P63 Anti-Alzheimer's drug, taurine transport through the blood-brain barrier in mice and pharmacokinetics

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Recently, evaluation of brain transport of taurine which is possible to effect on Alzheimer's disease has investigated in rats. Also, internal carotid artery perfusion (ICAP) method is very useful for measuring of blood-brain barrier (BBB) permeability in rats. But ICAP has difficulties to evaluate of BBB permeability in mice especially. In the present study examines neuropharmaceutials permeability through the BBB in mice by common carotid artery perfusion (CCAP) method that modify ICAP method and require simple surgery. The external carotid artery (ECA) is cannulated with coagulating pterygopalatine artery (PPA) on ICAP method, while CCA is cannulated without coagulating PPA on CCAP method. The CCAP method require 4-5 fold higher infusion rate than ICAP method because an additional factor of 2 must be incorporated to adjust for fluid loss to the extracerebral circulation.

At the result of CCAP method in mice at 2 ml/min for 10, 15, 30 second, the brain volume of distribution (V_D) of [^{3}H]taurine is similar to the result of ICAP method in rats at 4 ml/min, respectively. The permeability surface-area product (PS) for 15 second is more higher than that of other second in both of them. It could be followed by taurine efflux back into the blood after 15 second.

To compare of pharmacokinetic parameters, we used intravenous injection technique to mice and rats. The result of pharmacokinetic

experiment obtained from the intravenous injection with plasma volume marker, [^{14}C]sucrose and [^{3}H]taurine, area under the curve (AUC) in the plasma and brain uptake (%ID/g) are 65.5 ± 9.7 %ID*min/ml, 0.52 ± 0.09 %ID/g in mice, respectively. PS value of [^{3}H] taurine is similar to mice and rats.

In conclusion, the CCAP method in mice is able to take the place of ICAP method in rats, and there is species difference of drug permeability to the brain.