*Article*

# For Same-Day Bidirectional Endoscopy in Children, Propofol-based Sedation Shortened the Patient Time Requirement Compared to Midazolam

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**Abstract:** The aim of this study was to compare the effectiveness of propofol-based sedation and midazolam sedation in same-day bidirectional endoscopy (BDE) in children. The charts of children (≤15 years old) who had undergone same-day BDE were retrospectively reviewed. Demographic data, indications, sedatives and their dosages, clinical outcomes, endoscopic findings, adverse events, and patient time requirements were compared in cases with propofol-based and midazolam sedation. A total of 91 children [51 boys, mean age 13 years (range 9-15)] were enrolled. Propofol alone or in combination with midazolam and/or pentazocine was given in 51 (propofol-based sedation group) while midazolam alone or in combination with pentazocine was given in 40 (midazolam sedation group). The mean doses of propofol, midazolam and pentazocine were 96 mg (range 40–145 mg), 4.1 mg (range 3–5 mg) and 7.5 mg in the propofol group while the mean doses of midazolam and pentazocine were 6.2 mg (range 4–10 mg) and 15 mg in the midazolam group, respectively. The total procedure times and endoscopic findings between the two groups were similar, but the median patient time requirement in the propofol group was significantly shorter than that of the midazolam group (7.3 h vs. 8.4 h, P<0.001). No adverse events occurred in either group. Propofol-based sedation shortened patient time requirements in same-day BDE compared with midazolam sedation in children.

**Keywords:** bidirectional endoscopy; children; propofol; patient time requirements

## Introduction

The effectiveness of same-day bidirectional endoscopy, i.e., the execution of both esophagogastroduodenoscopy (EGD) and colonoscopy procedures, has been previously reported in adults [1–3]. The benefits include a shorter hospital stay, reduced medical costs, and a reduction of the total sedation dose. Regardless of which comes first, EGD or colonoscopy, same-day bidirectional endoscopy may also contribute to quicker diagnosis of gastrointestinal disease such as gastrointestinal bleeding, inflammatory bowel disease, or eosinophilic gastroenteritis, and arguably improves the quality of health care [4].

Propofol is a short-acting sedative drug with a short recovery time [5]. Based on its characteristics, we have previously reported that propofol sedation is safe and that recovery including driving ability occurs within 60 min [6]. In addition, we demonstrated that our hospital has safely established the policy of routine discharge of healthy subjects to normal activity 1 hour following sedated EGD or colonoscopy using propofol sedation

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[7,8,9]. We previously reported the results of our 11-year experience based on the hospital policy and showed the safety and effectiveness of propofol sedation for outpatient EGD or colonoscopy in adults [10]. This hospital policy may have contributed to a decrease in the patient time requirement for this dual procedure. The "patient time requirement" includes all phases of the patient's involvement: in-hospital bowel preparation, waiting and preparing, procedure, and recovery.

Propofol has successfully been utilized during endoscopic procedures in children [11,12,13,14]. We found that propofol-based sedation for EGD greatly improved visualization of the Z line using induction of esophageal peristalsis in children and adolescents [15]. In addition, sedation practices could reduce the time requirement for these patients. However, there is no available data on the effectiveness and safety of propofol sedation for bidirectional endoscopy in children. The aim of this study was to compare the effectiveness of propofol-based and midazolam sedation for same-day bidirectional endoscopy in children.

## 2. Materials and Methods

### *2.1. Study design*

This was a retrospective, cross-sectional analysis of endoscopy results from a single center (Showa Inan General Hospital in Komagane, Japan). The Institutional Review Board of the hospital approved the retrospective chart review study protocol on December 15, 2022 (2022-05). All subjects or their guardians had given written informed consent for the original procedures. The study was conducted in accordance with the latest version of the Helsinki Declaration. In addition, we confirmed that all examinations in this study were performed in accordance with relevant guidelines/regulations [16].

