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Propofol infusion for sedation during spinal anesthesia

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Abstract

Purpose. The dose and time course of propofol infusion required to induce rapid sedation without oversedation during spinal anesthesia were investigated.

Methods. Forty patients scheduled for spinal and epidural anesthesia were studied. After premedication with intramuscular midazolam 0.04 mg·kg^{-1}, an epidural catheter was inserted, followed by spinal anersthesia at L4-L5 with 0.5% hyperbaric tetracaine with epinephrine. The infusion of propofol was started with 10 mg·kg^{-1}·h^{-1} and was decreased to 5 mg·kg^{-1}·h^{-1} at spontaneous eye closure. According to the increase or decrease of the sedation level, the infusion does was decreased or increased to half or twice the initial dose, respectively, to keep the Observer's Assessment of Alertness Sedation (OAAS) score at 3 or 4.

Results. Eye closure was observed at 1.0 ± 0.4 min after the start of insusion. The maintenance insusion dose to keep the OAAS score at 3 or 4 was about 2.5 mg·kg^{-1}·h^{-1}.

Conclusion. Propofol infusion, starting with 10 mg·kg^{-1}·h^{-1}, decreasing to 5 mg·kg^{-1}·h^{-1} after 1 minute, and then decreasing to 2.5 mg·kg^{-1}·h^{-1} after another min induced rapid onset of sedation and kept the OAAS score at 3 or 4 during spinal anesthesia.

Key words Sedation · Propofol · Spinal anesthesia · Propofol concentration

Introduction

The continuous infusion of propofol can provide constant sedation, but prolongs onset time [1–3]. Bolus administration has a rapid onset, but sometimes induces deep sedation and respiratory depression [4]. Many studies have investigated the dose of propofol that is suitable for maintaining good sedation [4–6]. However, no studies are available of an infusion protocol that considers both rapid onset and adequate sedation. The purpose of this study was to investigate an infusion protocol for propofol that would be suitable to induce rapid onset and adequate sedation during spinal anesthesia.

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Patients and methods

After approval was given by the relevant research committee and informed consent was obtained from the patients, 40 patients, aged 30 to 70 years, of American Society of Anesthesiologists (ASA) physical status I or II, scheduled for spinal anesthesia were enrolled. Those who had hepatic, renal, cardiovascular, respiratory, or neurological disease, and those who had taken hypnotics were excluded form the study.

Premedication with intramuscular midazolam 0.04 mg·kg^{-1}, was carried out 30 min before an epidural catheter was inserted into L1-L2, L2-L3, or L3-L4; and spinal anesthesia was performed at L4-L5 with 0.5% hyperbaric tetracaine 10 to 12 mg with epinephrine 0.1 mg. The anesthesia level was checked according to cold sensation for 20 min before surgery was began. A catheter was inserted into the radial artery to measure blood pressure and to draw blood samples. When the anesthesia level was adequate for surgery but lower than T4, an infusion of propofol 10 mg·kg^{-1}·h^{-1} was started. We asked the patients to keep their eyes open. Oxygen, 6 l·min^{-1}, was administered by a mask. When the patients closed their eyes spontaneously, the infusion dose was decreased to 5 mg·kg^{-1}·h^{-1}. Every min for the first 5 min, then at 2.5-min intervals for the next 10 min, at 5-min intervals for the following 30 min, and at 15-min intervals until the end of surgery, according to the increase or decrease of the sedation level, judged by the Observer's Assessment of Alertness Sedation

Table 1. The Observer's Assessment of Alertness/Sedation (OAAS) score

Score	Responsiveness
5	Responds readily to name spoken in normal tone
4	Lethargic response to name spoken in normal tone
3	Responds only after name is called loudly and/or repeatedly
2	Responds only after mild prodding or shaking
1	Responds only after painful trapezius squeeze
0	No response after painful trapezius squeeze

(OAAS) score (Table 1) [7], the infusion dose was decreased or increased to half or twice, respectively, to keep the OAAS score at 3 or 4.

