

MEETING ABSTRACTS

EFFECTS OF MEMANTINE AND ITS METABOLITE Mrz 2/373 ON SOMAN-INDUCED INHIBITION OF BOVINE ERYTHROCYTE ACETYLCHOLINESTERASE *IN VITRO*

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Background: Memantine is the non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, used in the treatment of Alzheimer's disease. Memantine pretreatment assured protection of skeletal muscles from poisoning with nerve agents and an interaction between memantine and AChE was proposed [1].

Aim: Memantine and its main metabolite (1-amino-3-hydroxymethyl-5-methyl adamantane, Mrz 2/373) were used to ascertain their interaction with erythrocyte acetylcholinesterase (AChE) *in vitro*. The effect of these two compounds on the kinetics of the soman-induced AChE inhibition and on the aging of the soman-AChE complex was also investigated.

Methods: Bovine AChE activity was measured titrimetrically and the effect on aging of the soman-AChE complex was studied [2].

Results: Memantine and Mrz 2/373 exerted concentration-dependent inhibition of AChE, with Mrz 2/373 being a more potent inhibitor than the parent compound.

Addition of soman 2.5×10^{-8} mol/l induced gradual AChE inhibition that became almost 100% after 20 min. Memantine (0.1, 0.5 and 1 mmol/l) and Mrz 2/373 (0.1 and 1 mmol/l) concentration-dependently slowed down the AChE inhibition.

Neither memantine nor Mrz 2/373 prevented the aging of the soman-AChE complex. After 5 min incubation with AChE and soman, AChE activity was 11%, 36% and 30% in control medium and after adding of 1 mmol/l of memantine and Mrz 2/373, respectively.

Conclusion: Since high micromolar and low millimolar concentrations of memantine can be achieved in rats [3], it is quite possible that memantine and Mrz 2/373 can prevent AChE from inhibition by soman, which could, along with known memantine's neuroprotective activity, explain its potent antidotal effect in soman poisoning.

Keywords: *acetylcholinesterase; memantine; Mrz 2/373; soman; pretreatment*

References

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