Original Article

The influence of initial target effect-site concentrations of propofol on the similarity of effect-sites concentrations at loss and return of consciousness in elderly female patients with the Diprifusor system

Satoshi Shibuta, Seitetsu Kanemura[1], Osamu Uchida, Takashi Mashimo

Department of Anesthesiology and Intensive Care Medicine, Graduate School of Medicine D7, Osaka University, Yamadaoka, Suita, [1]Department of Anesthesia, Gratia Hospital, Awaomadaninishi, Mino, Japan

Abstract

Background: Whether effect-site concentrations of propofol (Cep) at loss of consciousness and return of consciousness (LOC and ROC, respectively) in elderly women using Diprifusor are similar is unclear. We investigated whether differences in initial target Cep (Ctarget) alter similarities between Cep values at LOC and ROC.

Materials and Methods: In this study, female patients (n = 58, age = 72.5 ± 1.1 years) undergoing knee arthroplasty were administered propofol with Diprifusor. Cep at LOC and ROC were estimated for different Ctarget values (3.0–4.5 μg/ml). Pearson's correlation coefficient analysis and simple regression were performed to assess the relationship between Cep at LOC and ROC for each Ctarget. Differences in correlation coefficients of regression lines obtained from each Ctarget group were determined using the *t*-test.

Results: The different Ctarget groups did not show significant differences in total propofol levels and in Cep values at LOC or ROC. However, Cep at ROC was significantly higher than Cep at LOC when Ctarget was 4.0 and 4.5 μg/ml, whereas these Cep values were not significantly different in low Ctarget groups.

Strong positive correlations were observed between Cep at LOC and ROC for all Ctarget groups. Regression coefficients for the different Ctarget groups were not significantly different. Compared to low (≤3.5 μg/ml) Ctarget groups, high Ctarget groups showed significantly shorter time until LOC. Induction quality was not significantly different among the groups.

Conclusions: In elderly women, Cep values at LOC are strong predictors of Cep at ROC when Ctarget is 3.0–4.5 μg/ml. High Ctarget groups (≥4.0 μg/ml) exhibited shorter induction times with normal cardiovascular stability.

Key words: Diprifusor, elderly female, initial target concentration, loss and return of consciousness, propofol

Introduction

Propofol is widely used as an intravenous anesthetic agent to induce and maintain general anesthesia using target-controlled infusion (TCI) techniques.[1] The Diprifusor® system, the first commercial TCI device used worldwide, displays effect-site concentration of propofol (Cep) as well as plasma concentration calculated according to the Marsh model, which is one of the most frequently used pharmacokinetic models for propofol.[2] However, the Marsh model does not adjust for age and weight is the only model covariate. Increased bias and inaccuracy were observed in a TCI study involving elderly patients.[3-5]

The default setting for the displayed initial target effect-site concentration (Ctarget) on the Diprifusor Graseby Anesthesia Pump 3500 is 4.0 μg/ml, which is thought to be a reasonable initial value for an average patient. A high Ctarget often leads to decreased cerebral blood flow[6] and hemodynamic instability, including hypotension and bradycardia, particularly in elderly patients with cardiovascular complications.[7] When using a bolus injection, the performance index of the three-compartment model, during the induction phase, is clearly

Address for correspondence: Dr. Satoshi Shibuta, Department of Anesthesiology and Intensive Care Medicine, Graduate School of Medicine D7, Osaka University, 2-2, Yamadaoka, Suita-city, Osaka 565-0871, Japan.
E-mail: shibuta@anes.med.osaka-u.ac.jp

Access this article online	
Quick Response Code:	Website: www.joacp.org
	DOI: 10.4103/0970-9185.94851

overpredicted.[8] On the other hand, a lower Ctarget (≤2.5 μg/ml) results in lengthening of the time required to induce anesthesia, and some patients complain of anxiety during anesthesia induction. Occasionally, there are patients who do not lose consciousness even when Ctarget ≤2.5 μg/ml.