### *2.2. Patients*

Cases of children between the ages of 9 and 15 who had undergone diagnostic bidirectional endoscopy (EGD + colonoscopy) with either propofol-based or midazolam sedation at the Digestive Disease Center, Showa Inan General Hospital between January 2005 and December 2022 were enrolled. The indications for bidirectional endoscopy were gastrointestinal symptoms (recurrent abdominal pain, vomiting, nausea, regurgitation, and dyspepsia), screening and surveillance for peptic ulcer, inflammatory bowel disease or eosinophilic gastroenteritis, gastrointestinal bleeding, and anemia. Patients with therapeutic endoscopy including foreign body removal, hemostasis, and percutaneous endoscopic gastrostomy or endoscope-guided duodenal tube placement were excluded. Repeat bidirectional endoscopies on already-included subjects were included but counted as separate cases. Data regarding age, gender, weight, height, indications for bidirectional endoscopy, drugs used, endoscopic findings, and adverse events were obtained from electronic medical records.

### *2.3. In-hospital bowel preparation method*

All subjects were allowed regular meals the day before; no pretreatment was required the day before colonoscopy. The regimen used in our hospital involved the first intake of 5-10 mL of sodium picosulfate and/or 50 g of magnesium citrate (Horii Pharmaceutical Co., Tokyo, Japan) dissolved in 0.2 L of water, and the subsequent intake of 0.2 L of PEG-Asc +0.2 L of water repeated 6-7 times with 15 minutes between administrations.

### *2.4. Procedures*

All bidirectional endoscopies in this study were carried out without tracheal intubation and were performed by experienced endoscopists. The sedation drugs and dosages and the sequence of EGD and colonoscopy were determined at the endoscopist's discretion. EGDs or ileocolonoscopies were performed using either a small caliber or standard upper endoscope (GIF-XP 240, XP260, or H290; Olympus, Tokyo, Japan) or PCF-Q260AZI, or PCF-H290ZI; Olympus, Tokyo, Japan) with an endoscopic video information system

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(CV 240, CV260, or CV290, Olympus, Tokyo, Japan). The endoscopic images were recorded by both computer image and a text reporting system. All patients had cardiovascular monitoring and continuous oximeter measurement. Respiratory or cardiovascular complications were recorded by the nurse at the time of the procedure. Supplemental oxygen was given to all patients to maintain oxygen desaturation levels above 93% during endoscopic procedures.

### *2.5. Evaluated outcomes*

Demographic data, indications, anesthetic drugs and dosages, endoscopic sequence, procedure times, adverse events, endoscopic findings and total patient time requirements (the total time in which patients stay in our hospital) were compared between cases with propofol-based sedation or and midazolam sedation.

### *2.6. Statistical analysis*

Differences in the categorical variables were analyzed using chi-square tests or, when appropriate, Fisher's exact test. The continuous data were expressed as means ± SDs and were compared using Student's *t* -test. Non-parametric data were analyzed by Wilcoxon rank sum test. Statistical significance was taken as a two-sided p-value <0.05. The statistical analyses were performed using GraphPad Prism ver. 9.3.1 (GraphPad Software, La Jolla, CA, USA).

## 3. Results

### *3.1. Characteristics of the enrolled patients and sedation drugs used*

Table 1 shows baseline characteristics and indications in pediatric patients with bidirectional endoscopy in the propofol-based sedation and midazolam sedation groups. A total of 91 children [51 boys, mean age 13 years (range 9–15)] were enrolled. The demographic characteristics and indications were similar between the two groups. Propofol alone or in combination with midazolam and/or pentazocine was administered in 51 patients (propofol-based sedation group) while midazolam alone or in combination with pentazocine was given in 40 patients (midazolam sedation group) (Table 2). The mean doses of propofol, midazolam and pentazocine were 96 mg (range 40–165 mg), 4.1 mg (range 3–5 mg) and 7.5 mg in the propofol-based sedation group while the mean doses of midazolam and pentazocine were 6.2 mg (range 4–10 mg) and 15 mg in the midazolam sedation group.

