CHOLINESTERASE INHIBITORS PLUS ASSOCIATED HOMOTAURINE TREATMENT FOR PROLONGING THE EFFECTIVENESS OF PHARMACOTHERAPIES IN ALZHEIMER'S DISEASE

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Objective: To evaluate efficacy and tolerability of homotaurine, a patented variant of the aminoacid taurine, as add-on therapy to cholinesterase inhibitors (ChEIs) in patients with mild-to-moderate Alzheimer's disease (AD).

Methods: This was a prospective, randomized, 12 month, parallel-group study comparing ChEIs vs homotaurine(100 mg/die) + ChEIs. Cognitive functions were assessed cross-sectionally at baseline, 6 and 12 months using two rating scales: MMSE and ADAS-Cog.

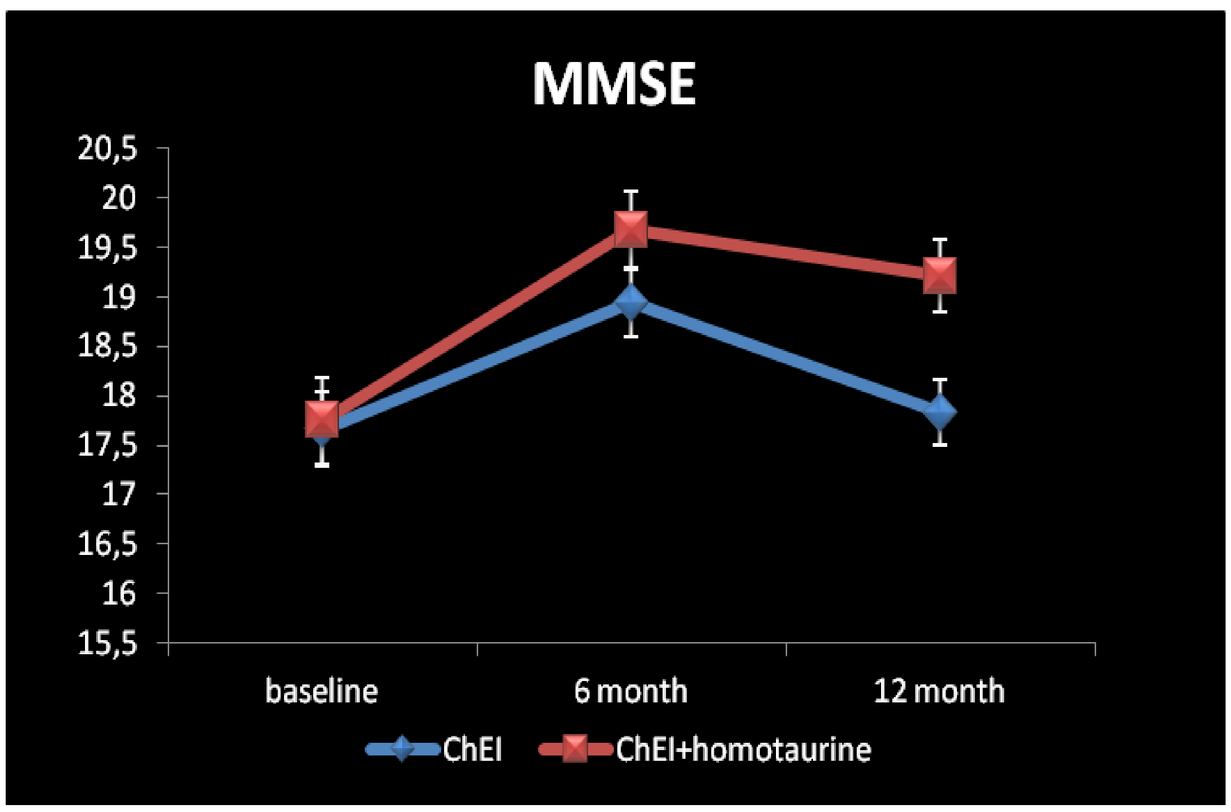
Results: 132 (80.4%) of 164 patients completed the study. 90 (54.8%) were female and 74 (45.2%) were male. 32 (19.6%) patients discontinued treatment prematurely. The most frequent reason for premature discontinuation was multiple failed appointments or non compliance. Patients treated with a combination therapy scored better on MMSE and ADAS-Cog at the study end compared with those who received a monotherapy. The MMSE score for combination therapy showed a mean improvement versus baseline of +2.46 points compared with monotherapy that showed a mean improvement of +0.28 points. MMSE score for combination therapy reached statistical significance vs baseline ($p > 0.05$). The ADAS-Cog score for combination therapy showed a mean improvement versus baseline of -2.42 points compared with monotherapy that showed a mean improvement of -0.83 points. The ADAS-Cog scores for combination differed significantly from baseline ($p > 0.05$). The between-group difference in MMSE change reached statistical significance ($p>0.05$) in favour of combination therapy, while in ADAS-Cog change showed a trend for superiority but did not reach statistical significance ($p \leq 0.1$). Adverse events occurred in 39.2% and in 42.5% of patients on combination and monotherapy groups respectively. Nausea, vomiting, and diarrhea were the most frequent in both groups.