The bispectral index (BIS) of the electroencephalogram is a sensitive method used to measure the depth of anesthesia and degree of suppression of the central nervous system. Because of its utility and reliability, BIS monitoring has been widely used. However, a BIS sensor sticker is disposable and expensive, costing 3600 JPY ($45 USD) per patient.

Iwakiri *et al.* have reported similar individual Cep values at loss of consciousness (LOC) and at return of consciousness (ROC) in healthy adult volunteers.[9] Nunes *et al.* showed that Cep values during ROC were related to the Cep values at LOC and patient age (19–76 years) and could be estimated by combining information of the Cep values at LOC and the patient's age.[10] However, whether an inter-relationship exists between Cep values at LOC and ROC in elderly patients undergoing elective surgeries is still unclear. There is no study investigating whether the differences in Ctarget values alter the similarity between individual Cep values at LOC and ROC.

The objective of this study was to identify whether a similarity exists between Cep values at LOC and at ROC in elderly female patients who underwent knee arthroplastic surgery using the Diprifusor system. When a similarity was observed, we investigated whether Ctarget of the Diprifusor system altered the similarity between Cep values at LOC and ROC. For Cep values at ROC were predicted using LOC values, statistical correlation analyses and linear regression models were determined to compare these Cep values for each Ctarget group.

Materials and Methods

After the study was approved by the Research Ethics Committee and written informed consent was obtained from each patient, 58 female patients (mean age, 72.5 ± 1.1 year; range, 50–81 year), who were to undergo knee arthroplasty and who had American Society of Anesthesiologists Physical Status Classification System scores ≤ II, were enrolled in this open study. Patients were excluded from the study if they had any of the following characteristics: Serious impairment of neuronal, respiratory, cardiovascular, hepatic, renal, hemostasis, or endocrine function; a body mass index that was more than 30% above the ideal value; history of problems during previous anesthesia or current medication likely to influence the course of anesthesia; or incompatibility with epidural anesthesia.

Patients received no premedication. Thirty minutes before entering the operating room, a 20 G venous cannula was placed in one forearm, lactate ringer solution was administered at 400 ml/h, and the solution was infused at this rate until the end of anesthesia induction. In the operating room, the patients underwent standard monitoring including noninvasive blood pressure, oxygen saturation by pulse oximetry, and electrocardiography.

An epidural catheter was placed using a 19G Tuohy needle through the L3–4 interspace, with the patient in the lateral position. The catheter was inserted 5 cm into the epidural space and aspiration test was performed to exclude the possibility an intravascular or arachnoid space placement.

After patients were preoxygenated with 100% O_2 for 3 min, general anesthesia was induced using TCI of propofol in a prefilled syringe (1% Diprivan; AstraZeneca Corporation, Osaka, Japan) using the Diprifusor system (Software version 2.0, Graseby 3500 Syringe Pump, Smiths Medical International Ltd., Watford, UK). Patients were randomly allocated to receive Ctarget of 3.0, 3.5, 4.0, and 4.5 μg/ml using the Diprifusor system. Lidocaine (1 mg/kg) was administered intravenously 1 min before propofol administration to prevent pain during propofol administration. When an anesthesiologist pushed the start button of the Diprifusor, a stopwatch was also started in order to measure time until LOC.

Both LOC and ROC were monitored by the responsiveness component of the Observer's Assessment of Alertness/Sedation (OAA/S) scale [Table 1].[11,12] LOC was defined as the first OAA/S score of 1 (loss or no response to mild shaking), while ROC was defined as the first OAA/S score of 2 (recovery or response to mild shaking). After identifying LOC, the LOC time, which was from the start of propofol infusion to LOC, and the Cep value, which was displayed on the Diprifusor system, were recorded. Any other medications, except lidocaine, were not used before LOC in order to minimize an effect on the propofol-required concentration.

