Sustained cholinesterase inhibition in AD patients receiving rivastigmine for 12 months

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Abstract:

OBJECTIVE: To study the long-term dual inhibitory effects of rivastigmine on acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) in patients with AD. METHODS: Eleven patients with mild AD received rivastigmine for 12 months. Cholinesterase (ChE) activities in the CSF and plasma were assessed colorimetrically. Immunoblot analysis was used to evaluate AChE isoforms. Neuropsychiatric tests were performed throughout the study. RESULTS: At 12 months, the mean dose of rivastigmine was 8.6 mg/d and specific activities of ChE in the CSF were lower than baseline values (by 36% for AChE and 45% for BuChE), correlating with parallel reductions in the plasma (27% for AChE and 33% for BuChE). The reduction of specific activities in the CSF, but not in the plasma, appeared to be dependent on the dose and duration of treatment. Scores of some of the neuropsychological tests associated with memory and attention were correlated with both plasma and CSF AChE and BuChE inhibition for up to 6 months. Immunoblot analysis revealed up-regulation of the "read-through" AChE isoform (AChE-R), whereas levels of the synaptic isoform were unchanged. CONCLUSIONS: Rivastigmine causes persistent inhibition of AChE and BuChE in CSF as well as plasma. The persistent CSF inhibition contrasts with earlier findings after long-term treatment by the reversible ChE inhibitor tacrine, which demonstrated increased AChE activity in the CSF but not in the blood. Rivastigmine's effects on the preferential up-regulation of the AChE-R isoform may have a favorable effect on disease stabilization.

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