At the start of skin closure, the propofol infusion was stopped. Blood pressure, heart rate, respiratory rate, percutaneous oxygen saturation (SpO_2), arterial oxygen tension (PaO_2), and arterial carbon dioxide ($PaCO_2$) tension, end-tidal carbon dioxide tension ($ETCO_2$), serum concentration of propofol, and the OAAS score were monitored. The serum propofol concentration was measured by high-performance liquid chromatography at BML Laboratory (Tokyo, Japan). The time to return to an OAAS score of 5 after the infusion was stopped was measured as the recovery time. The number of patients with involuntary body movements during surgery was also checked. Amnesia was checked on the next morning by asking the patients whether they remembered the verbal contact used to check the OAAS score during surgery.

Data values are expressed as means ± SD. Statistical analysis was performed with repeated-measures analysis of variance followed by the Student-Newman-Keuls test as a post-hoc test for measured parameters. A P value of less than 0.05 was considered to be statistically significant.

Results

Of the 40 patients, 18 were male and 22 were female; the age was 52 ± 13 years and body weight was 61 ± 15 kg. Twenty-one patients received stripping of varicose veins, 11 received bypass grafting of the femoral to the popliteal artery, and 8 received open reduction of a fracture of the lower extremities. The duration of surgery was 216 ± 39 min.

Eye closure was observed at 1.0 ± 0.4 min after the starting of the infusion. Blood pressure, heart rate, respiratory rate, and PaO_2 decreased significantly during the propofol infusion (Figs. 1, 2), but no treatment was necessary. SpO_2 was kept at more than 98% in all patients. $PaCO_2$ and $ETCO_2$ did not change significantly from the control values of 38.5 ± 6.4 mmHg and 42 ± 4 mmHg, respectively. Serum concentrations of propofol were 0.75 ± 0.14 μg·ml^{-1} at eye closure, 1.37 ± 0.43 μg·ml^{-1} at the end of infusion, and 0.32 ± 0.16 μg·ml^{-1} 30 min after the end of infusion (Fig. 3). Recovery time was 3.3 ± 2.1 min. Fifteen patients had involuntary body movements, but this did not interfere with the surgical procedure. Thirteen patients had a memory of