Table 1. Baseline characteristics and indications in pediatric patients with bidirectional endoscopy with either propofol-based sedation or midazolam sedation

| **Group** | **Propofol-based** | **Midazolam** | ***p* value** |
|---|---|---|---|
| Number of patients | 51 | 40 | |
| Mean (SD) age (yr) * | 12.7(1.8) | 13.1(1.5) | 0.54 |
| Gender (boy)** | 30 | 21 | 0.67 |
| Mean body height (cm)* | 158 | 154 | 0.29 |
| Mean body weight (kg)* | 47.1 | 45.1 | 0.28 |
| Indications:** | | | 0.33 |
| GI symptoms | 39 | 29 | |
| Screening | 4 | 3 | |
| Surveillance | 2 | 6 | |
| GI bleeding | 5 | 2 | |
| Anemia | 1 | 0 | 0 |

GI: gastrointestinal. *Differences between propofol-based sedation group and midazolam sedation group compared by Student's t-test for continuous variables. **Differences between propofol and midazolam groups compared by chi-square test or, when appropriate, Fisher's exact test for categorical data.

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**Table 2.** Sedation drugs and doses used in pediatric patients with bidirectional endoscopy with either propofol-based sedation or midazolam sedation.

| Group | Propofol-based. (N=51) | Midazolam (N=40) | *p* value |
|---|---|---|---|
| Sedation drugs and doses used: | | | |
| Propofol alone (40-145 mg) | 8 | | |
| Propofol + pentazocine 7.5 mg | 2 | | |
| Propofol + midazolam 3-5 mg | 29 | | |
| Propofol + midazolam 4 mg | 12 | | |
| + pentazocine 7.5 mg | | | |
| Midazolam (4-10 mg | | 5 | |
| Midazolam (4-10 mg) | | | |
| + pentazocine (15 mg) | | 35 | |
| Mean propofol (mg) | 96 | | |
| Mean midazolam (mg) | 4.1 | 6.2 | <0.001 |
| Mean pentazocine (mg | 7.5 | 15 | <0.001 |

Differences between propofol-based sedation group and midazolam sedation group compared by Student's t-test for continuous variables.

*3.2. Clinical outcomes of enrolled patients*

Table 3 shows clinical outcomes in pediatric patients with bidirectional endoscopy with either propofol-based sedation or midazolam sedation. Although the endoscopic sequence differed significantly between the two groups (<0.001), the mean EGD procedure time, mean colonoscopy time and mean total procedure time were similar between the two groups. No adverse events such as cardiopulmonary events, perforation, nausea, or vomiting occurred in either group in this study (Table 3).

Table 4 shows endoscopic findings in pediatric patients with bidirectional endoscopy with either propofol-based sedation or midazolam sedation. There were no significant differences in EGD or colonoscopy endoscopic findings between the two groups.

**Table 3.** Clinical outcomes in pediatric patients with bidirectional endoscopy with either propofol-based sedation or midazolam sedation.

| Group | Propofol-based. (N=51) | Midazolam (N=40) | *p* value |
|---|---|---|---|
| Endoscopic sequence:** | | | |
| EGD to colonoscopy | 19 | 30 | <0.001 |
| Colonoscopy to EGD | 2 | 6 | |
| Mean EGD procedure time, min* | 9 | 8 | 0.34 |
| Mean colonoscopy procedure time, min* | 17 | 15 | 0.54 |
| Cecal intubation rate, %** | 94.1 | 97.5 | 0.50 |
| Mean cecal intubation time, min* | 9 | 6 | 0.44 |
| Mean withdrawal time, min* | 8 | 8 | 0.88 |
| Mean total procedure time, min* | 27 | 23 | 0.65 |
| Biopsy taken** | 48(94%) | 40(100%) | 0.25 |
| Mask ventilation required | 0 (0%) | 0 (0%) | |
| Heart rate <50 beats/min | 0 (0%) | 0 (0%) | |
| Perforation | 0 (0%) | 0 (0%) | |
| Nausea and vomiting | 0 (0%) | 0 (0%) | |

GI: gastrointestinal, EGD: esophagogastroduodenoscopy. *Differences between propofol group and midazolam group compared by Student's t-test for continuous variables. **Differences between propofol group and midazolam group compared by chi-square test or, when appropriate, Fisher's exact test for categorical data.

