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ORIGINAL ARTICLE

Predominant effects of midazolam for conscious sedation: benefits beyond the early postoperative period

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Abstract
Purpose Conscious sedation with intravenous sedative–hypnotic drugs has the advantage of relaxing patients before invasive procedures. Preoperative anxiety has been suggested to correlate with postoperative comfortableness. In this study, we chose midazolam and droperidol as well-established intravenous sedative–hypnotic drugs. We evaluated the preoperative anxiolytic effect on postoperative memories and emotions up to the first postoperative morning.
Methods In a prospective, double blind study, 120 patients requiring epidural anesthesia were randomly assigned to one of three groups to receive saline, midazolam (0.04 mg/kg), or droperidol (0.1 mg/kg). Cardiovascular and respiratory measurements, observer's assessment of alertness/sedation scale, level of anxiety and discomfort of the patients, pain during the infiltration of local anesthetics, and incidence of adverse effects were recorded. Amnesia, anxiety, and discomfort during the epidural procedure were re-assessed between 12 and 20 h postsurgery.
Results Patients who received sedatives were significantly more sedated ($P < 0.0001$), but the pain score was significantly higher in the droperidol group ($P = 0.0007$) at epidural catheterization. On the first postoperative morning, patients receiving midazolam had a significantly lower pain score ($P < 0.0001$) with less anxiety and discomfort. Patients in both the midazolam and droperidol groups showed a significant decrease in blood pressure ($P < 0.0167$), but no respiratory impairment. No adverse effects were experienced throughout the study period.
Conclusion Conscious sedation with intravenous midazolam 0.04 mg/kg significantly decreased the anxiety and discomfort scores of the patients on the day following surgery but had no effect on these immediately following the epidural catheterization procedure.

Keywords Conscious sedation · Early postoperative · Midazolam · Droperidol

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Introduction

Intravenous sedative–hypnotic drugs, such as propofol, benzodiazepine, ketamine, and droperidol, have often been used to make patients comfortable and relaxed before invasive procedures. Epidural catheter placement is a minimally invasive procedure accompanied with anxiety or discomfort, and several studies have shown the predominant beneficial effects of conscious sedation during this procedure [1–6]. It has been also reported that preoperative anxiety may correlate with both the postoperative pain response and recovery profile [7, 8]. Consequently, preliminary medication has been administered while the patient is in the ward as a means to readily make patients undergoing invasive procedures more comfortable and relaxed, whereas there has been a reconsideration of its use for perioperative safety management [9]. In one study,

patients who were not premedicated felt more comfortable than the sedated ones in terms of being able to converse with the medical staff prior to the surgical procedure. No premedication also had the advantage of avoiding patient misunderstandings [10].

Midazolam, a member of the benzodiazepine family, has a rapid onset after intravenous injection (with clinical effects appearing within 3 min) and a short elimination half-life (1.5–3.0 h) [11]. It is widely used for conscious sedation because it can produce significant anterograde amnesia [12]. It has also been suggested that preoperative midazolam possibly provides patients with postoperative benefits in the 24 h following surgery [13]. Droperidol is a butyrophenone that produces mild sedation, reduced anxiety, and indifference to one's surroundings [14]. The onset of action for droperidol administered either intramuscularly or intravenously occurs within 3–10 min, and the half-life is approximately 2 h [15]. It does seem to have a place in difficult-to-sedate patients, including alcoholics, intravenous drug abusers, and habitual benzodiazepine users [14, 16]. Moreover, droperidol has been recognized as a valid remedy for patients with emergence agitation from general anesthesia [17], patients with acute undifferentiated agitation in the emergency department [18], and patients undergoing therapeutic endoscopy [19].

In the study reported here, we hypothesized that the administration of intravenous midazolam would reduce postoperative discomfort and pain memory due to its property of anterograde amnesia, whereas droperidol would not alter postoperative outcomes. We therefore compared the effects of conscious sedation for epidural catheterization with midazolam and droperidol in terms of patients' anxiety, comfortableness, and pain intensity during local anesthetic infiltration. We also tested the hypothesis that the levels of anxiety, discomfort, and pain immediately following the epidural procedure are similar in patients administered midazolam and those receiving droperidol, but that those of the midazolam patients are lower than those of the droperidol ones at 20 h postsurgery.