Following LOC, 4% sevoflurane was administered for 4 min until a ProSeal laryngeal mask was inserted. No muscle

Table 1: Responsive component of Observer Assessment of Alertness/Sedation score

Score	Responsiveness
5	Responds readily to name spoken in a normal tone.
4	Lethargic response to name spoken in a normal tone.
3	Responds only after name is spoken loudly or repeatedly, or both.
2	Responds only after mild prodding or shaking.
1	Does not respond to mild prodding or shaking.
0	Does not respond to noxious stimulus.

relaxants were used during induction of anesthesia. After an anesthesiologist identified that spontaneous respiration of the patient had stopped, the patient's lungs were mechanically ventilated using air and oxygen (2 and 1l/min, respectively) to maintain an end-tidal CO_2 concentration between 30–35 mmHg.

Induction quality, including cardiovascular stability (The quality of induction score: QIS), was assessed as good (0; smooth induction without problems), adequate (1; minor problems which were easily managed), or poor (2; significant problems).

Fifteen minutes prior to the surgical incision, 0.75% ropivacaine (5–7 ml) was administered through an epidural catheter to provide analgesia. No analgesic agents, except ropivacaine, were used throughout the anesthesia. If a patient had required additional analgesia except supplied through epidural anesthesia, the patient would have been excluded from the study. However, all patients acquired sufficient analgesia with epidural anesthesia.

General anesthesia was maintained using propofol. During maintenance of anesthesia, the Cep value was titrated to value of 0.5–1.5 μg/ml over the Cep value at LOC to prevent intraoperative awareness during operation. Following surgery, the intravenous infusion of propofol was discontinued. The Cep value calculated by the TCI system was recorded at the time of ROC (OAA/S = 2).

Hypotension (systolic blood pressure < 75 mmHg) was treated using a rapid intravenous infusion of colloid solution and/or intravenous administration of etilefrine hydrochloride. The conduct of anesthesia, including fluid management, was determined by the attending anesthesiologist.

Patients were actively warmed using forced air on the upper body to maintain intraoperative normothermia.

Data Analysis: To investigate statistical differences between Cep at LOC and ROC for each Ctarget group, two-sided paired *t*-test was performed. For QIS score, the statistical difference was determined using two-sided Mann-Whitney's *U*-test. $P < 0.05$ was considered significant. Other data were analyzed using one- or two-way analysis of variance, and the differences among the means were analyzed using Tukey-Kramer multiple comparison tests. Pearson's correlation coefficient analyses and simple regressions were performed to evaluate relationships between LOC and ROC in each Ctarget group. Differences in the correlation coefficients of regression lines obtained for each Ctarget group were determined by performing the *t*-test.

Results

Anesthetic characteristics are shown in Table 2. The groups did not show significant differences in age, weight, height, anesthesia time, operation time, tourniquet period, infusion volume, loss of blood, total ropivacaione dose, and total etilefrine hydrochloride dose. Table 3 shows induction and propofol-related characteristics. The time from the start of propofol infusion until LOC for high Ctarget groups (91.1 ± 4.2 s at 4.0 μg/ml; 84.1 ± 6.5 s at 4.5 μg/ml) was significantly shorter ($P < 0.05$) than that for the low Ctarget group (141.2 ± 19 s at Ctarget = 3.0 μg/ml). The different Ctarget groups did not show significant difference in total propofol levels and in Cep values at LOC or ROC. However, Cep at ROC was significantly higher than Cep at LOC when Ctarget was 4.0 μg/ml (Cep at LOC = 1.19 ± 0.06 μg/ml vs. Cep at ROC = 1.49 ± 0.07 μg/ml; $P < 0.01$) and 4.5 μg/ml (Cep at LOC = 1.17 ± 0.09 μg/ml vs. Cep at

Table 2: The anesthetic characteristics. anesthesia time, operation time, tourniquet period, infusion volume, loss of blood, total ropivacaine dose, and total etilefrine hydrochloride dose