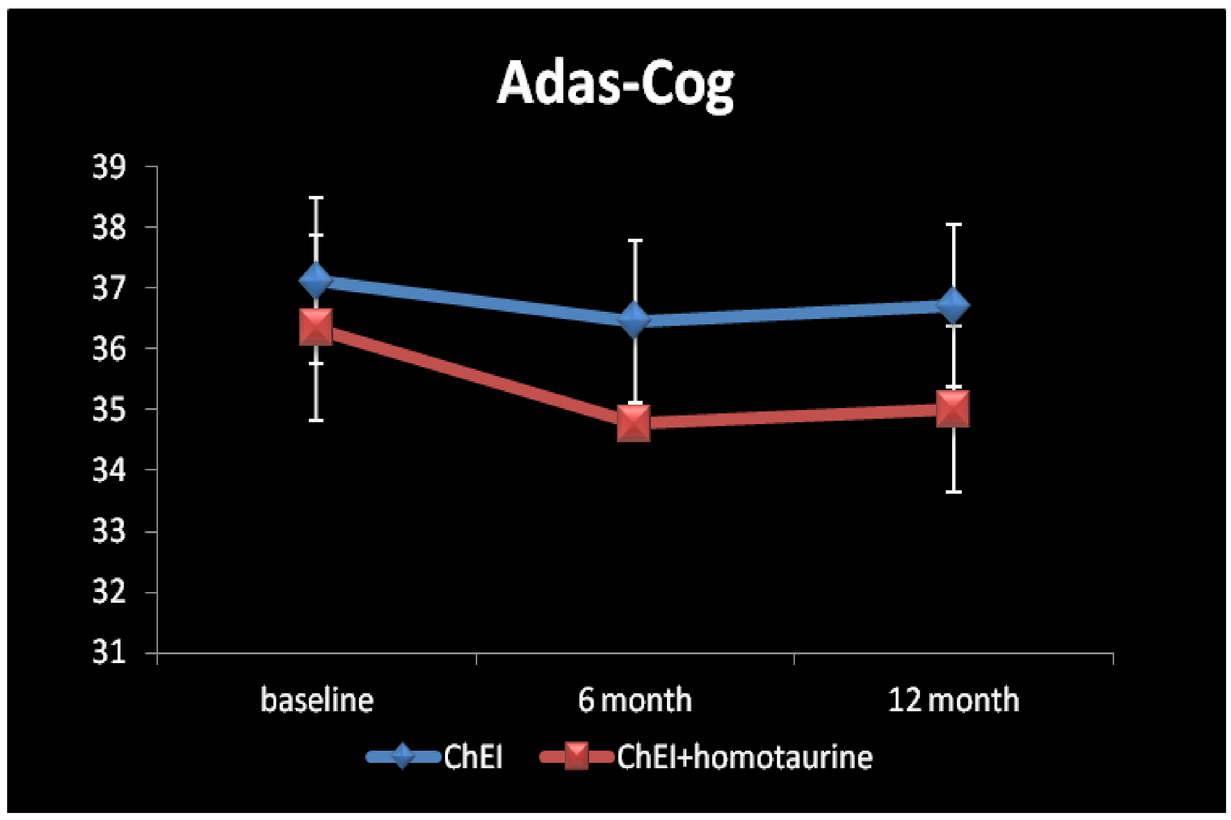
Discussion*:* Homotaurine has been shown, in both in vitro and in vivo models, to provide a relevant neuroprotective effect by its specific anti- amyloid activity and by its GABA A receptor affinity. The results of our study suggest a positive effect of homotaurine on cognitive function among patients suffering from AD, by slowing down cognitive decline during a 12 month follow-up period. No major side effects were reported.

Conclusions: The addition of this compound to the current standard treatments for AD may represent a way to prolong on time the beneficial effects of cholinergic therapies.

Baseline characteristics of the patient population (n=164)

	ChEIs+ homotaurine (n=84)	ChEIs (n=80)
MALES (n, %)	38 (42.72)	36 (44.85)
FEMALES (n, %)	46 (57.27)	44 (55.14)
MEAN AGE (yr ± SD)	76.4 ± 8.1	75.6 ± 8.2
MEAN EDUCATION (yr ± SD)	5.1 ± 2.9	5.3 ± 2.8
MEAN AD DURATION (yr ± SD)	5.6 ± 1.2	5.3 ± 1.4
MMSE (total mean score ± SD)	17.7 ± 2.8	17.6 ± 2.4
ADAS Cog (total mean score ± SD)	36.3 ± 1.5	37.1 ± 1.5
HIS (total mean score ± SD)	3.5 ± 2.9	3.8 ± 2.1
GDS (total mean score ± SD)	4.7 ± 0.5	4.8 ± 0.6





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