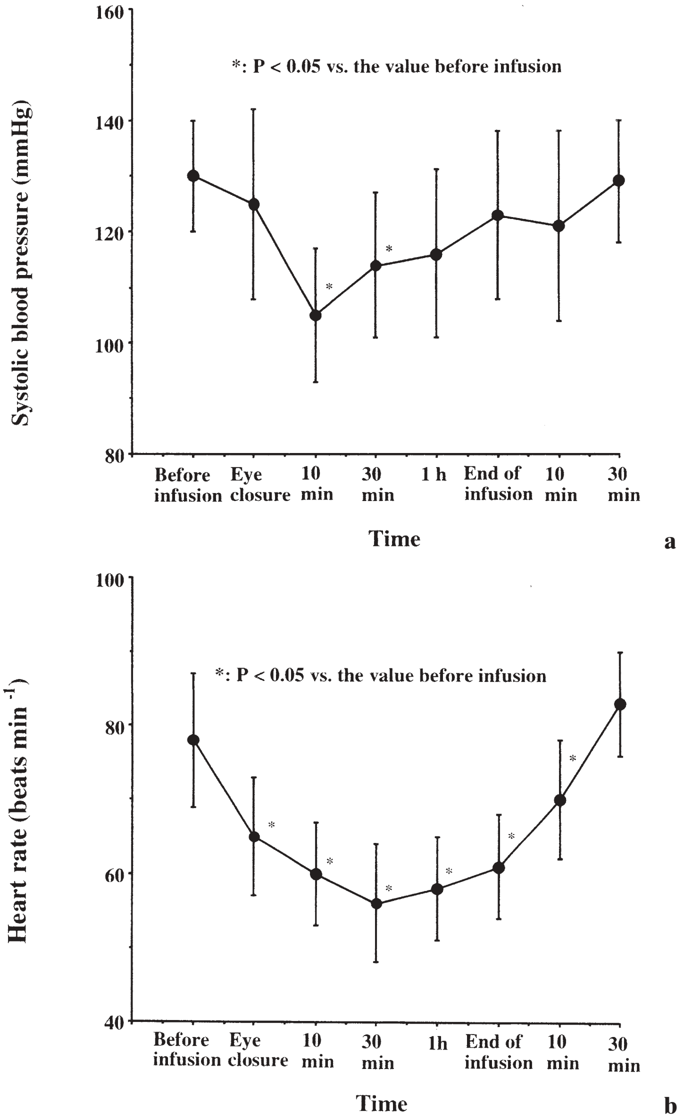

Fig. 1. **a** Blood pressure and **b** heart rate. Values are means ± SD

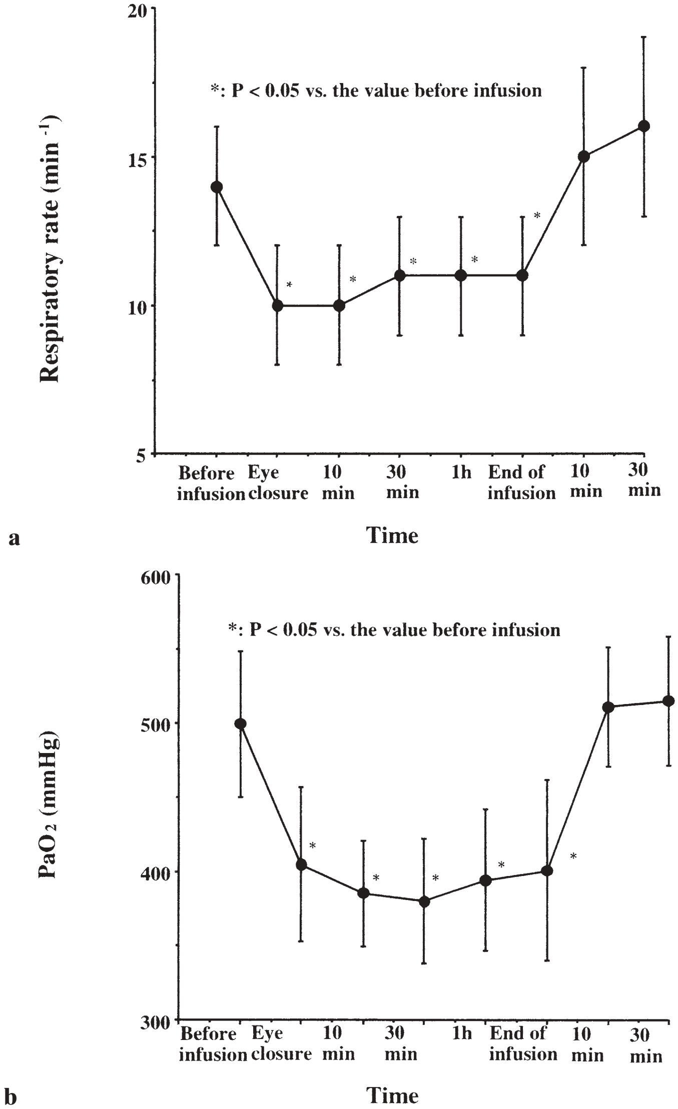

Fig. 2. **a** Respiratory rate and **b** arterial oxygen tension (PaO_2). Values are means ± SD