Ctarget (μg/mL)	3.0	3.5	4.0	4.5
Anesthesia time (min)	235 ± 6.2	231 ± 3.7	233 ± 5.5	230 ± 5.8
Operation time (min)	169 ± 5.9	167 ± 4.4	169 ± 5.0	168 ± 5.0
Infusion volume (mL)	1711 ± 83	1740 ± 77	1763 ± 43	1683 ± 49
Urine (mL)	935 ± 117	902 ± 126	879 ± 128	931 ± 93
Blood loss (mL)	187 ± 45	252 ± 31	294 ± 68	247 ± 50
Ropivacaine (mg)	98.9 ± 4.2	96.8 ± 5.5	98.8 ± 3.7	99.0 ± 5.3
Etilefrine (mg)	2.23 ± 0.80	2.2 ± 0.60	2.73 ±0.	453.4 ±0.53

Ctarget: Initial target effect-site concentration of propofol

Table 3: The induction and propofol-related characteristics

Ctarget (μg/mL)	3.0	3.5	4.0	4.5
Cep at LOC (μg/mL)	1.26 ± 0.13	1.23 ± 0.11	1.19 ± 0.06	1.17 ± 0.09
Cep at ROC (μg/mL)	1.40 ± 0.07	1.48 ± 0.09	1.49 ± 0.07#	1.51 ± 0.08#
Total PPF (mg/kg)	18.4 ± 0.98	17.6 ± 0.52	18.1 ± 0.63	18.1 ± 0.52
Time till LOC (sec)	141.2 ± 19	114.1 ± 12	91.1 ± 4.2*	84.1 ± 6.5*
QIS	0.24 ± 0.12	0.13 ± 0.10	0.43 ± 0.14	0.40 ± 0.13

** P <0.05 vs Ctarget = 3.0 (μg/mL) # P <0.05 vs Cep at LOC each Ctarget group. The induction and PPF-related characteristics. Ctarget: Initial target effect-site concentration of propofol. Cep: The effect-site concentration of propofol. QIS: The quality of induction score*

ROC = 1.51 ± 0.08 μg/ml; $P < 0.01$), whereas these Cep values were not significantly different in low Ctarget groups. Statistically significant correlations were observed between Cep at LOC and Cep at ROC in all Ctarget groups [Figure 1]. Strong positive correlations were observed between Cep at LOC and Cep at ROC in all Ctarget groups (Ctarget = 3.0 μg/ml, $r = 0.722$, $P = 0.005$; Ctarget = 3.5 μg/ml, $r = 0.861$, $P < 0.001$; Ctarget = 4.0 μg/ml, $r = 0.569$, $P = 0.027$; Ctarget = 4.5 μg/ml, $r = 0.563$, $P = 0.029$). Regression lines incorporating ROC as an outcome variable (y) and LOC as a predictor variable (x) were $y = 0.387x + 0.9111$ for Ctarget = 3.0 μg/ml, $y = 0.686x + 0.634$ for Ctarget = 3.5 mg/ml, $y = 0.604x + 0.775$ for Ctarget = 4.0 μg/ml, and $y = 0.537x + 0.884$ for Ctarget = 4.5 μg/ml. There were no significant differences in regression coefficients among all Ctarget groups [Table 4].

Although cardiovascular adverse effects such as hypotension during the induction phase were more frequent when the infusion rate was >4.0 μg/ml, significant differences were not observed in the QIS for the different Ctarget groups. Hypotension and other adverse effects were easily treated in all cases. Epidural anesthesia was effective in all patients, and complete analgesia was achieved in all patients. No patients required additional analgesics other than ropivacaine during perioperative periods. No patients complained of pain at the end of anesthesia. No patients reported memory of the operation either spontaneously or when questioned about it on the day after the operation.