Methods

With the approval of the local ethics committee and written informed consent from the participants, 120 patients (33 men, 87 women) scheduled for abdominal surgical procedures under general anesthesia with epidural analgesia were enrolled in the study. Exclusion criteria were: (1) any significant hepatic, renal, cardiovascular (including preexisting conduction defects or prolonged frequency-corrected QT interval), or respiratory diseases; (2) use of medications known to affect central nervous system activity; (3) neurological diseases. All patients were stratified using the American Society of Anesthesiologists (ASA) Classification of Physical Status, as Class 3 or less.

Protocols

No premedication was given. After arrival at the operating room, each patient received an intravenous infusion of 500 ml hydroxyethylated starch solution at 10 ml/kg/h. After baseline vital signs and sedation score were recorded, patients were randomly assigned to one of three groups to receive saline, midazolam, or droperidol.

Patients in the control group were given 10 ml saline solution as placebo. For patients in the midazolam group and droperidol group, midazolam 0.04 mg/kg or droperidol 0.1 mg/kg dissolved in 10 ml of saline was administered intravenously over 30 s, respectively. Each drug was given 5 min prior to the epidural procedure by a blinded observer. Patients were then placed in a lateral decubitus position and underwent epidural catheterization by the median approach technique. A total of 12 Japanese Society of Anesthesiologists Board physicians, who were blinded to the case assignment, performed the epidural procedures. Local infiltration anesthesia with 10 ml of 1% lidocaine using a long 25-gauge needle was followed by puncture with an 18-gauge Tuohy needle, and 2 ml of 2% lidocaine was administered through the catheter as a test dose. If peripheral oxygen saturation (SpO_2) decreased to <90% or if the respiratory rate (RR) decreased to <5 breaths/min, oxygen was supplied at 6 l/min via a facemask. Patients' hemodynamic changes were adjusted by the discretion of the attending anesthesiologists.

Patients returned to a supine position. A blinded observer evaluated each patient's pain level, anxiety, and discomfort scores during the infiltration of local anesthetics prior to anesthetic induction. Anesthesia was induced with 0.25 μg/kg/min remifentanil and the propofol target plasma concentration at 4.0 μg/ml using the target-controlled infusion (TCI) system (Graseby 3500 TCI incorporating Diprifusor; Sims Graseby, Watford, UK). After confirmation of facemask ventilation, rocuronium 0.6 mg/kg was given. The patient's trachea was then intubated, and general anesthesia was maintained with propofol and remifentanil. The propofol target concentration was adjusted to achieve the target Bispectral Index (BIS; Aspect Medical Systems, Natick, MA) value, which was 50, and remifentanil infusion was titrated according to the surgical stimuli. Lidocaine and ropivacaine, but not opioids, were used for epidural analgesia during the surgical period. At the beginning of fascia closure, fentanyl 2.0 μg/kg was administered intravenously. Patients were discharged from the operating room after their emergence. Patient-controlled epidural analgesia was used for postoperative pain management. The postanesthetic round was performed

between 12 and 20 h after the operation. Pain level of local anesthetic infiltration, amnesia, anxiety, and discomfort during the epidural procedure were reevaluated by a blinded observer on the first postoperative morning. The subjects with protocol violation were excluded from the study.

Measurements

Morphometric data and cardiorespiratory measurements, including electrocardiogram, heart rate (HR), SpO_2, and RR were monitored continuously throughout the procedure. Blood pressure (BP) was measured every 2.5 min. Observer's assessment of alertness/sedation scale (OAA/S) [20] score was adopted to evaluate the level of sedation. OAA/S measures the level of alertness in sedated subjects based on an assessment of four categories: responsiveness, speech, facial expression, and ocular appearance. A composite score ranged from 1 to 20 is obtained, and a lower score indicates a higher degree of sedation. The following data were recorded by a blinded observer: (1) OAA/S score on arrival at the operating room; (2) OAA/S score at the end of the epidural procedure; (3) visual analog scale (VAS; evaluated as 0–100 by a sliding cursor 100-mm scale; 0 = no pain, 100 = the worst pain imaginable) [21] score for pain during the infiltration of local anesthetic; (4) level of anxiety of patients on a three-point scale (0 = not at all anxious, 1 = slightly anxious, 2 = anxious); (5) level of discomfort of patients on a three-point scale (0 = comfort, 1 = slight discomfort, 2 = discomfort); (6) incidence of adverse respiratory events (defined as SpO_2 decrease to <90% or RR decrease to <5 breaths/min); (7) total epidural procedure time (the total time the patient is in a lateral decubitus position); (8) emergence time from general anesthesia (the time from the end of the operation until the modified Aldrete score [22] surpasses 9 points); (9) amnesia, any recall of injection being administered into the patient's back; (10) incidence of adverse effects from the time of administering the test drug to the first postoperative morning.

