Intrathecal Pharmacokinetics of ARTCEREB® Irrigation and Perfusion Solution for Cerebrospinal Surgery in the Rat
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[Purpose] We investigated the pharmacokinetics of ARTCEREB® irrigation and perfusion solution (Artcereb) during intrathecal perfusion in a lateral ventricle-cisternal perfusion model in rats. [Methods] In this perfusion model we investigated the pharmacokinetics of electrolytes and also performed whole body autoradiography with 14C-inulin-labeled Artcereb. The perfusion rate was set at 0.35 mL/kg/h, taking into consideration the clinical perfusion rate (500 mL/60 kg/day). [Results and Discussion] In the absorption study, K⁺, Na⁺, and Cl⁻ concentrations in blood and in the effluent perfusion solution were determined to investigate the influence of perfusion with Artcereb on blood electrolytes. The concentrations of K⁺, Na⁺, and Cl⁻ in blood remained almost constant at close to baseline levels throughout perfusion. Output of K⁺, Na⁺, and Cl⁻, was very similar to input of these electrolytes as Artcereb. Recovery rates of K⁺, Na⁺, and Cl⁻ after perfusion were 102%, 105%, and 100% when calculated using the recovered perfusion solution. In the distribution study, whole body autoradiography was performed using 14C-inulin-labeled Artcereb to confirm the area perfused. Radioactivity was detected in the entire cerebrospinal fluid space, the brain, and the cribriform plate in the nasal cavity, confirming the area perfused with Artcereb. Radioactivity was seen in the bladder, suggesting that some of the perfusion solution transferred to blood via a physiological route, and that 14C-inulin was excreted renally. [Conclusions] We demonstrated that perfusion with Artcereb does not affect electrolyte (K⁺, Na⁺, and Cl⁻) concentrations in blood or CSF.

DETERMINATION OF THALIDOMIDE BLOOD CONCENTRATION IN PATIENTS BY LCMS
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[Purpose] Thalidomide was put on the market in Feb. 2009 in Japan for the treatment of multiple myeloma. The study on the relationship among the blood concentration, effect, and side effect, might be necessary for effective and safety clinical use. However, satisfactory determination method has not been developed for total thalidomide and/or both enantiomers. We have established determination method of total thalidomide and both enantiomers by LCMS, and determined the concentration in patients. [Methods] Serum or plasma was mixed with citrate buffer and stored at -30°C. Trichloroacetic acid was used as deproteinazation reagent for total thalidomide. Solid phase extraction (C18) was used for both enantiomers determination. Phenacetin was used as internal standard. Mobile phase was mixed solution of methanol and 5 mM ammonium acetate at proper ratio. The column was ODS for total thalidomide and CHIRALPACK-IA for enantiomers. The LCMS conditions: ESI(+), M/Z 259 for thalidomide and 180 for phenacetin, cone 30 V, capillary 3.5 V. [Results and Discussion] 45 samples were analyzed without problem. Around trough value at steady state were from 0.2 to 1.0 µg/ml, some patients exhibited high concentration over 1.5 µg/ml. The ratio of R and S enantiomers will be presented in poster.