Table 4 Differences in the correlation coefficients of the regression lines obtained from each Ctarget groups were determined by testing the t-values

Ctarget (μg/mL)	t-value	*P*
3.0-3.5	0.381	0.707
3.0-4.0	1.559	0.890
3.0-4.5	1.143	0.897
3.5-4.0	1.290	0.950
3.5-4.5	1.171	0.900
4.0-4.5	1.713	0.969

Ctarget: initial target effect-site concentration of propofol

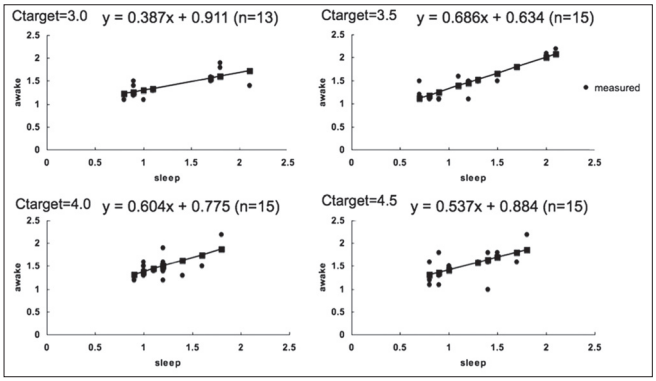

Figure 1: Linear regression between Cep values at ROC and LOC in each Ctarget group. Strong positive correlations were found between Cep values at LOC and Cep values at ROC in all Ctarget groups. The regression lines used ROC as an outcome variable (y) and LOC as a predictor variable (x)

Discussion

We examined whether Ctarget using the Diprifusor system is related to the similarity between Cep at LOC and ROC in elderly female patients who underwent elective knee surgery and who were anesthetized using propofol and epidural anesthesia. Our results showed that Cep at LOC could be used to accurately predict Cep at ROC when Ctarget was set between 3.0 and 4.5 μg/ml. Although Cep at ROC was higher than that at LOC when Ctarget was ≥4.0 μg/ml, no significant differences were observed for lower Ctarget values. Compared to low Ctarget values, high Ctarget values did not elicit hemodynamic instability and resulted in a shorter induction.

TCI systems facilitate the clinical management of intravenous anesthesia. Anesthesiologists set the desired plasma concentration as Ctarget, and the TCI pump adjusts the rate of delivery of the anesthetic agent according to a pharmacokinetic (PK) model. The first-available commercial propofol TCI pump, the "Diprifusor," was based on the Marsh PK model. Recently, models such as the Schnider model have been introduced into clinical practice.[10,13] The Diprifusor Graseby Anesthesia Pump 3500 uses the Marsh model and was used in the present study. Anesthesiologists are instructed to enter the body weight and age into the settings of this pump; however, the age variable was not used to adjust the plasma and effect-site concentration predictions displayed by this pump.

We used the OAA/S score to evaluate the hypnotic effect of propofol. The rate of achieving a specific level of sedation or time course of sedation should reflect the rate of effect-site equilibration.[13] However, the reliability of the TCI model, such as the high incidence of intraoperative awareness for total intravenous anesthesia[14] and BIS monitoring, is assessed to evaluate the depth of anesthesia and sedation. BIS has been used for monitoring adequate sedation levels under anesthesia using propofol. However, the sensors used for this monitoring are expensive and the present study explored the possibility of monitoring Cep values at ROC and LOC instead. The similarity of effect-site concentrations of propofol at LOC and ROC was investigated in young healthy volunteers.[9] However, whether these results are compatible for elderly patients and the influence of Ctarget on this similarity was unclear. In our study, we proved that Cep values at LOC are strong predictors of Cep at ROC when Ctarget is 3.0–4.5 μg/

ml. These results mean that monitoring Cep might be a good option when BIS is not available.

Predicting the time course of propofol in the first minutes after beginning drug administration is difficult.[6,8,15] Our results showed that when Ctarget was set to a high value, Cep at LOC increased, although the difference was not significant. When Ctarget was set to a high value, infusion rate during induction of anesthesia also increased. Rapid injection (2.5 mg/kg administered within 10 s) showed an obvious overprediction for 5 min of the study when using the Marsh model. Masui *et al.*[8] reported that the Marsh model performed poorly in predicting the time course of Cep after rapid injection. However, when Ctarget was low, a long time was required to obtain proper depth of anesthesia, and we experienced that some patients complained of anxiety during induction of anesthesia.