Data analysis

In our preliminary study, standard deviation (SD) of VAS in the control (saline) group was approximately 20. Assuming that the SD of the other two groups (midazolam or droperidol) would also be 20, 35 patients in each group would be necessary to detect a 15-point difference in VAS between any two study groups with an $\alpha = 0.05$ and a $\beta = 0.2$.

Patient characteristics and physiological data were analyzed using one-way analysis of variance (ANOVA). Significant ($P < 0.0167$) differences were subsequently analyzed using the Bonferroni post hoc test. Time required for the epidural procedure, emergence from general anesthesia, operation, and anesthesia among the three groups were also tested by one-way ANOVA. Non-parametric data were compared with the Kruskal–Wallis test.

Statistical analysis was performed using StatView ver. 5.0 (SAS Institute, Cary, NC) and Sample Power 2.0 (SPSS, Chicago, IL). Values were expressed as the mean ± SD (SD given in parenthesis) unless otherwise specified; $P < 0.05$ was considered to indicate a statistically significant difference.

Results

A total of 120 patients were enrolled in this study, of whom six were excluded after randomization due to protocol violation: (1) two patients in the control group due to failure of epidural catheter placement in one patient and the administration of an inhalational agent in the other; (2) two patients in the midazolam group due to failure to extubate the trachea because of a surgical problem in one patient and discontinuation of epidural catheterization in another patient because blood was aspirated from the catheter; (3) two patients in the droperidol group due to failure of tracheal extubation in one patient because of unexpected blood loss and the refusal of one patient to undergo the epidural procedure prior to catheter insertion because of emotional instability. Of the 114 remaining patients, 38 received saline as placebo, 38 received midazolam, and 38 received droperidol. Morphometric and demographic characteristics and operative background of these patients are given in Table 1. There were no significant differences among the three groups, including diagnosis ($P = 0.513$), type of operation ($P = 0.333$), level of epidural puncture ($P = 0.095$), and total amounts of intraoperative anesthetics consumption (propofol, $P = 0.168$; remifentanil, $P = 0.739$; total local anesthetics volume, $P = 0.964$; lidocaine, $P = 0.441$; ropivacaine, $P = 0.690$).

The sedation level of each patient was evaluated according to the OAA/S score. All patients were fully alert on arrival at the operating room ($P = 0.066$). Following intravenous sedation, patients in both the midazolam [4.0 (median); 3.0 (25th percentile); 4.0 (75th percentile)] and droperidol groups (4.0; 5.0; 3.0) were significantly more sedated than those in the control group (5.0; 5.0; 5.0) ($P < 0.0001$).

Pain during the infiltration of local anesthetic was evaluated using VAS scores (Fig. 1). Both midazolam and droperidol failed to reduce the pain during local infiltration anesthesia, and the VAS scores were significantly higher in the droperidol group than in the control or midazolam group (36.6 ± 20.1 vs. 23.6 ± 14.1 or 21.4 ± 21.2, $P = 0.0007$) when epidural catheterization was accomplished. On the

