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Usefulness of oral hypnotic premedication for volatile induction of anesthesia in adults

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Abstract

Purpose. We investigated the effects of oral hypnotic premedication for smooth anesthetic induction and for the patient's comfort under anesthesia, using sevoflurane without nitrous oxide.

Methods. Adult patients were divided into four groups: control ($n = 12$), triazolam (0.25 mg; $n = 12$), zopiclone (7.5 mg; $n = 12$), and clonidine (0.15 mg; $n = 12$) groups. Each premedication was given to each patient 1 h before the anesthesia. The patients breathed out to residual volume and then the anesthetic mask was fitted. The repeated vital capacity breathing technique was used, with 5% sevoflurane in 10 l·min^{-1} oxygen. Induction time, specific induction side effects, and acceptability of this technique by the patients were recorded by an independent observer.

Results. Induction time in the premedicated groups ranged from 66 ± 12 s (mean ± SD) to 76 ± 14 s, and these values were significantly shorter than that in the control group (92 ± 16 s). The number of patients in whom adverse effects occurred during anesthetic induction was significantly greater in the control group (4 patients; 33%) than in the premedicated groups (1 patient each; 8%). Acceptability of the smell of sevoflurane was significantly higher in the premedicated groups (8–10 patients; 67%–83%) than in the control group (5 patients; 42%).

Conclusion. Oral hypnotic premedications with either triazolam (0.25 mg), zopiclone (7.5 mg), or clonidine (0.15 mg) are recommended for smoother volatile anesthetic induction and for the patient's comfort in adults.

Key words Sevoflurane · Volatile induction and maintenance of anesthesia (VIMA) · Premedication · Triazolam · Zopiclone · Clonidine

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Introduction

Induction of anesthesia can be achieved rapidly using the vital capacity ("single breath") technique with 8% sevoflurane and 50%–66% nitrous oxide, which typically produces loss of consciousness in 45–55 s [1,2]. This technique, using sevoflurane, is associated with minimal complications compared with the technique using halothane [3,4] or isoflurane [5]. Although sevoflurane has little pungency, patients sometimes complain about the discomfort of the induction. On the other hand, there has been a recent tendency to avoid the use of nitrous oxide in the clinical setting because of the air pollution it causes and its high costs [6,7]. However, volatile induction of anesthesia without nitrous oxide would prolong the duration of anesthetic induction and increase the risk of adverse effects during anesthetic induction [8–10]. It has been reported that hypnotic premedication (midazolam i.m.) significantly shortened the anesthetic induction time, using the vital capacity technique with 5% sevoflurane with nitrous oxide [11].

We, therefore, investigated the effects of some oral hypnotic premedications for the smoother induction of anesthesia and for the patient's comfort during anesthetic induction, using sevoflurane without nitrous oxide.

Patients and methods

After obtaining institutional approval and informed consent from each patient, 48 ASA physical status I or II adult patients who required general anesthesia with laryngeal mask insertion for minor surgery were enrolled in this study. Patients with a history or evidence from laboratory or physical examination indicating hepatic, renal, or significant respiratory/cardiovascular disease were excluded from the study. The patients were randomly (by card technique) divided into four

groups: control ($n = 12$), triazolam ($n = 12$), zopiclone ($n = 12$), and clonidine ($n = 12$) groups. Oral premedication with triazolam (0.25 mg), zopiclone (7.5 mg), or clonidine (0.15 mg) was given to each group 1 h before the anesthesia, whereas no premedication was given to the control group. The does of each hypnotic agent was selected according to previous reports [12–18]. While the patients were breathing room air before the induction of anesthesia, the anesthetic circuit was circulated with 10 l·min^{-1} oxygen and 5% sevoflurane for 1 min, and the hypnotic level of each patient was evaluated by use of the Ramsay scale [19]. The anesthetic concentration was adjusted with a calibrated vaporizer. The patients were instructed to breathe out to residual volume, and then the anesthetic mask was fitted tightly. They were then told to take repeated vital capacity breaths through the mouth, as deeply as possible, and anesthesia was induced by 5% sevoflurane in oxygen (10 l·min^{-1}) via the mask. Loss of consciousness was defined as loss of eyelash reflex. Eyelash reflex was checked at 5-s intervals. After loss of consciousness was confirmed, the fresh gas flow rate of oxygen was decreased to 6 l·min^{-1}, and the patient's breathing was assisted thereafter. The laryngeal mask was inserted in each patient 5 min after the application of sevoflurane. Anesthesia was maintained with 2%–3% sevoflurane and 30%–40% oxygen. After the operation, the patients breathed 100% oxygen, and the laryngeal mask was pulled out when the patients responded to a verbal command.

