for diagnostic esophagogastroduodenoscopy and endoscopic procedures in patients aged ≥ 90 years[13-16]. In addition, we have allowed our patients to drive home after colonoscopy, based on the experience with diagnostic esophagogastroduodenoscopy in our endoscopy unit[13,14]. Here, we report a prospective evaluation of the safety and effectiveness of propofol sedation with follow-up for 24 h after outpatient colonoscopy.

MATERIALS AND METHODS

Patients

The study was done at the Showa Inan General Hospital and included outpatients who underwent only colonoscopy. Emergency procedures were excluded. Patients were also excluded if they were < 20 years old, pregnant, assigned to American Society of Anesthesiologists (ASA) class Ⅲ and Ⅳ, overweight (> 100 kg), or allergic to the drugs used or their components (soybeans or eggs). Routine standard monitoring at this unit included continuous assessment of peripheral oxygen saturation (SpO_2) and heart rate. Clinical assessment of the patients included measurement of respiratory effort by visual assessment and by palpation of the chest wall and abdominal excursion and/or palpation of exhaled breath. When oxygen desaturation (SpO_2 < 90%) continued for > 20 s, supplemental oxygen was given. The endoscopic team consisted of the nurse who administered the drugs and was responsible for the patient, the endoscopist, and a second nurse to assist the endoscopist and the patient-monitoring nurse.

Propofol was administered for endoscopic sedation by nurses supervised by endoscopists. Both the nurses and endoscopists had advanced cardiac life support certification, advanced airway training, didactic training on propofol, observation of cases, and supervised administration of propofol by anesthesiologists before beginning propofol administration supervised by the endoscopist. The training period typically lasted about 2 wk.

The study was conducted in accordance with the Helsinki Declaration and was approved by the ethics committee at the hospital. Verbal and written informed consent was obtained from all patients.

All colonoscopies were performed by six skilled endoscopists (Horiuchi A, Nakayama Y, Kajiyama M, Kato N, Kamijima T, Ichise Y) who each perform > 300 colonoscopies/year. All the procedures were conducted under propofol sedation (AstraZeneca, Osaka, Japan)[13,14]. The standard bowel preparation was a polyethylene glycol solution (Ajinomoto Pharmaceutical Co, Tokyo, Japan).

Study design

Colonoscopy was performed in the lateral decubitus position. A butterfly needle for the bolus injection of propofol was placed on the patient's forearm shortly before the start of colonoscopy and was removed after completion of the procedure. Propofol was given by bolus injection with an age-adjusted standard protocol of 60 mg for patients aged < 70 years, 40 mg for patients aged 70-89 years, and 20 mg for those aged ≥ 90 years. Adequate sedation was considered achieved when the patients passed through the following sequence: eyes closing, one or two yawns, and cessation of body movements. The target level of sedation was moderate conscious sedation with the patients still being able to respond purposefully to verbal commands. When the target level was not obtained or the patients were undersedated, additional injections of 20 mg propofol were given up to a maximum of 200 mg.

A decline in SpO_2 to < 90% that continued for > 20 s was regarded as respiratory depression associated with sedation. Vital signs were frequently assessed but not on a periodic basis. In addition to monitoring of vital signs, the patient's condition was assessed more globally by visual inspection. Monitoring and complications were recorded by a registered nurse. SpO_2 was routinely captured by visual inspection of the monitor and the value was recorded on the vital sign sheet.

After the procedure, patients were moved to a waiting room after they could stand by themselves and they were discharged after they were fully awake. Full recovery, including consciousness and psychomotor function was assessed using three criteria: (1) Level of consciousness (fully awake and responding to questions from the recov-

Table 1 Demographic and clinical data in 2101 patients who underwent colonoscopy using propofol sedation

	n (%)
Sex: Male	1149 (55)
Mean age (range) (yr)	66 (20-94)
Mean body weight (range) (kg)	56.7 (32-98)
Indication	
Screening	785 (37)
Hemopositive stool	538 (26)
Abdominal symptoms	406 (19)
Hematochezia	140 (7)
Surveillance	133 (6)
Anemia	70 (3)
Others	29 (1)
Propofol dose (mg):	
About 40	110 (5)
60	239 (11)
80	623 (30)
100-120	973 (46)
140-160	131 (6)
180-200	25 (1)
Successful procedure	2101 (100)
Mean procedure time (range) (min)	14 (8-46)
Oxygen administered	5 (0.2)
Mask ventilation required	0 (0)
Heart rate < 50 beats/min	0 (0)
Complications	0 (0)
Full recovery 60 min after the procedure	2101 (100)

