

MEETING ABSTRACT

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Penetration of polar organic compounds through the blood-brain barrier

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Background

The effect of polar organic xenobiotics in the central nervous system depends on blood-brain barrier (BBB) penetration of these compounds. Newly synthesized pyridinium aldoximes (K-compounds) are promising antidotes for organophosphate intoxications. However, being highly polar, their BBB penetration is questionable. Using an *in vivo* model we aimed to characterize the BBB penetration of K-compounds.

Methods

Male Wistar rats were injected intramuscularly with various doses of pyridinium aldoximes, blood, cerebrospinal fluid (CSF), and brain samples were collected after 5, 15, 30, 60 and 180 min. A recently developed and optimized RP-HPLC method was used for analysis. Samples of brain homogenate, blood serum and CSF were subjected to clean-up using precipitation by perchloric acid (pH < 1) and centrifugation at 14,000 rpm at 4°C for 20 min. Before load onto Zorbax Rx-C18 stationary phase, the pH of the supernatants was adjusted to 2. As mobile phase a mixture of acetonitrile and aqueous buffer pH 4.5, also containing ion-pairing agent, was used.

Results

Dose- and time-dependent BBB penetration of pyridinium aldoximes was experimentally found.

Conclusions

Dose- and time-dependent brain and CSF levels of these highly polar K-compounds following intramuscular administration suggest contribution of active transport or specific transporters in their BBB penetration. The BBB transport may also depend on the size and charge of the solutes.

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