J Anesth (2006) 20:57–59
DOI 10.1007/s00540-005-0355-8

Journal of
Anesthesia

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The effect of gynecologic laparoscopy on propofol concentrations administered by the target-controlled infusion system

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Abstract
The purpose of this study was to assess the effect of gynecologic laparoscopy on propofol concentrations administered by the target-controlled infusion (TCI) system. Thirteen patients undergoing gynecologic laparoscopy (intraabdominal pressure of 10 mmHg) were enrolled in this study. Anesthesia was induced with vecuronium 0.1 mg·kg^{-1} and propofol, then maintained by 60% nitrous oxide and sevoflurane in oxygen and a constant infusion of propofol. Propofol was administered to all subjects by means of a target-controlled infusion to achieve propofol plasma concentration at 6.0 μg·ml^{-1} at intubation and 2.0 μg·ml^{-1} after intubation. Before and during laparoscopy, plasma propofol concentration was determined using high-performance liquid chromatograhy. Cardiac output (CO) and effective liver blood flow (LBF) were also measured using indocyanine green as an indicator. Before and during pneumoperitoneum, there were no significant differences in propofol concentations between each point. Propofol concentrations were well achieved to predicted concentrations administered by the TCI system during gynecologic laparoscopy under propofol and sevoflurane anesthesia.

Key words Propofol · Cardiac output · Gynecologic laparoscopy · Pharmacokinetics

Introduction

Propofol has been widely used for anesthesia during surgical procedure and for sedation of patients. It is a short-acting drug with a large volume of distribution and a high total body clearance [1]. Because the hepatic extraction ratio of propofol is very high [2], hepatic metabolism is considered as the main elimination pathway and the metabolism depends on liver blood flow (LBF). Recently, we reported that a pseudo-steady state was established during the anhepatic phase of living related donor liver transplantation [3]. Furthermore, we found that the human kidneys played an important role in the elimination of propofol [4].

Pharmacokinetic parameters incorporated into Diprifusor target-controlled infusion (TCI) systems were proposed by Gepts et al. [5] and later modified by Marsh et al. [6]. The pharmacokinetic parameters of Diprifusor might be influenced by gynecologic laparoscopy because previous researchers reported that cardiac output (CO) and liver blood flow (LBF) decreased during laparoscopy [7,8]. We reported increase of the predictive performance error of TCI system by dopamine infusion due to the change of CO and LBF [9]. The purpose of this study was to assess the effect of gynecologic laparoscopy on propofol concentrations administered by the TCI system.

Materials and methods

Subjects

After institutional approval, informed consent was obtained from 13 patients undergoing gynecologic laparoscopy (age range, 25–38 years; height range, 151–167 cm; weight range, 43–64 kg). Sample size was determined according to our previous study [9]. All patients were American Society of Anesthesiology (ASA) I–II, and individuals who had severe hepatic or renal insufficiency, significant hemodynamic instability, or a known allergy to eggs or propofol were excluded from the study.

Sampling procedure

Before induction of anesthesia, an IV catheter was placed in an antecubital vein for infusion of anesthetics and for fluid replacement. Anesthesia was induced with

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Received: May 10, 2005 / Accepted: August 31, 2005

vecuronium 0.1 mg·kg^{-1} and propofol and was maintained by 60% nitrous oxide and sevoflurane in oxygen and a constant infusion of propofol. Propofol was administered to all subjects by means of a target-controlled infusion (Diprifusor; TE-371TM, Terumo, Tokyo, Japan) to achieve propofol plasma concentration at 6.0 μg·ml^{-1} at intubation and 2.0 μg·ml^{-1} after intubation. Sevoflurane was kept constant at 2% throughout the study. After predicted propofol concentration at 2.0 μg·ml^{-1} was achieved, injection of 20 mg indocyanine green was performed for the measurement of CO and effective LBF. Blood samples were collected from a cannula inserted in the radial artery for measurement of plasma propofol concentration. At 30 and 60 min after the start of pneumoperitoneum (intraabdominal pressure of 10 mmHg), injection of 20 mg indocyanine green for the measurement of CO and effective LBF and the collection of a blood sample for the analysis of propofol concentration were performed again.