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**Table 4.** Endoscopic findings in pediatric patients with bidirectional endoscopy with either propofol-based sedation or midazolam sedation.

| Group | Propofol-based. (N=51) | Midazolam (N=40) | *p* value |
|---|---|---|---|
| EGD | | | |
| Normal | 27 | 17 | 0.29 |
| Reflux esophagitis | 9 | 15 | |
| Chronic gastritis | 6 | 1 | |
| Duodenal ulcer & duodenitis | 4 | 5 | |
| Crohn's disease | 2 | 2 | |
| Eosinophilic gastroenteritis | 1 | 2 | |
| Others | 6 | 6 | |
| Colonoscopy | | | 0.43 |
| Normal | 30 | 32 | |
| Ulcerative colitis | 6 | 2 | |
| Crohn's disease | 2 | 3 | |
| Proctitis | 2 | 1 | |
| Nonspecific colitis | 3 | 1 | |
| Others | 4 | 1 | |

EGD: esophagogastroduodenoscopy. Differences between propofol group and midazolam group compared by chi-square test or, when appropriate, Fisher's exact test for categorical data.

*3.5. Patient time requirements*

Table 5 shows patient time requirements in pediatric patients with bidirectional endoscopy with propofol-based sedation or midazolam sedation. With regard to median durations of in-hospital bowel preparation, waiting and preparing, and the sum of the two endoscopy procedures themselves, there were no significant differences between the two groups. However, the median total patient time requirement, including these three components plus the recovery time, was significantly shorter in the propofol-based group than the midazolam group (7.3 h vs. 8.4 h, P<0.001). Note that the recovery time could not be precisely measured because our hospital has no specific recovery room.

**Table 5.** Patient time requirements in pediatric patients with bidirectional endoscopy with either propofol-based sedation or midazolam sedation.

| Median number of hours (range) | | | |
|---|---|---|---|
| **Group** | **Propofol-based. (N=51)** | **Midazolam (N=40)** | ***p* value** |
| In-hospital bowel preparation | 3.2(3-5) | 3.5(3-5) | 0.57 |
| Waiting and preparing | 1.5(1-2) | 1.8(1-2) | 0.42 |
| Total procedure time | 0.5 | 0.5 | 0.73 |
| Total patient time requirements | 7.3(6-9) | 8.4(7-10) | <0.001 |

EGD: esophagogastroduodenoscopy. Total patient time requirements: the total staying time in which patients stayed in our hospital for bidirectional endoscopy.

Differences between propofol group and midazolam group compared by Wilcoxon rank sum test.

**4.. Discussion**

Patient time requirements in clinical practice are always critical. This study demonstrated that patient time requirements in bidirectional endoscopy depended on the sedation agents used. As shown in Table 2, the mean doses of midazolam and pentazocine

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used in the propofol-based sedation group were much less than those of midazolam group (4.1 mg and 7.5 mg in propofol group vs. 6.2 mg and 15 mg in midazolam group). Because of the obstacles to measuring "recovery time" per se from the existing medical records, we simply evaluated the total patient time requirement, essentially the time spent in the hospital, in this study. As a result, we found that the median total patient time requirement in the propofol-based sedation group was significantly shorter than that of the midazolam sedation group (7.3 h vs. 8.4 h, P<0.001), although no significant between-group differences were found for three of the four components of total patient time requirement: i.e., the in-hospital bowel preparation time, the waiting and preparing time, and the total procedure time. The most likely reason is that the use of propofol allowed a decrease in the dose of midazolam and/or pentazocine, resulting in a decrease in the recovery time required. Midazolam, a sedative, and pentazocine, an anesthetic with sedation effects, are longer-acting than propofol, and are generally given together for a synergistic effect; however, the synergistic effect of these drugs also delays recovery, necessitating a longer hospital stay. Our previous study using a driving simulator demonstrated that driving ability recovered to the basal level within 60 min of propofol sedation [6,8,9]. In addition, after a propofol-only dose < 200 mg, psychomotor recovery was confirmed at 1 hour after colonoscopy using the number connection test and a driving simulator test [9]. Therefore, children enrolled in this study also may have been permitted to go home or to school after propofol-based sedation sooner than after midazolam sedation at our endoscopy unit.