Values are numbers (percentages) of patients except for mean age, mean body weight, and mean procedure time.

ery room nurse); (2) Ability to stand on one-foot; and (3) Ability to walk in a straight line without instability for 5 m. These three criteria were assessed every 15 min starting 30 min after the procedure; full recovery was defined as meeting all three criteria. The nurses reconfirmed the absence of re-emerging sedative effects and finally permitted patients to leave the endoscopic unit.

In addition, we provided questionnaires. Within 2 wk after the procedure, patients were contacted by telephone and asked about overall satisfaction for this procedure, whether they drove home or to their office after colonoscopy, the occurrence of any accidents within 24 h after colonoscopy and their willingness to repeat the same procedure next time (yes/no).

Study parameters

The principal parameters were the occurrence of adverse events within 24 h after colonoscopy and overall satisfaction for the procedure. Secondary parameters included successful procedure, respiratory depression, and other complications. Respiratory depression was defined as the need of oxygen supply due to an oxygen desaturation (SpO_2 < 90%) that continued more than 20 s.

Instruments

The Olympus PCF-Q260AI videoscope used has an insertion diameter of 11.3 mm, an accessory channel diameter of 2.8 mm, a total length of 1335 mm, and a working length of 1030 mm.

Table 2 Relationship between age or sex and dose of propofol used in 2101 patients who underwent colonoscopy

Age (yr)	No. (M/F)	Propofol dose (mg)			*P* value
		Total (range)	Male	Female	
20-40[1]	150 (89/61)	115.3 ± 32 (40-200)	113.4 ± 27	118.2 ± 24	0.43
41-60	563 (316/247)	107.7 ± 27 (40-200)	106.9 ± 28	108.7 ± 25	0.19
⩾ 61	1388 (744/644)	89.7 ± 21 (40-200)	87.7 ± 23	92.1 ± 19	0.32
Total	2101 (1149/952)	96.4 ± 27	95.0 ± 26	98.1 ± 25	0.18

Values are mean ± SD except for number of patients and range of dose used of propofol. *P* value shows the difference between male and female patients. [1]There were significant differences in the doses of propofol in each group between age 20-40 and ⩾ 61 years ($P < 0.001$).

Statistical analysis

Data are presented as mean ± SD. The χ^2 test, with Yates' correction for continuity where appropriate, was used for comparison of categorical data. Fisher's exact test was used when the numbers were small. For parametric data, Student's *t* test was used when two means were compared. Analysis of variance was used when the three groups were compared and positive results were confirmed using Tukey's Honestly Significantly Different procedure. A value of $P < 0.05$ was regarded as significant. Statistical analysis was performed by using JMP® 9.0.2 version software (SAS Institute Inc., Cary, NC, United States).

RESULTS

Between January 2010 and December 2010, 2101 consecutive patients received outpatient colonoscopy based on a standard protocol of age-adjusted doses of propofol (Table 1). All procedures were completed successfully. The patients' ages ranged from 20 to 94 years. The most common indications for colonoscopy were: colorectal cancer screening in 785 (37%), hemopositive stools in 538 (26%), and abdominal symptoms in 406 (19%). Mean procedure time was 14 min (range, 8-46 min). A biopsy and/or polypectomy was performed in 775 patients (37%). Oxygen desaturation requiring supplemental oxygen (1-3 L/min) occurred in 0.2% (five patients); mask ventilation or endotracheal intubation was not required in any case. In no case did respiratory event or laryngospasm occur. No other complications occurred (Table 1). Full recovery within 60 min after the procedure was present in 100%.