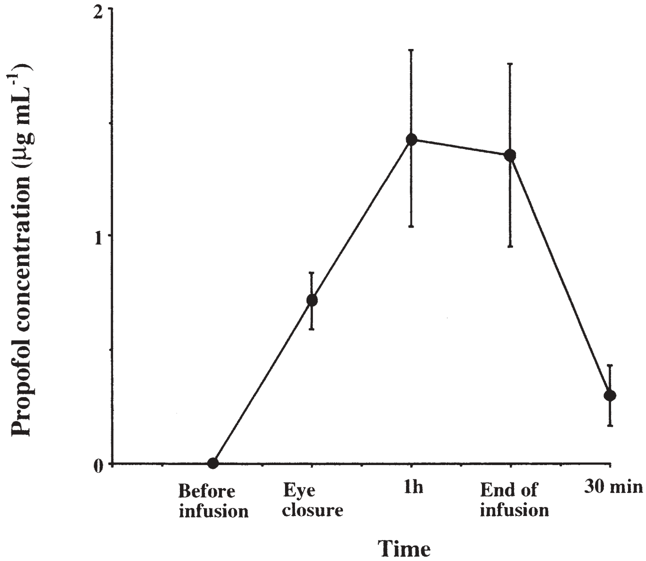

Fig. 3. Serum propofol concentrations. Values are means ± SD

the surgery. The propofol infusion dose and OAAS scores are shown in Table 2.

Discussion

The onset time of sedation with propofol infusion is very slow, and was reported to be 9 to 27 min when starting at 6 mg·kg^{-1}·h^{-1} followed by 4 mg·kg^{-1}·h^{-1} after 10 min [1, 3]. In addition, with this method a transient respiratory arrest occurred, probably due to a high total dose of the infusion. In contrast, with bolus administration, the onset time of sedation is shorter. With propofol 0.5 mg·kg^{-1} followed by infusion with 5 mg·kg^{-1}·h^{-1}, adequate sedation was obtained within 5 min [8] . Time to reach adequate sedation was shortened to 4 min with a propofol bolus of 0.75 to 1.0 mg·kg^{-1} followed by the infusion of 2 to 4 mg·kg^{-1}·h^{-1}, and the time was shortened to 1.8 min with a bolus of 0.75 to 1.0 mg·kg^{-1} and intermittent bolus of 0.25 mg·kg^{-1} [2]. However, transient respiratory depression occurred with propofol bolus administration [9]. In the present study, we used only an infusion, but it had a very rapid onset without causing significant respiratory depression. The starting dose (10 mg·kg^{-1}·h^{-1}) was as high as the dose used for the induction of general anesthesia, but the dose was decreased to half the starting dose in 1 minute when the patients showed spontaneous eye closure. This dose and setting was obtained by carrying out a preliminary trial using various doses and time combinations.

Mackenzie and Grant [5] reported that a mean infusion rate of 3 to 4.1 mg·kg^{-1}·h^{-1} propofol sedated patients, with preservation of the eyelash reflex and purposeful reaction to verbal or mild physical stimulation, in spinal anesthesia, but no details were given of the infusion regimen; their doses were higher than those used in the present study. They administered oral benzodiazepine as premedication (details were not shown), whereas intramuscular midazolam was used in the present study. When midazolam 2 mg was administered intramuscularly as premedication, the dose of propofol infusion required to keep adequate sedation decreased to 2.86 mg·kg^{-1}·h^{-1}, compared with the dose with no premedication (3.47 mg·kg^{-1}·h^{-1}) [4]. In a study by Geddes et al. [10], the mean propofol dose required to sedate patients to slurring of speech and ptosis was 2.2 mg·kg^{-1}·h^{-1} under local anesthesia with no premedication. Without any premedication, the bolus administration of 0.2 mg·kg^{-1} propofol, twice, followed by infusion at

Table 2. Changes in the Observer's Assessment of Alertness/Sedation (OAAS) score and propofol dose

	Time (min)								
Score	0	1	2	3	4	5	7.5	10	15
5	40[a]	36	3	2	1	0	0	0	0
4	0	3	29	26	24	25	25	24	26
3	0	1	7	10	14	13	13	13	13
2	0	0	1	2	1	2	2	3	1
1	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0
Propofol dose ($mg \cdot kg^{-1} \cdot h^{-1}$)	10 (0)	5.3 (1.3)	2.6 (0.7)	2.4 (0.6)	2.5 (0.6)	2.4 (0.7)	2.6 (0.7)	2.5 (0.5)	2.7 (0.4)