As various sedation protocols were included in this study, they were classified as either propofol-based or midazolam sedation. Although propofol-based sedation group included midazolam, the effectiveness of sedation protocols was compared based on the presence or absence of propofol in this study. Both propofol and midazolam doses are usually expressed per kg body weight. However, propofol or midazolam was nurse-administered by bolus injection using an age-adjusted standard protocol in our previous studies [6-10]. As there were no significant differences in both body heights and body weights between the two groups (Table 1), comparisons of mean doses of sedation drugs used in this study may be accepted. In addition, there were not any hospital guidelines or local policy in placeprescribing a particular sedation protocol which may bias the results.

It was previously reported that same-day bidirectional endoscopy with administration of midazolam and pethidine significantly increases the incidence of hypoxia and post-endoscopic nausea compared to propofol administration [17]. Nausea and vomiting might be the result of stimulation of the medullary chemoreceptor trigger zone by pethidine [18]. The observed sex differences in that prior study may be explained by the presence of different socialization processes for men and women influencing their respective willingness to communicate distress [19]. Other possible explanations include the interaction between opioids and the sexual hormonal fluctuations associated with the menstrual cycle [18]. In this study nausea and vomiting were not recognized as adverse events in enrolled children, irrespective of the sedation used. However, mild post-endoscopic nausea may have occurred, and it may have delayed recovery as greater doses of midazolam and pentazocine were used in the midazolam sedation group than the propofol-based sedation group.

In addition, the financial balance of sedation depends on the drugs used [20]. Even if sedation is safe, it requires an extra nurse and a team educated for monitoring, resulting in higher costs when the recovery time is long. In this study the social costs of conventional sedation with the combination of midazolam and pentazocine, such as increased recovery time, inability to go home or return to school, and need for a companion may have been higher than those of propofol-based sedation.

Based on a systematic review and meta-analysis, the optimal sequence of same-day bidirectional endoscopy is EGD followed by colonoscopy [4]. In this study, sequences of bidirectional endoscopy were significantly different between the two groups. However, sequences of bidirectional endoscopy were not associated with the total patient time requirements, because the sequence did not affect recovery time after sedation.

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In the U.S. bowel preparation is done by the patient at home. Typically in the U.S. it is "no food for 12 hours, plus use of magnesium citrate". On the other hand, bowel preparation is commonly an in-hospital experience in Japan. In this study all subjects were allowed regular meals the day before; no pretreatment was required the day before colonoscopy. As all children experienced bowel preparation in our hospital, we described our bowel preparation method as "in-hospital bowel preparation".

This study has some limitations. It was retrospective and was conducted at an endoscopy unit in a community hospital in Japan where nurses and technicians were highly trained. The number of pediatric patients enrolled in this study was small. In addition, it might be not possible to eliminate the influence of the patients' background or other potential confounding factors. The recovery time was not measured directly. A follow-up study should be performed prospectively to confirm and clarify the characteristics of adverse events after bidirectional endoscopy.

## 5. Conclusions

The benefits of same-day bidirectional endoscopy in children may be enhanced by propofol-based sedation rather than midazolam sedation because of the shorter patient time requirement.

**Author Contributions:** Study concept and design; S.N., T.K., A.H., data acquisition; S.N., A.H., data analysis and interpretation; S.N., T.K., A.H., drafting of the manuscript; S.N., T.K., A.H., critical revision of the manuscript for important intellectual content; S.N., T.K., I.H, K.Y, S.K. and A.H., statistical analysis; A.H., obtained funding; A.H. All authors have read and agreed to the published version of the manuscript.

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**Institutional Review Board Statement:** I The study was conducted in accord with the latest version of the Helsinki Declaration and was approved by the Showa Inan General Hospital's Ethics Committee on December 15, 2022 (2022-05). In addition, we confirmed that all examinations in this study were performed in accordance with relevant guidelines/regulations. All authors had access to the study data and reviewed and approved the final manuscript.

**Informed Consent Statement:** All subjects or their guardians had given written informed consent for the original procedures. .

**Data Availability Statement:** The data underlying this article will be shared on reasonable request to the corresponding author.