The mean dose of propofol used was 96.4 mg (Table 2). There were no significant differences in the dose of propofol used between men and women (95.0 ± 26 mg *vs* 98.1 ± 25 mg, $P = 0.18$), however younger patients required higher doses of propofol than older patients (20-40 years *vs* ⩾ 61 years, 115.3 ± 32 mg *vs* 89.7 ± 21 mg, $P < 0.001$). Of the 2101 patients, 495 (24%) had at least an adenoma detected. Fifty-two (3%) had invasive colorectal cancer. Colorectal adenomas with high-grade dysplasia were found in 32 (2%) patients. The detection rate of adenoma in this study was 53 adenomas/100

Table 3 Demographic data and results of questionnaires in 1820 patients who underwent colonoscopy using propofol sedation

Sex: Male	954 (52)
Mean age (range) (yr)	65 (33-80)
Mean body weight (range) (kg)	58.7 (45-98)
Did you find propofol sedation for your colonoscopy satisfactory?	
Excellent	1456 (80%)
Good	309 (17%)
No	11 (0.6%)
NA	8 (2.4%)
Did you drive home or to the office after your colonoscopy?	
Yes	1183 (65%)
No	637 (35%)
Did you experience any accidents within 24 h after your colonoscopy?	
Yes	0 (0%)
No	1820 (100%)
Do you want to repeat the same procedure next time?	
Yes	1805 (99%)
No	15 (1%)

Values are numbers (percentages) of patients except for mean age and mean body weight. NA: Not available.

colonoscopies. Adenomas were distributed evenly in the colon and rectum.

The questionnaires were completed by 1820 (87%) of 2101 patients (Table 3). Their mean age and mean body weight were 65 years and 58.7 kg. The majority rated their overall satisfaction for this procedure as excellent (80%) or good (17%). The majority (65%) of subjects drove home or to their office after their colonoscopy. No associated incidents within 24 h after colonoscopy occurred. Most (99%) were willing to repeat the same procedure.

DISCUSSION

This study describes the safety and outcomes of propofol sedation given to 2101 patients for outpatient colonoscopy. Previous studies have involved propofol dosages ranging from 60 to 300 mg using an indwelling catheter for endoscopic sedation[9-12,17-21]. In the present study, the mean dose of propofol used was 96.4 mg, which corresponded to that of a previous study in the Japanese population[17]. On the basis of our pervious experiences[13,14], the protocol adopted here focused on safety with the initial dose of 40 or 60 mg propofol designed to minimize hypoxemia during the procedure; only 0.2% required oxygen, which is less than previous studies[9-12]. No subject required mechanical ventilation during the procedures via either endotracheal intubation or a mask (Table 1). The routine use of supplemental oxygen during colonoscopy may mask respiratory depression[22], therefore, we chose to administer supplemental oxygen only when needed. No subjects experienced bradycardia (heart rate < 50 beats/min). Other studies with low-dose propofol have reported rates of bradycardia up to 10%[23]; the differences may relate to difference in the sedation method because studies with bradycardia have typically used a combination of propofol, midazolam and meperidine. All procedures were done with pediatric variable stiffness colonoscope, thus, it is impossible to assess whether the pediatric variable stiffness colonoscope, or the lower dose of propofol required, was responsible for the low incidence of cardiopulmonary depression.

Generally, patients are not permitted to drive themselves within the first day after endoscopic sedation. Riphaus *et al*[24] have reported that current recommendations that patients should be refrain from driving and unescorted use of public transport for 24 h after sedation may need to be reconsidered in patients who receive propofol sedation. Based on our previous study using a driving simulator showing that driving ability recovered to the basal level within 60 min of low-dose propofol sedation[13], patients have been permitted to drive themselves after colonoscopy as well as esophagogastroduodenoscopy at our endoscopy unit. In this study, the majority (65%) of patients drove home or to their office after their colonoscopy. No sedation-associated incidents within 24 h after colonoscopy occurred in the 1820 subjects responding.