	Time (min)									
Score	20	25	30	45	60	75	90	105	120	End
5	0	1	0	0	0	0	0	0	0	2
4	24	23	22	26	24	23	25	26	25	22
3	15	15	17	13	14	15	14	13	14	16
2	1	1	1	1	2	2	1	1	1	0
1	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
Propofol dose ($mg \cdot kg^{-1} \cdot h^{-1}$)	2.6 (0.5)	2.6 (0.6)	2.6 (0.4)	2.5 (0.3)	2.5 (0.4)	2.4 (0.5)	2.4 (0.4)	2.3 (0.5)	2.3 (0.6)	2.3 (0.6)

Values are means (SD)
End, at the end of propofol infusion
[a] Number of patients (total number, 40)

$1.7\,mg \cdot kg^{-1} \cdot h^{-1}$ gave adequate sedation, while keeping the verbal response, in patients with spinal anesthesia [6]. From these studies, there appears to be some variation, from $1.7\,mg \cdot kg^{-1} \cdot h^{-1}$ to $4.1\,mg \cdot kg^{-1} \cdot h^{-1}$, in the dose of propofol infusion required to sedate patients adequately.

In the present study, the serum propofol concentration was 1.0 to $1.8\,\mu g \cdot ml^{-1}$ during adequate sedation. This result is very similar to that in other reports. The serum propofol concentration in patients sedated but responding to verbal stimulation was around $1.5\,\mu g \cdot ml^{-1}$, using a target-controlled infusion system for dental surgery [11]. Using a target-controlled infusion, an OAAS score of 4 was obtained with a propofol concentration of $1.35\,\mu g \cdot ml^{-1}$ and an OAAS score of 1 was obtained with a propofol concentration of $1.62\,\mu g \cdot ml^{-1}$ [12]. Loss of verbal response occurred with a plasma propofol concentration of $1.6\,\mu g \cdot ml^{-1}$ and loss of consciousness occurred with a plasma propofol concentration of $1.9\,\mu g \cdot ml^{-1}$ [7]. Skipsey et al. [13] reported that the mean blood propofol concentration necessary to achieve adequate sedation was $1.05\,\mu g \cdot ml^{-1}$. Therefore, in the light of the above data to induce adequate sedation, a propofol concentration of 1.0 to $1.8\,\mu g \cdot ml^{-1}$ is necessary.

Inappropriate movements were observed in 10 of 20 patients sedated with propofol in a study by Manninen et al. [14]. In another study, about 25% of the patients sedated with propofol had motor activity that interfered with surgery [15]. In the present study, we observed movement in about 40% of the patients. This is a disadvantage. There is controversy regarding the amnesic properties of propofol, with some studies reporting little amnesia [16], whereas others showed significant amnesia [17]. In the present study, about 30% of the patients had a memory of surgery. The memory effects of propofol and midazolam were reported to be similar [12]; however, while in a study using midazolam, no patients had had a memory of surgery [18]. Therefore, amnesic effects may be smaller with propofol than with midazolam.

Mackenzie and Grant [5] reported that patients regained full consciousness approximately 4 min after the end of a propofol infusion. The recovery was faster in the present study. This is the most important advantage of propofol sedation.

In conclusion, propofol infusion, starting with $10\,mg \cdot kg^{-1} \cdot h^{-1}$, decreasing to $5\,mg \cdot kg^{-1} \cdot h^{-1}$ after 1 min, and then decreasing to $2.5\,mg \cdot kg^{-1} \cdot h^{-1}$ after another min, induced rapid onset of sedation and kept the OAAS score at 3 or 4 during spinal anesthesia in patients premedicated with intramuscular midazolam $0.04\,mg \cdot kg^{-1}$.

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