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**The Citicholinage Study: Citicoline Plus Cholinesterase Inhibitors in Aged Patients Affected with Alzheimer's Disease Study**

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**Abstract**

**Background:** Citicoline can have beneficial effects both in degenerative and in vascular cognitive decline in a variety of ways (apoptosis inhibition, neuroplasticity potentiation, phospholipid, and acetylcholine (ACh) synthesis). Acetylcholinesterase inhibitors (AChEIs) have been used for treatment of Alzheimer's disease (AD). When co-administered with cholinergic precursors, they are able to increase the intrasynaptic levels of ACh more than when the single drugs given alone.

**Objective:** The aim of the present study was to show the effectiveness of oral citicoline plus AChEIs in patients affected with AD.

**Methods:** This was a retrospective multi-centric case-control study, involving seven Centers for Cognitive Impairment and Dementia in Italy, on 448 consecutive patients aged 65 years old or older affected with AD. 197 patients were treated with an AChEI while 251 were treated with an AchEI + citicoline 1000 mg/day given orally. Cognitive functions were assessed by MMSE, daily life functions by ADL and IADL, behavioral symptoms by NPI, comorbidities by CIRS, and mood by GDS-short form. Tests were administered at baseline (T0), after 3 (T1), and 9 months (T2). The primary outcomes were effects of combined administration versus AChEIs given alone on cognitive functions assessed by MMSE. The secondary outcomes were possible side effects or adverse events of combination therapy versus AChEIs alone.

**Results:** Patients treated with citicoline plus an AChEI showed a statistically significant increase in MMSE between T0 and T1 ( $16.88 \pm 3.38$  versus  $17.62 \pm 3.64$ ;  $p = 0.000$ ) and between T1 and T2 ( $17.62 \pm 3.64$  versus  $17.89 \pm 3.54$ ;  $p = 0.000$ ).

**Conclusion:** The present study encourages the role of combined administration in disease management by slowing disease progressio

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