Induction time, specific induction adverse effects, recovery time, and acceptability of this technique by the patients were recorded by an independent observer. Induction time was defined as the duration from sevoflurane exposure to loss of consciousness. Definitions of induction adverse effects were those reported by Lamberty and Wilson [5] and by Philip et al. [20]. Briefly, possible side effects were categorized into six groups: hypotension (below −25% of preanaesthetic systolic blood pressure), coughing, laryngospasm, breath-holding, movement of limbs, and excessive secretions. Recovery time was defined as the duration from discontinuance of sevoflurane exposure to verbal response. Acceptability of this technique was assessed on the day after the operation by asking the patients to characterize the smell of the anesthetics and asking whether they would be willing to receive the same technique again.

All data valves are expressed as means ± SD or numbers (percentages). Statistical analyses were performed using the unpaired *t*-test or λ^2-test. A P value of less than 0.05 was considered statistically significant.

Results

All groups were comparable with respect to sex, age, height, weight, and ASA physical status (Table 1). Durations of operation and anesthesia were also comparable. There were no significant differences between the premedicated groups in the hypnotic levels at the anesthetic induction. Induction time, details of the specific adverse effects during induction, and the acceptability of this technique are shown in Table 2. Induction time in the premedicated (triazolam, zopiclone, and clonidine) groups ranged from 66 ± 12 s to 76 ± 14 s, and these values were significantly shorter than that in the control group (92 ± 16 s). Coughing occurred in the control and triazolam groups (1 patient in each group). Movement of limbs occurred in the control, zopiclone, and clonidine groups (3, 1, and 1 patients respectively). None of the patients showed hypotension, laryngospasm, or percutaneous arterial oxygen desaturation below 90%. The number of patients in whom adverse effects occurred during anesthetic induction was significantly greater in the control group (4 patients; 33%) than in the premedicated groups (1 patient in each group; 8%). Recovery time was not different between

Table 1. Demographics of the subjects in each group

	Control group ($n = 12$)	Triazolam group ($n = 12$)	Zopiclone group ($n = 12$)	Clonidine group ($n = 12$)
Sex (F/M)	6/6	5/7	5/7	5/7
Age (years)	45 ± 7	47 ± 8	43 ± 7	46 ± 8
Height (cm)	160 ± 14	162 ± 13	165 ± 16	164 ± 12
Weight (kg)	63 ± 8	64 ± 10	65 ± 11	66 ± 12
ASA physical status I	9	10	10	9
Duration of operation (min)	125 ± 34	134 ± 23	131 ± 32	129 ± 28
Duration of anesthesia (min)	160 ± 41	169 ± 34	165 ± 39	167 ± 29
Hypnotic level at anesthetic induction (level: 1/2/3/4)[a]	0/0/8/4	0/2/8/2	0/1/9/2	0/3/8/1

Data valves are expressed as means ± SD or numbers

[a] Ramsay scale [19]; level 1; anxious, level 2, calm and cooperative; level 3, responds to order; level 4; sleeping but responding to stimuli

Table 2. Induction time, adverse effects during induction of anesthesia, recovery time, and the acceptability of this technique

