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Patient-controlled sedation using propofol in eight patients with endstage renal failure

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Introduction

Surgical procedures performed under local or regional anesthesia are associated with varying degrees of patient discomfort and apprehension. Patient-controlled sedation (PCS) with propofol has been used successfully in local and regional anesthesia [1–4]. The advantages cited in favor of PCS generally parallel the advantages cited for patient-controlled analgesia (PCA) for postoperative pain. PCS allows patients to titrate the drug dose on an individual basis, reducing the risk of over- or underdosage, a potential disadvantage of anesthestetist-administered sedation. Although the advantages of PCS include adequate efficacy, safety, and a high degree of satisfaction, little information is available on the safety and efficacy of PCS in patients with endstage renal failure. The aim of this study was to evaluate the safety and efficacy of PCS in patients with endstage renal failure undergoing arteriovenous (A-V) shunt construction by investigating the patients' respiratory and circulatory conditions, and the patients' satisfaction, during PCS with propofol.

Patients and methods

After the granting of approval by the institutional ethics review board at the Okinawa Prefectural Miyako Hospital and the acquisition of written informed consent, eight patients scheduled to undergo an elective A-V shunt construction in the forearm received propofol PCS. All patients were premedicated with atropine sulfate 0.01 mg·kg^{-1} intramuscularly 30 min before arrival at the operating room. After the placement of routine monitors (ECG, NIBP, and a pulse oximeter for arterial hemoglobin oxygen saturation [S_{PO_2}]), axillary blockade was performed by the standard approach, with an injection of 20 ml of 1.5% lidocaine with epinephrine 5 μg/ml.

The PCS setting consisted of 0.2 mg·kg^{-1} of propofol with a lockout interval of 3 min. The basal infusion used was 2 mg·kg·h^{-1} following a 0.4 mg·kg^{-1} bolus injection. All patients were shown how to use the device and were instructed to use the pump (Baxter AP-II PCA pump; Baxter, Chicago, IL, USA) if they felt anxious or wished to be more sedated during their operation.

The cardiorespiratory condition (blood pressure [BP], heart rate [HR], respiratory rate, arterial blood gas analysis) was recorded during the surgical procedure. The degree of sedation was assessed at 1, 15, 30, and 60 min after the loading dose and 15 min after the end of PCS. The level of sedation was assessed by a five-point scale: 1, fully awake; 2, drowsy; 3, eyes closed, but arousable by command; 4, eyes closed, but arousable by mild physical stimulation; and 5, eyes closed and nonarousable by mild physical stimulation [5]. A sedation score of 4 or more was considered to be oversedation in this study. To collect arterial blood for the analysis of arterial blood gas and the plasma propofol level, an arterial catheter was inserted into the right dorsal is pedis artery. Arterial blood gas analysis was performed before the start of PCS as a control value. For the analysis of plasma propofol levels, blood was collected in tubes containing ethylene diamine tetraacetic acid (EDTA) at 1, 15, 30, and 60 min after the start of PCS and 15 min after the end of PCS. Each sample was then centrifuged at 1500 *g* for 15 min and

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the plasma was collected and frozen at −30°C for later analysis. Plasma propofol levels were determined by high-performance liquid chromatography in our laboratory.

The day after the operation, each patient was asked to evaluate the degree of satisfaction, according to a visual analogue scale (VAS) consisting of a 100-mm line, with 0 equaling "fair" and 100 equaling "excellent".

Statistical analysis for BP and HR was performed by repeated measures analysis of variance (ANOVA), followed by Dunnett's test to assess differences between pre- and intra-PCS. Analyses were performed using SPSS (SPSS, Chicago, IL, USA). Values for results were reported as medians for the sedation scores and as mean values ± standard deviation (SD) for other parameters. $P < 0.05$ was considered statistically significant.