Table 1 Characteristics of the three study groups

Characteristics of the patient cohort	Control ($n = 38$)	Midazolam ($n = 38$)	Droperidol ($n = 38$)	P value
Demographics				
Age (years)	59 (17)	58 (16)	58 (14)	0.912
Gender (M/F)	10/28	10/28	11/27	0.974
Height (cm)	158 (9)	158 (8)	159 (7)	0.929
Weight (kg)	53 (9)	56 (10)	57 (9)	0.140
Body mass index (kg/m^2)	21.2 (2.8)	22.4 (3.5)	22.7 (2.8)	0.094
ASA-PS (1/2/3)	15/19/4	19/18/1	12/25/1	0.370
Operative backgrounds				
Diagnosis (benign/malignant)	17/21	20/18	15/23	0.513
Operation (upper abdomen/lower abdomen)	7/31	6/32	11/27	0.333
Level of epidural puncture (thoracic/lumbar)	19/19	17/21	26/12	0.095
Dose of anesthetics				
Propofol (mg)	960.5 (300.0)	913.2 (348.9)	1094.6 (454.0)	0.168
Remifentanil (mg)	2.8 (1.6)	3.0 (2.1)	3.1 (2.0)	0.739
Total local anesthetics volume (ml)	15.1 (25.3)	15.2 (20.5)	16.4 (27.0)	0.964
Lidocaine (mg)	114.5 (170.0)	120.1 (138.4)	133.6 (201.3)	0.441
Ropivacaine (mg)	26.5 (48.4)	26.8 (42.7)	26.6 (47.9)	0.690
Operative data				
Operative time (min)	143 (77)	130 (76)	161 (102)	0.171
Anesthesia time (min)	216 (85)	205 (84)	239 (109)	0.203
Total epidural procedure time (min)	11.1 (5.0)	11.8 (4.3)	11.8 (4.3)	0.765
Emergence time (min)	14.0 (7.4)	14.2 (8.3)	13.2 (6.7)	0.766

Data are presented as the mean and standard deviation (SD; in parenthesis) or as the number of patients. There were no significant differences among the three groups

ASA-PS American Society of Anesthesiologists Classification of Physical Status

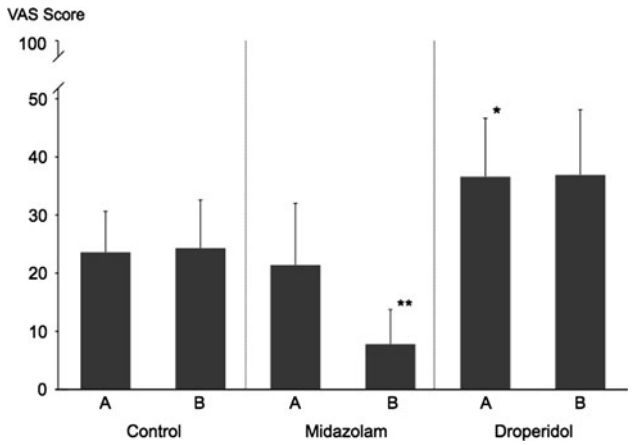

Fig. 1 Comparison of visual analog scale (VAS) scores after epidural catheterization and on the first postoperative morning. Pain during the infiltration of local anesthetic was evaluated using VAS scores (0 = no pain, 100 = the worst pain imaginable) following completion of the epidural catheterization procedure (*A*), and the postanesthetic round was performed on the day after surgery (*B*). Values are given as the mean ± standard deviation (SD). $*P = 0.0007$, $**P < 0.0001$ compared with data of the other two groups at the same points. Pain was significantly reduced in the midazolam group not only after catheterization but also on the first postoperative morning compared with the control and droperidol groups

first postoperative morning, about 60% of the patients ($n = 23$) in the midazolam group could not recall being injected in the back, while only a small number of patients in the control group ($n = 1$) and droperidol group ($n = 4$) could not recall the injection ($P < 0.0001$). Compared with other two groups (control group; 24.3 ± 16.6, droperidol group; 36.9 ± 22.4), patients receiving midazolam indicated a significantly lower VAS score at the postanesthetic round (7.8 ± 11.9, $P < 0.0001$).

