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Poster

## [P26-2] P26-2: Central nervous system drugs (1)

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### [P26-2-9] Effect of lipid emulsion infusion on paliperidone

#### pharmacokinetics in the acute overdose rat model: a potential emergency treatment for paliperidone intoxication

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Keywords: intravenous lipid emulsion, paliperidone, acute overdose, detoxification therapy, lipid rescue

#### Background

Paliperidone, established as a potent human *ether-a-go-go-related gene* blocker, prolongs cardiac repolarization in a concentration-dependent manner. Meanwhile, continuous infusion of intravenous lipid emulsion (ILE) has been established as a detoxification therapy for several lipophilic drugs. However, this change in pharmacokinetics of various lipophilic drugs following ILE administration remains to be clarified. The objective of this study is to clarify the effect of continuous ILE on the pharmacokinetics of overdosed paliperidone in rats.

#### Methods

Paliperidone (20 mg/kg) was administered orally to free-moving male Wistar rats. Continuous infusion (initial loading dose: 4 mL/kg for 10 min, followed by 4 mL/kg/h for 12 h) of ILE or acetated Ringer's solution (AR) was initiated 30 min after paliperidone administration. Plasma concentration profile of paliperidone was monitored for 12 h after administration. The plasma concentration and tissue/plasma concentration ratio of paliperidone were compared between ILE and AR groups. The effect of lipid emulsion on the free fraction of paliperidone in serum was also examined by in vitro experiment.

#### Results

The rat group infused with ILE showed a higher area under the concentration–time curve (mean [SD]: 6102 [900.9] vs. 3407 [992.1] ng·h·mL<sup>-1</sup>,  $p = 0.02$ ) and longer elimination half-time ( $t_{1/2}$ ) (4.1 [0.9] vs. 2.2 [0.4] h,  $p = 0.02$ ) of paliperidone, compared with the AR group. Tissue/plasma concentration ratios of paliperidone were lower in ILE rats than in AR rats (1.98 [0.70] vs. 3.82 [1.47] in the heart,  $p = 0.04$ ; 0.28 [0.29] vs. 1.27 [0.58] in the brain,  $p < 0.001$ ). Observed free fraction of paliperidone in serum containing 1.0% lipid emulsion was lower than that in the control serum (0.75 vs. 1.29%,  $p < 0.05$ ).

#### Conclusions

Continuous infusion of ILE would reduce tissue distribution and prolong the  $t_{1/2}$  of paliperidone in rats. Therefore, continuous infusion of ILE as an emergency treatment may reduce the incidence of QT prolongation following paliperidone overdose.