Since nearly all patients in this study experienced complications such as hypertension, hyperlipidemia, and diabetes, we were concerned about instability of hemodynamics during induction of anesthesia at extremely high Ctarget. However, incidences of adverse cardiovascular effects were not observed to occur at a significant level even at the highest Ctarget (4.5 μg/ml) in the present study, and all adverse effects were easily treated. Compared to high Ctarget, low Ctarget was associated with a significantly longer time from beginning propofol infusion until LOC. The highest displayed Cep at LOC was 2.4 μg/ml. Due to the increased sensitivity to propofol in elderly patients, the dose of propofol administered to elderly patients should be lesser than that administered to younger patients.[10,16,17]

Statistically significant correlations were observed between Cep at LOC and Cep at ROC in all Ctarget values (range, 3.0–4.5 μg/ml), and no significant differences were observed in the regression coefficients of all groups. However, Cep at ROC was significantly higher than Cep at LOC when Ctarget was 4.0 and 4.5 μg/ml, while these values were not significant different at low Ctarget. Thus, setting Ctarget values in a range of 3.0–4.5 μg/ml was appropriate.

Nunes *et al.*[18] identified variables related to Cep at ROC for anesthesia with propofol and remifentanil until the end of anesthesia. The use of an analgesic alters the requirement for propofol during induction.[19] Analgesic and hypnotic drugs, including premedication, interact with each other to achieve an adequate depth of anesthesia and analgesia[20] in the presence of surgical stimuli. In our study, because the analgesic effect of epidural anesthesia was sufficient in all patients, we used propofol as the only sedative without the need of any other medication, such as opioids, which could have influenced the required propofol concentrations for Cep at LOC and ROC.

Our study has several advantages. Since the type of surgery and patient variability are important in TCI anesthesia, patient characteristics were nearly the same, and the same operation was performed by the same group of anesthesiologists and surgeons. We used a laryngeal mask to avoid strong airway stimulation by intubation. In addition, in our study, no patient had a risk of severe adverse events.

However, this study has some limitations. Although not statistically significant, incidences of cardiovascular adverse effects were more frequently observed at high Ctargets. Therefore, we did not examine the correlation between Cep values at LOC and ROC at high Ctargets (e.g., 5.0 μg/ml) for patient safety. Second, there were more female patients than male patients who have undergone knee arthroplasty. There may be gender differences in pharmacokinetics and propofol sensitivity.[21] Therefore, further studies on more patients, particularly male patients, would provide a more powerful clinical correlation between variables. Third, stimulation of the laryngeal mask remained. This may explain why Cep values at ROC were slightly higher than Cep values at LOC.

In conclusion, Cep at LOC can be used to accurately predict Cep at ROC when the Ctarget is between 3.0 and 4.5 μg/ml. Ceps at ROC were significantly higher than Ceps at LOC when Ctarget was greater than 4.0 μg/ml, while at a lower Ctarget, these values were not significantly different.

References

1. Shibuta S, Varathan S, Inoue T, Shimizu T, Tomi K, Mashimo T. The effects of propofol on NMDA- or nitric oxide-mediated neurotoxicity *in vitro*. Neuroreport 2001;12:295-8.
2. Marsh B, White M, Morton N, Kenny GN. Pharmacokinetic model driven infusion of propofol in children. Br J Anaesth 1991;67:41-8.
3. Swinhoe CF, Peacock JE, Glen JB, Reilly CS. Evaluation of the predictive performance of a 'Diprifusor' TCI system. Anaesthesia 1998;53:61-7.
4. Absalom AR, Mani V, De Smet T, Struys MM. Pharmacokinetic models for propofol–defining and illuminating the devil in the detail. Br J Anaesth 2009;103:26-37.
5. Coppens M, Van Limmen JG, Schnider T, Wyler B, Bonte S, Dewaele F. Study of the time course of the clinical effect of propofol compared with the time course of the predicted effect-site concentration: Performance of three pharmacokineticdynamic models. Br J Anaesth 2010;104:452-8.
6. Struys MM, Coppens MJ, De Neve N, Mortier EP, Doufas AG. Influence of administration rate on propofol plasma-effect site equilibration. Anesthesiology 2007;107:386-96.
7. Coates D. Diprifusor for general and day-case surgery. Anaesthesia 1998;53:46-8.
8. Masui K, Upton RN, Doufas AG, Coetzee JF, Kazama T, Mortier EP. The performance of compartmental and physiologically based recirculatory pharmacokinetic models for propofol: A comparison using bolus, continuous, and target-controlled infusion data. Anesth Analg 2010;111:368-79.