A three-point scale was used to evaluate the level of anxiety and discomfort, respectively. Each patient was able to establish contact with a blinded observer and give his/her verbal answer clearly. Following completion of the epidural catheterization procedure, patients' anxiety (Fig. 2a) and discomfort scores (Fig. 2b) were similar among the three groups. However, on the morning of postoperative day 1, both patients' anxiety ($P < 0.0001$) (Fig. 2a) and discomfort scores ($P = 0.0002$) (Fig. 2b) were significantly lower in patients of the midazolam group than in those of the control and droperidol groups, respectively. No adverse effects, such as palpitation, syncope, and psychological or extrapyramidal reactions, were experienced by any of the patients included in all groups

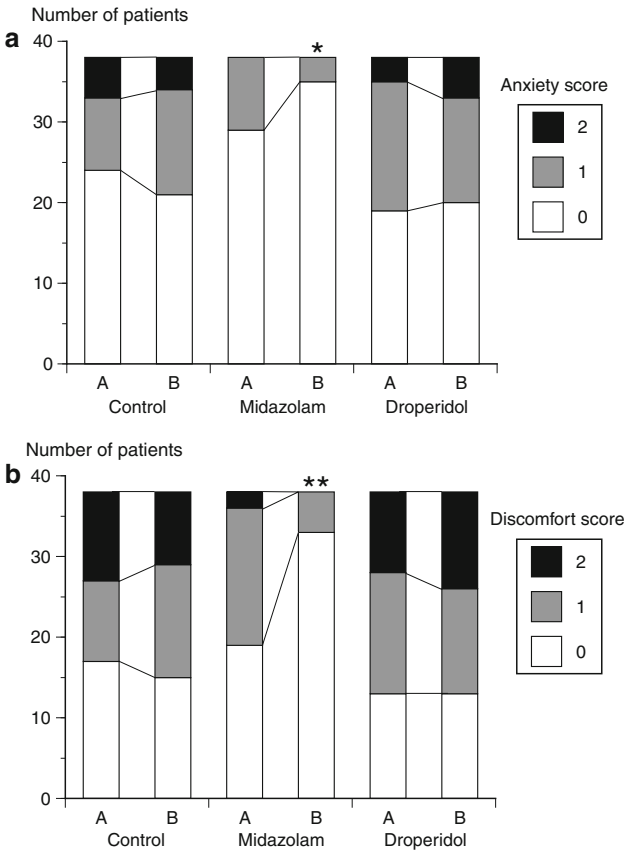

Fig. 2 Intergroup comparison of patient's anxiety and discomfort scores. Patient's anxiety (**a**; 0 = not at all anxious, 1 = slightly anxious, 2 = anxious) and discomfort (**b**; 0 = comfort, 1 = slight discomfort, 2 = discomfort) were evaluated according to a three-point scale. *A* Just after epidural catheterization, *B* the first postoperative morning. $*P < 0.0001$, $**P = 0.0002$ compared with data of the other two groups at the same points. Patients who received midazolam had significantly lower anxiety and discomfort scores than patients who received the placebo or droperidol

from the time of drug administration to the first postoperative morning.

The cardiorespiratory variables are described in Table 2. Baseline vital signs, including BP, HR, RR, and SpO_2, were not significantly different among the three groups. Following insertion of the epidural catheter, systolic and diastolic BP both significantly decreased within clinically acceptable levels in the midazolam and droperidol groups ($P < 0.0167$) compared with the control group. There were no statistical differences in HR ($P = 0.356$), RR ($P = 0.253$), and SpO_2 ($P = 0.194$) among the three groups when catheterization was achieved. No patient required any supplemental vasoactive agent during the epidural procedure. However, sinus tachycardia (108 beats per minute tachycardia) was seen in one patient in the placebo group immediately after the patient returned to the supine position, requiring 12.5 mg landiolol. Oxygen administration was required during epidural catheterization in one patient in the control group and four patients in the midazolam group, but there was no statistical difference between groups ($P = 0.067$). No patients required active airway management, such as assisted ventilation or endotracheal intubation. Flumazenil was not required for patients in the midazolam group, neither during epidural catheterization nor at emergence. One patient in the midazolam group and four patients in the droperidol group required 0.5 mg atropine, while three other patients in the midazolam group required 8 mg ephedrine intravenously during anesthetic induction.

Discussion

Although preoperative anxiety reportedly correlates with the postoperative recovery profile [7, 8], a study assessing the usefulness of preoperative intravenous midazolam showed limited effects [13]. Therefore, in this study, we compared the effects of midazolam and droperidol on patients' anxiety, comfortableness, and pain intensity during local infiltration anesthesia for an epidural procedure at two time points: immediately after completion of the catheterization procedure and 20 h postoperatively. Our results show that preoperative intravenous midazolam reduced patients' anxiety, discomfort, and pain memory on the first postoperative morning.