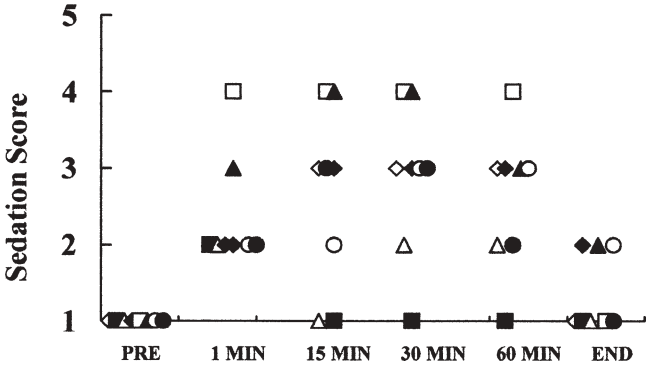

Fig. 1. Plot of the sedation score of each patient before and after patient—controlled sedation (PCS). *Open diamonds*, patient 1; *closed squares*, patient 2; *open triangles*, patient 3; *closed diamonds*, patient 4; *open squares*, patient 5; *closed triangles*, patient 6; *open circles*, patient 7; *closed circles*, patient 8

Results

The median sedation scores were 2, 3, 3, and 3 at 1, 15, 30, and 60 min, respectively, after the start of PCS (Fig. 1). Two of the eight patients had episodes of oversedation (sedation score, ≧4) during the PCS. There was no request for additional propofol administration after the start of propofol infusion in patient 5 (Table 1), because of oversedation.

The respiratory rate was not significantly decreased at any point compared with the pre-PCS value (Table 2). Although blood gas analysis revealed that the mean Pa_{O_2} was decreased (maximum ΔPa_{O_2}, 17.5 mmHg) at 15, 30, and 60 min after the start of PCS, Sp_{O_2} remained at more than 92% throughout, without oxygen administration. The mean Pa_{CO_2} was significantly increased (maximum ΔPa_{CO_2}, 4.5 mmHg) at 30 and 60 min compared with pre-PCS values. Respiratory acidosis was not observed during the operation. At 15 min after the end of the PCS, both Pa_{O_2} and Pa_{CO_2} had recovered to the level of pre-PCS values.

Table 1. Demographic data and the number of patient-controlled sedation (PCS) attempts and hits in individual patients

Patient no.	Age (years)	Sex	Body weight (kg)	PCS	
				Attempts	Hits
1	59	M	59	12	7
2	45	F	52	3	2
3	40	M	66	4	4
4	55	M	61	7	4
5	63	M	72	0	0
6	60	F	57	1	1
7	65	F	61	3	3
8	50	M	65	6	2

Table 2. Respiratory and hemodynamic conditions and plasma propofol concentrations before and after patient—controlled sedation (PCS)

	Pre-PCS	1 min	15 min	30 min	60 min	End-PCS
RR (/min)	15.8 ± 3.3	16.1 ± 3.6	16.3 ± 2.2	15.3 ± 1.7	15.3 ± 2.7	16.8 ± 3.5
pH	7.35 ± 0.07	7.34 ± 0.07	7.33 ± 0.08	7.33 ± 0.08	7.34 ± 0.08	7.35 ± 0.07
Pa_{CO_2} (mmHg)	36.6 ± 5.8	38.1 ± 6.0	38.3 ± 4.7	39.1 ± 4.5*	39.3 ± 4.4*	38.0 ± 5.0
Pa_{O_2} (mmHg)	90.4 ± 9.2	85.7 ± 6.7	82.6 ± 5.9*	78.5 ± 7.5*	82.9 ± 9.3*	88.6 ± 10.1
Sp_{O_2} (%)	95.5 ± 1.0	95.4 ± 0.6	94.9 ± 0.9	94.2 ± 1.1	95.0 ± 1.4	95.6 ± 0.7
SBP (mmHg)	173 ± 22.1	162 ± 24.0*	158 ± 20.9*	150 ± 18.8*	148 ± 20.4*	157 ± 19.9*
DBP (mmHg)	90 ± 12.8	88 ± 11.4	88 ± 14.7	86 ± 12.8*	87 ± 11.1*	88 ± 9.1*
HR (bpm)	88 ± 8.1	76 ± 10.9	73 ± 7.1	71 ± 9.0	69 ± 6.5	72 ± 8.9
Plasma propofol concentration ($\mu g \cdot ml^{-1}$)		1.01 ± 0.2	0.95 ± 0.1	1.08 ± 0.4	0.98 ± 0.3	0.90 ± 0.2

* $P < 0.05$ vs pre-PCS value
Data values are presented as means ± SD
RR, respiratory rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate

The mean arterial BP was decreased significantly from the pre-PCS value at 30 and 60 min after the start of PCS ($P < 0.05$). Heart rate (HR) at 30 and 60 min of PCS and 15 min after the end of PCS was significantly lower than the pre-PCS value ($P < 0.05$). Neither hypotension nor bradycardia requiring medication was observed during the PCS period (Table 2).