9. Iwakiri H, Nishihara N, Nagata O, Matsukawa T, Ozaki M, Sessler DI. Individual effect-site concentrations of propofol are similar at loss of consciousness and at awakening. Anesth Analg 2005;100:107-10.
10. Nunes CS, Ferreira DA, Antunes L, Lobo F, Santos IA, Amorim P. Individual effect-site concentrations of propofol at return of consciousness are related to the concentrations at loss of consciousness and age in neurosurgical patients. J Clin Anesth 2009;21:3-8.
11. Chernik DA, Gillings D, Laine H, Hendler J, Silver JM, Davidson AB. Validity and reliability of the Observer's Assessment of Alertness/Sedation Scale: Study with intravenous midazolam. J Clin Psychopharmacol 1990;10:244-51.
12. Doufas AG, Bakhshandeh M, Bjorksten AR, Shafer SL, Sessler DI. Induction speed is not a determinant of propofol pharmacodynamics. Anesthesiology 2004;101:1112-21.
13. Barakat AR, Sutcliffe N, Schwab M. Effect site concentration during propofol TCI sedation: A comparison of sedation score with two pharmacokinetic models. Anaesthesia 2007;62:661-6.
14. Morimoto Y, Nogami Y, Harada K, Tsubokawa T, Masui K. Awareness during anesthesia: The results of a questionnaire survey in Japan. J Anesth 2011;25:72-7.
15. Masui K, Kira M, Kazama T, Hagihira S, Mortier EP, Struys MM. Early Phase Pharmacokinetics but Not Pharmacodynamics Are Influenced by Propofol Infusion Rate. Anesthesiology 2009;111:805-17.
16. Schnider TW, Minto CF, Gambus PL, Andresen C, Goodale DB, Shafer SL. The influence of method of administration and covariates on the pharmacokinetics of propofol in adult volunteers. Anesthesiology 1998;88:1170-82.
17. Olmos M, Ballester JA, Vidarte MA, Elizalde JL, Escobar A. The combined effect of age and premedication on the propofol requirements for induction by target-controlled infusion. Anesth Analg 2000;90:1157-61.
18. Nunes CS, Ferreira DA, Antunes L, Amorim P. Clinical variables related to propofol effect-site concentrations at recovery of consciousness after neurosurgical procedures. J Neurosurg Anesthesiol 2005;17:110-4.
19. Vuyk J, Mertens MJ, Olofsen E, Burm AG, Bovill JG. Propofol Anesthesia and Rational Opioid Selection: Determination of Optimal EC sub 50 -EC sub 95 Propofol-Opioid Concentrations that Assure Adequate Anesthesia and a Rapid Return of Consciousness. Anesthesiology 1997;87:1549-62.
20. Vuyk J. Drug interactions in anaesthesia. Minerva Anestesiol 1999;65:215-8.
21. Hoymork SC, Raeder J. Why do women wake up faster than men from propofol anaesthesia? Br J Anaesth 2005;95:627-33.

How to cite this article: Shibuta S, Kanemura S, Uchida O, Mashimo T. The influence of initial target effect-site concentrations of propofol on the similarity of effect-sites concentrations at loss and return of consciousness in elderly female patients with the Diprifusor system. J Anaesthesiol Clin Pharmacol 2012;28:194-9.

Source of Support: Nil, **Conflict of Interest:** None declared.