Analytical procedure

The dilution curve of indocyanine green was simultaneously recorded at the nasal wing using a specially designed optimal sensor that sandwiched the nasal wing between light-emitting diodes with a photodiode that measured the intensity of the light transmitted through the nasal wing. CO, blood volume and indocyanine green clearance slope (K) were measured by a pulse dye densitometer (R470; Nihon-kohden, Tokyo, Japan) [10]. Effective LBF was calculated using the following formula: effective LBF = K × blood volume. The propofol concentrations in plasma were measured using high-performance liquid chromatography (HPLC) as we reported previously [2].

Statistical analysis

Data are expressed as mean ± SD. Analysis of variance for repeated measurements was used to detect significant changes. When significance was found, the Scheffe test was used as a post hoc comparison procedure. A P value <0.05 was considered statistically significant.

Results

The transition of mean arterial pressure, heart rate, CO, effective LBF, and propofol concentrations are shown in Table 1. There were no significant differences of mean arterial pressure, heart rate, CO, effective LBF, or propofol concentrations between each point. Propofol concentration at before pneumoperitoneum and 30 and 60 min after the start of pneumoperitoneum was 2.13 ± 0.41, 2.12 ± 0.43, and 2.21 ± 0.40 μg/ml, respectively. Propofol concentrations were well achieved to predicted concentrations before and during pneumoperitoneum.

Table 1. Hemodynamics before pneumoperitoneum and at 30 and 60 min after the start of pneumoperitoneum

	Baseline	30 min	60 min
HR	75 (14)	83 (22)	76 (27)
MAP	72 (17)	82 (15)	80 (21)
ELBF	0.78 (0.17)	0.81 (0.21)	0.76 (0.19)
CO	4.7 (1.5)	5.1 (1.4)	4.9 (1.2)
C-pro	2.13 (0.41)	2.12 (0.43)	2.21 (0.40)

Data are mean (SD)
HR, heart rate (beat/min); MAP, mean arterial pressure (mmHg); ELBF, effective liver blood flow (l·min^{-1}); CO, cardiac output (l·min^{-1}); C-pro, plasma concentration of propofol

Discussion

In the present study, we examined propofol concentrations in plasma before and during pneumoperitoneum in patients undergoing gynecologic laparoscopy. We found that propofol concentrations were well achieved to predicted concentrations administered by the TCI system during gynecologic laparoscopy under propofol and sevoflurane anesthesia.

Hoymork et al. reported that propofol concentrations were underestimated by a median of 60% during laparoscopic cholecystectomy [11]. Therefore, we hypothesized that propofol concentrations became higher than predicted during gynecologic laparoscopy. Contrary to our hypothesis, propofol concentrations were well achieved to predicted concentrations, and CO and effective LBF were kept constant even during pneumoperitoneum. In patients undergoing laparoscopic cholecystectomy, LBF might be reduced because of direct depression of liver perfusion by the pneumoperitoneum even if CO was kept constant. Another explanation is the presence of a kinetic interaction with remifentanyl.

Myburgh et al. and Kurita et al. have investigated the influence of CO on propofol concentrations during continuous infusion, demonstrating an inverse relationship between CO and propofol concentrations [12,13]. Previous researchers reported that CO and LBF decreased during laparoscopy [7,8] and that liver blood flow decreased by 39% when intraabdominal pressure elevated from 10 to 15 mmHg [8]. Therefore, if pneumoperitoneum was performed at a pressure greater than 10 mmHg, the possibility of overdosing of propofol cannot be denied.

In summary, propofol concentrations were well achieved to predicted concentrations even during

pneumoperitoneum in patients undergoing gynecologic laparoscopy when pneumoperitoneum was performed at a pressure of 10 mmHg.

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