Menstrual Cycle Phase Influences Propofol Pharmacokinetics

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Background: Previously, we found that menstrual cycle phase determined by questionnaire survey have no significant influence on propofol pharmacokinetics. To determine exact menstrual cycle phase, we used plasma levels of female hormones including luteinizing hormone, estradiol, and progesterone. in the present analysis. The aim of the study was to investigate whether peak plasma concentration of propofol by a bolus dose were different between the follicular and other phases in premenopausal female patients.

Method and Materials: Female patients who were ASA physical status I or II, aged 20-49 years, scheduled to undergo elective surgery under general anesthesia were enrolled. Patients with severe hepatic, renal, or cardiovascular disease, neuromuscular disease, a history of propofol allergy, and body mass index greater than 30 kg/m^2 were excluded. After oxygenation, the patients received propofol 2 mg/kg over 3 min. To measure plasma concentration of propofol, arterial blood samples (1 mL each) were collected before, and at 15, 30, 45, 60, 75, 90, 105, 120, 140, 160, 180, 195, 210, 225, 240, 260, 280, 300 s, and 5, 5.5, 6, 7, 8, 10, 12, 15, 20 min after the start of the infusion of propofol. Additionally, we took 4mL blood sample to measure plasma level of female sex hormones including luteinizing hormone, estradiol, and progesterone.
Plasma propofol concentrations were determined using high-performance liquid chromatography with fluorescence detection. The highest concentration among the measured concentrations in each patient was defined as the peak concentration. A patient with luteinizing hormone level between 5.7 and 64.3 mIU/ml, estradiol level between 6 and 37 pg/ml, and progesterone level ≤0.44 ng/ml was excluded from the analysis as being menopausal. A premenopausal patient with progesterone level ≤0.92 ng/ml and estradiol level ≥22 pg/ml was regarded as the follicular phase.
The data was expressed as mean ± SD. Unpaired Welch's t test was used to compare the peak plasma concentration between the patients in the follicular and other menstrual cycle phases. A P value <0.05 as regarded as significant.

Result: Fourteen patients in the follicular phase and forty-night patients in the others

phases were included for the analysis. Four patients were excluded due to menopause. Age, weight, height were as follows; 31 ± 8 years, 58 ± 9 kg, 162 ± 6 cm for the patients in the follicular phase, 36 ± 8 years, 57 ± 8 kg, 170 ± 5 cm for the patients in the other menstrual cycle phases.
The peak plasma concentration of propofol in follicular phase, 10.1 ± 3.1μg/ml, was significantly higher than that in the other phases, 8.0 ± 2.1g/ml (P =0.025). The level of each sex hormones not correlated with maximum plasma concentrations of propofol.

Conclusion: The peak plasma concentration of propofol was influenced by the menstrual cycle phase. Further pharmacokinetic analysis is desired to examine whether a menstrual cycle phase is a covariate on the pharmacokinetic model.