**Conflicts of Interest:** The authors declare no competing interests.

## References

1. Cao Y, Yang J, Li J, et al. Comparison of procedural sequences in same-day painless bidirectional endoscopy: Single-center, prospective, randomized study. Dig. Endosc. 2017; 29: 330–7.
2. Chen SW, Cheng CL, Liu NJ et al. Optimal procedural sequence for same-day bidirectional endoscopy with moderate sedation: A prospective randomized study. J. Gastroenterol. Hepatol. 2018; 33: 689–95.
3. Sui Y, Chen X, Ma T, et al. Comparison of three sedation models for same-day painless bidirectional endoscopy: A multicenter randomized controlled trial. J Gastroenterol Hepatol. 2022; 37:1603–1609
4. Laoveeravat P, Thavaraputta S, Suchartlikitwong S, et al. Optimal sequences of same-visit bidirectional endoscopy: Systematic review and meta-analysis. Dig Endosc. 2020; 32: 706–14.
5. Riphaus A, Gstettenbauer T, Frenz MB, etal. Quality of psychomotor recovery after propofol sedation for routine endoscopy: a randomized and controlled study. Endoscopy 2006; 38: 677–683.
6. Horiuchi A, Nakayama Y, Katsuyama Y, et al. Safety and driving ability following low-dose propofol sedation. Digestion 2008;78:190–4.
7. Horiuchi A, Nakayama Y, Hidaka N, et al. Low-dose propofol sedation for diagnostic esophagogastroduodenoscopy: results in 10,662 adults. Am J Gastroenterol. 2009;104: 1650–5.
8. Horiuchi A, Nakayama Y, Kajiyama M, et al. Safety and effectiveness of propofol sedation during and after outpatient colonoscopy. World J Gastrointest 2012;18:3420–5.
9. Horiuchi A, Nakayama Y, Fujii H, et al. Psychomotor recovery and blood propofol level in colonoscopy when using propofol sedation. Gastrointest Endosc 2012;75:506–12.

 doi:10.20944/preprints202306.0650.v1


10. Sato M, Horiuchi A, Tamaki M, et al. Safety and effectiveness of nurse-administered propofol sedation in outpatients undergoing gastrointestinal endoscopy. Clin Gastroenterol Hepatol. 2019; 17;1098–1104
11. Kaddu R, Bhattacharya D, Metriyakool K, et al. Propofol compared with general anesthesia for pediatric GI endoscopy: is propofol better? Gastrointest Endosc. 2002; 55:27–32.
12. Larsen R, Galloway D, Wadera S, et al. Safety of propofol sedation for pediatric outpatient procedures. Clin Pediatr. 2009; 48:819–23.
13. Lamond DW. Review article: safety profile of propofol for pediatric procedural sedation in the emergency department. Emerg Med Australas. 2010; 22:265–86.
14. Khalila A, Shavit I, Shaoul R. Propofol Sedation by Pediatric Gastroenterologists for Endoscopic Procedures: A Retrospective Analysis. Front. Pediatr. 2019; 7:98
15. Morita A, Nakayama Y, Horiuchi A, et al. Stimulating peristalsis improves esophagogastric junction observation during sedated esophagogastroduodenoscopy in children and adolescents. Acta Gastroenterol Belg 2022; 85: 15–19
16. Gotoda T, Akamatsu T, Abe S, et al .Guidelines for sedation in gastroenterological endoscopy (second edition). Dig Endosc. 2021 Jan;33:21-53.
17. Nishizawa T, Sakitani K, Suzuki H, et al. Adverse events associated with bidirectional endoscopy with midazolam and pethidine. J Clin Biochem Nutr 2020; 66: 78–81.
18. Nishizawa T, Suzuki H, Arita M, et al. Pethidine dose and female sex as risk factors for nausea after esophagogastroduodenoscopy. J Clin Biochem Nutr 2018; 63: 230–232.
19. Barsky AJ, Peekna HM, Borus JF. Somatic symptom reporting in women and men. J Gen Intern Med 2001; 16: 266–275.
20. Squires RH, Morriss F, Schluterman S, et al. Efficacy, safety, and cost of intravenous sedation versus general anesthesia in children undergoing endoscopic procedures. Gastrointest Endosc 1995; 41: 99–104