Patients who received midazolam did not recognize the epidural procedure as a painful experience on the first postoperative morning, although their VAS scores were comparable to those of patients receiving saline placebo before anesthetic induction. It has been reported that systemically administrated midazolam has possible antinociceptive effects. Iida et al. reported that intravenous midazolam significantly depresses somatosympathetic discharges in a dose-dependent manner in cats. They also suggested that the effect of midazolam on nociception depends on its dosage [23]. In a study carried out on healthy volunteers by Nakanishi et al. [24], the antinociceptive dose of midazolam was twofold higher than its sedative dose. In their study, both tactile and painful stimulation were measured by an esthesiometer; a 0.05 mg/kg intravenous bolus midazolam was required to alter both these thresholds, even though 0.025 mg/kg was sufficient for evident sedation. Our results demonstrate that intravenously administered 0.04 mg/kg midazolam was able to provide significant sedation but that this dose could not affect the pain level of local anesthetic infiltration during epidural catheterization. Both the type of subject and the device used for measuring pain sensitivity differed between our study and that of Nakanishi et al. [24], but current findings seem to be consistent with the latter report. On the other hand, in our study, midazolam dramatically reduced

Table 2 Cardiorespiratory variables

Cardiorespiratory variables	Control ($n = 38$)	Midazolam ($n = 38$)	Droperidol ($n = 38$)
Systolic blood pressure (mmHg)			
Arrival at the operating room	138 (21)	134 (22)	137 (21)
After insertion of the epidural catheter	133 (23)	112 (15)*	116 (19)*
Diastolic blood pressure (mmHg)			
Arrival at the operating room	76 (15)	79 (11)	81 (15)
After insertion of the epidural catheter	76 (18)	66 (13)*	66 (13)*
Heart rate (bpm)			
Arrival at the operating room	75 (13)	77 (13)	77 (14)
After insertion of the epidural catheter	76 (18)	72 (12)	76 (12)
Respiratory rate (bpm)			
Arrival at the operating room	15 (3)	16 (4)	16 (3)
After insertion of the epidural catheter	15 (4)	14 (5)	14 (5)
Peripheral oxygen saturation (%)			
Arrival at the operating room	98 (2)	98 (1)	98 (1)
After insertion of the epidural catheter	98 (1)	97 (2)	97 (2)

Data are presented as mean (SD)

* $P < 0.0167$ compared with data of the control group after the epidural catheter insertion

the VAS score compared to the other groups on postoperative day 1. The majority of patients receiving midazolam lacked recall of the epidural procedure. These results imply that the anterograde amnesic effect of midazolam may prevent the memory formation of pain sensation.

Neither midazolam nor droperidol decreased patients' anxiety or discomfort immediately following completion of the epidural catheterization procedure. Of the patients of the midazolam group, however, over half answered "not at all anxious" or "comfortable" despite the anxiety score not being statistically lower than that of the other groups; moreover, no one responded "anxious" at this time point. Previous studies did not evaluate the potential efficacy of midazolam pretreatment against anxious feelings prior to anesthetic induction [1, 4–6, 13], but this decreased anxiety response is considered to be a distinctive feature of midazolam. Intravenous bolus midazolam is able to rapidly provide conscious sedation for patients without emotional instabilities, and its preoperative anxiolytic effect extends into the early postoperative period. In our study, patients who received midazolam experienced a significant decrease in both anxiety and discomfort at the postanesthetic round. The number of patients who responded "not at all anxious" or "comfortable" at this time point decreased in both the control and droperidol groups, whereas it notably increased in the midazolam group. We did not ask the patients whether they would be willing to undergo the epidural under same medication; however, each patient who was given midazolam answered that they were satisfied. They expressed to the interviewer that he/she did not have any unfavorable impression of epidural procedure even though some of them had feared it before the operation. Bauer et al. suggested that the preoperative anxiolysis induced by intravenous midazolam probably persists up to 24 h after surgery. In their study, the patients' overall mean satisfaction score did not significantly decrease, but 0.04 mg/kg of midazolam was able to offer postoperative satisfaction [13]. Preoperative anxiety may also play a critical role in the chain-of-events that controls postoperative outcomes [7]. These results strongly support our findings of intravenous midazolam demonstrating a superiority to conscious sedation. Midazolam removes patients' psychological stress against invasive procedures and has benefits in terms of patients' postoperative memories and emotions.