Our recent study used a number connection test and a driving simulator test to assess psychomotor recovery before and 1 h and 2 h after colonoscopy[25]. Psychomotor recovery was evident as early as 1 h after propofol sedation. Additional studies are needed before it can be routinely recommended that patients be permitted to drive home after endoscopy using only propofol sedation. Effective endoscopic sedation depends on the type of procedure and the procedure time. In most patients, an appropriate level of sedation can be reached through the use of a benzodiazepine combined with a narcotic. In contrast, we gave propofol by bolus titration with an initial dose of 40-60 mg followed by dose of 20 mg beginning 30-60 s later. The appropriateness of additional bolus doses was determined by the level of sedation and the respiratory effect. When moderate conscious sedation was not obtained or the patients were undersedated, additional injections of 20 mg propofol were given up to a maximum of 200 mg; 180-200 mg were required in only 25 patients (1.2%). The advantages of propofol using a butterfly needle include immediate onset of action and fast recovery, which likely contributed to the high level of acceptability and cost-effectiveness for outpatient colonoscopy. In our facility, a butterfly needle has been used instead of an indwelling cannula for about 60 000 patients. Even if a patient in conscious sedation moves his/her arm, the butterfly needle is usually placed stably in the vein. This butterfly needle method is thought to be a safe and practical way to administer propofol over 15-30 min.

The average procedure time was 14 min and the detection rate of adenoma was 24% as the proportion of patients in whom at least one adenoma was identified in this study. The adenoma detection rate that was reported to be an independent predictor of the risk of interval colorectal cancer after screening colonoscopy was compatible to our

data[26]. Therefore, this sedation method is likely an important variable in ensuring quality in colonoscopy.

Unsedated colonoscopy is still the main type of procedure in many countries. Even if sedation is safe, it requires an extra nurse and a team educated for monitoring, resulting in higher costs. The requirement for an escort and time burden of recovery from sedation are both barriers to the acceptance of screening colonoscopy. Improved acceptance of colonoscopy is important to allow full use of colonoscopy in cancer screening and prevention. Colonoscopy can be completed without sedation in the majority of patients and undoubtedly there is a place for unsedated colonoscopy, especially in areas where cost containment is a primary concern[27-29].

This study had some limitations. The sedation level was assessed using minimal, moderate, and deep sedation on the basis of the ASA level[30], but this was not recorded for each patient during the study. Although the patients may have had amnesia after propofol sedation, the questionnaire in this study did not include any questions related to amnesia. Blood pressure monitoring was not routinely performed in this study. Blood pressure monitoring is generally a standard practice whenever administering propofol in the United States but not in Japan. We were therefore unable to comment on episodes of hypotension in our series. The monitoring used (e.g., continuous assessment of SpO_2 and heart rate) is the standard in Japan.

In conclusion, propofol sedation was associated with good acceptance of colonoscopy and willingness to repeat the procedure and enabled patients to drive home safely by themselves after colonoscopy. Propofol sedation using a dose < 200 mg was safe and practical. Increased use of this sedation method may improve the acceptability of colonoscopy, which may enable population wide screening and decrease colorectal cancer mortality.

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COMMENTS

Background

Despite the increasing usage of short-acting sedatives, the recommendations that patients should refrain from driving and the unescorted use of public transport for 24 h after sedation remain unchanged. The authors previously reported that recovery after low-dose propofol sedation for diagnostic esophagogastroduodenoscopy was such that the patients were able to drive home. In addition, the recent study using a number connection test and a driving simulator test demonstrated that psychomotor recovery was evident as early as 1 h after propofol sedation for outpatient colonoscopy.

Research frontiers

The authors report a prospective evaluation of the safety and effectiveness of propofol sedation with follow-up for 24 h after outpatient colonoscopy.

Innovations and breakthroughs

Propofol sedation was associated with good acceptance of colonoscopy and willingness to repeat the procedure and enabled patients to drive home safely by themselves after colonoscopy. Propofol sedation using a dose < 200 mg was safe and practical. Increased use of this sedation method may improve the acceptability of colonoscopy, which may enable population-wide screening and decrease colorectal cancer mortality.

Applications

The findings in this study indicate that patients sedated with propofol may be capable of safely driving 1 h after colonoscopy. The ability to drive home after sedation reduces the need for an accompanying individual and thus lowers the costs and burden associated with endoscopy.

Peer review

This is a well-written paper providing new data on safety of propofol sedation and new information about patients checking out and driving home after propofol sedation.

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