	Control group ($n = 12$)	Triazolam group ($n = 12$)	Zopiclone group ($n = 12$)	Clonidine group ($n = 12$)
Induction time (s)	92 ± 16*	72 ± 10	76 ± 14	66 ± 12
Adverse effects during induction				
Cough	1	1	0	0
Hypotension	0	0	0	0
Laryngospasm	0	0	0	0
Breath-holding	0	0	0	0
Movement of limbs	3	0	1	1
Excessive secretions	0	0	0	0
Total	4 (33%)*	1 (8%)	1 (8%)	1 (8%)
Recovery time (min)	7.5 ± 3.2	8.5 ± 3.0	9.0 ± 2.9	8.2 ± 3.2
Acceptability of the smell	5 (42%)*	8 (67%)	10 (83%)	9 (75%)
Acceptability of possible repeat anesthesia	7 (58%)	9 (75%)	10 (83%)	11 (92%)

* $P < 0.05$ vs the premedicated groups
Data valves are expressed as means ± SD or numbers (percentages)

groups. Acceptability of the smell of sevoflurane was significantly higher in the premedicated groups (8–10 patients; 67%–83%) than in the control group (5 patients; 42%). Most of the patients in the premedicated groups expressed willingness to receive the same technique again (10–11 patients; 83%–92%).

Discussion

In the present study, it was revealed that the induction times in the premedicated groups were significantly shorter than that in the control group. Because we had reported the same technique with the use of 5% sevoflurane with 67% nitrous oxide [11], and the anesthetic induction time in that study was 65 ± 6 s in patients without premedication, we could conclude that volatile induction of anesthesia without nitrous oxide significantly prolonged the duration of anesthetic induction. Because adverse effects during induction in the present study occurred in one-third of the patients in the control group (without hypnotic premedication), this technique does not seem to be appropriate for the volatile induction of anesthesia in adults. This study also revealed that oral hypnotic premedication shortened the duration of anesthetic induction by this technique and reduced the rate of induction adverse effects. Benzodiazepines are popular for preanesthetic medication because their anxiolytic, sedative, and amnesic properties are combined with minimal cardiovascular effects and depression [12,13]. Some investigations have demonstrated that a low dose of triazolam (0.125 or 0.25 mg) had no significant benefits with regard to anxiety, sedation, and amnesia [14,15]. Nonetheless, 0.25 mg of triazolam significantly shortened the duration of anesthetic induction in this study, and this effect seems to depend on its hypnotic effect. Zopiclone, a cyclopyrrolone agent, also binds to the benzodiazepine receptor, to a portion which is, however, different from that of benzodiazepine agents. Zopiclone has a much stronger anxiolytic effect than those of the benzodiazepines [16]. The high acceptability of the smell of sevoflurane and of this technique in the zopiclone group seems to be due to this characteristic. Kaukinen and Pyykko [17] first reported that clonidine potentiated halothane anesthesia. Inomata et al. [18] also reported that oral clonidine preanesthetic medication ($4.5\,\mu g \cdot kg^{-1}$) significantly reduced both vital capacity rapid inhalation anesthetic induction time and minimum alveolar anesthetic concentration awake (MAC_{awake}) for sevoflurane. Hypotension was expected to occur in the clonidine group, due to the blocking effect of this agent on catecholamine release. However, severe hypotension (below −25% of preanesthetic systolic blood pressure) was not observed in any patient in this group, presumably due to the low dose ($2–3\,\mu g \cdot kg^{-1}$) of clonidine used in this study.

Although the elimination half-lives of triazolam and zopiclone are very short (2–5 h) [21,22], that of clonidine is rather long (12 h) [23]. However, the recovery times in the groups in this study were indistinguishable. Although the hypnotic effect of clonidine may last for longer than the analgesic effect, the reason for this is not clear. These oral hypnotic premedications by no means seem to be appropriate for operations that require only a short stay in the hospital.

In conclusion, technique with sevoflurane, in anesthetic induction of adult patients using the vital capacity breathing oral hypnotic premedication with either triazolam, zopiclone, or clonidine is recommended for smoother anesthetic induction and for the patient's comfort.

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