Poster

[P26-3] P26-3: Central nervous system drugs (2)

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[P26-3-6] Effectiveness of barbiturate therapy for severely increased intracranial pressure based on pharmacokinetic analysis

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Background

Intracranial pressure has to be maintained quite constant by homeostasis, because increased intracranial pressure caused by cerebrovascular disease and head trauma leads to certain death. Although controlling intracranial pressure is critical in clinical,
only few therapies for increased intracranial pressure are currently available. Barbiturate acts on the central nervous system and shows therapeutic effects on general anesthesia and epilepsia. In some clinical cases and animal experiments, in addition to the therapeutic effect on high intracranial pressure, barbiturate also exhibited cerebral protective effect. However, barbiturate therapy sometime showed side effects such as cardiovascular depression and respiratory depression. The relationship between side effects, dosage, and blood concentration of barbiturates is totally unknown. The purpose of this study was to determine the effectiveness of barbiturate therapy for severely increased intracranial pressure by pharmacokinetic (PK) analysis.

Methods

Patients with severely increased intracranial pressure (Kurume University Hospital) were emrolled in this study. Among them, 9 patients undergoing surgery with thiamylal (ultra-short acting barbiturate) administration were assessed. We evaluated blood thiamylal concentration, intracranial pressure, cerebral perfusion pressure, body temperature, and blood pressure at before administration, and 6, 12, 24, 48, 72, 96 (administration ended), 120, 144 h after administration. Population PK modeling was performed by using NONMEM ver.7.3.0.

Results

With thiamylal administration, we could achieve the management target value of 20 mmHg or less, except for one patient after administration. The patients showed the systolic blood pressure (basically 90mmHg or more) and the body temperature (35-38˚C). During the drug administration, blood thiamylal concentration was maintained between 2.8 to 14.5 μg/mL. Clinically critical side effects were not observed in this study. Final PK model was CL_{tot} = 6.35 ×(Body weight /41)$^{2.32}$ (L/h), Vd = 177 (L), suggesting that thiamylal dosage need to be adjusted based on body weight.

Conclusions

The barbiturate therapy for severe intracranial hypertension using thiamylal PK analysis may be clinically effective.