The mean plasma concentrations of propofol at 1, 15, 30, and 60 min after the 0.4 mg·kg^{-1} bolus injection were 1.01 μg·ml^{-1} (range, 0.75–1.51 μg·ml^{-1}), 0.95 μg·ml^{-1} (range, 0.77–1.07 μg·ml^{-1}), 1.08 μg·ml^{-1} (range, 0.54–1.75 μg·ml^{-1}), and 0.98 μg·ml^{-1} (range, 0.50–1.55 μg·ml^{-1}), respectively.

The mean degree of satisfaction according to the VAS was 84.9 ± 10.9 mm (range, 79–100 mm) the day after the operation.

Discussion

The results of our study showed that propofol PCS provided stable respiratory and circulatory conditions and a high degree of satisfaction in eight patients with endstage renal failure.

There is no information on the safe PCS dose for patients with endstage renal failure. In our study, the PCS parameters (PCS dose of 0.2 mg·kg^{-1} of propofol with a delay interval of 3 min; basal infusion of 2 mg·kg·h^{-1} following 0.4 mg·kg^{-1} bolus injection) was selected based on our experience with this technique, and based on evidence [6] for the normal pharmacokinetics and pharmacodynamics of propofol even in endstage renal failure. Although these dosages were not associated with any clinically serious complications, a deeper sedation than we anticipated was observed in two of the eight patients after the start of PCS. This result suggests that a 0.4 mg·kg^{-1} bolus injection and 2 mg·kg·h^{-1} infusion of propofol may be the upper limit of safety for some patients with endstage renal failure.

Respiratory depression might be expected during propofol sedation. While Pa_{O_2} at 15, 30, and 60 min during PCS was decreased significantly compared with pre-PCS values, oxygen desaturation ($Sp_{O_2} < 92\%$) was not observed at any time. Respiratory rate was maintained at 10–21 per min during the sedation. Although propofol has been reported to be a respiratory depressant, tidal volume was decreased by propofol infusion (6 mg·kg·h^{-1}) without a decrease in the respiratory rate [7]. Our results showed that Pa_{CO_2} was increased significantly (maximum ΔPa_{CO_2}, 4.5 mmHg) at 30 and 60 min compared with pre-PCS values, but there were no significant changes in pH. Although pH was decreased to a level of less than 7.35 during the PCS, no adverse effects caused by acidosis were observed clinically. The data for arterial blood gas analysis suggest that our method of PCS has little effect on respiratory function in endstage renal failure, and, especially, the PCS had little effect on the acid-base balance.

We did not find any hemodynamic disadvantages with our PCS method. It has been reported that, in humans, propofol decreased the preload and afterload by a direct effect on vascular smooth muscle [8] and that it decreased the level of sympathetic activity and depressed myocardial contractility [9]. Also, a concentration-dependent decrease in regional myocardial contractility has been shown with propofol [10]. Therefore, our results from the measurement of plasma propofol levels suggest that the plasma propofol concentrations with the PCS setting used in this study were too low to adversely affect the hemodynamic condition in our patients.

In this study, all of our patients had an excellent degree of satisfaction (VAS, 84.9 ± 10.9 mm [mean ± SD]). The majority of patients said that the operative procedure seemed to be of a shorter duration than they expected. Although low-dose infusion of propofol is widely used for sedation in the clinical situation, amnesia and sedation in an individual patient is not reliably produced by a fixed infusion rate of propofol [11,12]. On the other hand, the PCS technique can allow patients to be given a sedative whenever required and can eliminate the chance of deeper sedation by negative-feedback technology in a closed-loop system. This high degree of satisfaction could be a result of the technique of "patient-controlled" sedation, which can provide an adequate level of sedation.

The patients' satisfaction, without any adverse effects on cardiorespiratory conditions, indicates that the propofol PCS setting described here (PCS dose of 0.2 mg·kg^{-1} with a delay interval of 3 min; 2 mg·kg·h^{-1} basal infusion following 0.4 mg·kg^{-1} bolus injection) may produce the safe intraoperative sedation in patients with endstage renal failure. However, the optimal PCS setting for patients with endstage renal failure should be investigated by comparative studies.

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