In comparison, droperidol enhanced the pain of local anesthetic infiltration during the epidural catheterization procedure. This painful memory persisted into the early postoperative period, as indicated by the significantly high VAS score. Although the analgesic effect of droperidol has yet to be verified, there is one report of the pain threshold being affected by droperidol. Siker et al. [25] demonstrated the time course of the pain threshold caused by droperidol 0.075 mg/kg: from 15 to 25 min following intravenous injection, the threshold of pain gradually decreased, and the average pain threshold was lower in the droperidol group than in the placebo group from 15 to 50 min following the administration of the study drugs. Because both of these phenomena and time courses are exactly the same as in our study, it is possible that droperidol modified the reaction against pain stimuli in our patients as well. Droperidol also failed to reduce patients' postoperative anxiety or discomfort; nevertheless, it did provide a comparable level of sedation to midazolam. We evaluated levels of pain, anxiety, discomfort, and amnesia during the epidural procedure up to 20 h postsurgery. Eberhart et al. [26] reported

that patients receiving droperidol (5.0–7.5 mg intravenously) showed impaired postoperative mood and well-being 6 h after surgery and that the well-being scores returned to preoperative baseline values 24 h postoperatively. Compared to midazolam, this lack of anterograde amnesic effect might correlate with patients' postoperative discomfort. It is therefore possible that patients receiving droperidol retain their painful memory of local anesthetic infiltration. It has been reported that droperidol rarely but potentially leads to unidentified panic attacks, even it has been recognized as a useful adjunct to premedication [27]. In our study, all patients who could be followed up to the end of the study did not complain of the unusual physical sensations, restlessness, or nervousness noted in former reports. However, in terms of droperidol being used as a valid remedy for difficult-to-sedate situations [14, 16–19], its psychological effects should be taken into account. In our study, one patient showed emotional instability following intravenous droperidol administration.

Hemodynamic changes caused by intravenous sedatives are a cause of frequent concern during conscious sedation. In our study, the BP significantly decreased in patients of the midazolam and droperidol groups following completion of the epidural procedure, while the HR remained unchanged. Several studies have investigated the effects of lumbar epidural block upon cardiovagal baroreflex function [28–30]. Compared with the doses reported in these studies, our dose of local anesthetic, 2 ml of 2% lidocaine, was clearly low. Therefore, the epidural anesthesia itself was unlikely to have affected the baroreceptor activity in our patients. Likewise, midazolam and droperidol have been suggested to cause hemodynamic changes through alteration of the baroreceptor reflex [31–34]. As Balagny et al. [33] have reported, 0.2 mg/kg of intravenous droperidol affected the baroreflex function with a transient increase in plasma norepinephrine concentrations. Following droperidol administration, the systolic BP significantly decreased but diastolic BP was stable for 20 min. Additionally, HR increased at 5 min and then returned to control levels at 10 and 15 min. It has also suggested that 0.15 mg/kg droperidol induced a marked decrease in preload, which led to a reduction in mean arterial pressure [34]. Similarly, effects on the baroreflex activity were elicited by the induction dose of midazolam, which caused a decrease in the BP without affecting the HR [31, 32]. Our doses of midazolam and droperidol were lower than those used in these earlier human studies; however, it an be considered that both midazolam and droperidol altered the cardiovagal baroreflex function even though their doses were insufficient for general anesthesia.

In conclusion, based on our results, conscious sedation with intravenous midazolam provide more benefits to patients than previously suggested. Among our patients, a 0.04 mg/kg bolus midazolam reduced anxiety and discomfort associated with the epidural catheterization on the first postoperative morning, although it did not affect these emotions immediately after the epidural catheterization procedure. Moreover, conscious sedation with droperidol significantly enhanced pain intensity during the epidural procedure.

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Conflict of interest None of the authors have any financial interests in products related to this study.

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