Neither vitamin E nor donepezil delays progression from amnestic mild cognitive impairment to Alzheimer’s disease in the long term


Do vitamin E or donepezil delay the clinical diagnosis of Alzheimer’s disease in people with the amnestic form of mild cognitive impairment?

METHODS

Design: Randomised controlled trial.

Allocation: Unclear.

Blinding: Double blind.

Follow up period: Three years.

Setting: Sixty nine sites in the United States and Canada; March 1999 to January 2004.

Patients: 790 people aged 55–90 years, with amnestic mild cognitive impairment of a degenerative nature. Other inclusion criteria: Clinical Dementia Rating of 0.5; Mini-Mental State Examination score 24 to 30; impaired memory; and Logical Memory delayed recall score about 1.5 to 2 standard deviations below education adjusted norm.

Intervention: Donepezil (10 mg daily) plus placebo vitamin E; vitamin E (2000 IU daily) plus placebo donepezil; or placebo vitamin E plus placebo donepezil for three years. All participants received a daily multivitamin tablet that contained 15 IU of vitamin E.

Outcomes: Possible or probable Alzheimer’s disease (National Institute of Neurological and Communicative Disorders and Stroke, and the Alzheimer’s Disease and Related Disorders Association clinical criteria); adverse events.

Patient follow up: 68% completed the study, 97% included in analyses.

MAIN RESULTS

Compared with placebo, neither vitamin E nor donepezil altered the probability of progression to Alzheimer’s disease after three years (vitamin E v placebo: HR for progression 1.02, 95% CI 0.74 to 1.41; donepezil v placebo: HR for progression 0.80, 95% CI 0.57 to 1.13). However, there was some indication that donepezil slowed progression to Alzheimer’s disease over the first two years compared with placebo (p = 0.03). Donepezil increased adverse events compared with placebo (diarrhoea, muscle cramps, insomnia, nausea, abnormal dreams: p < 0.01; loose stools, vomiting, arthritis: p < 0.05).

CONCLUSIONS

Neither vitamin E nor donepezil were associated with a lower rate of progression to Alzheimer’s disease after three years for people with mild cognitive impairment, although donepezil may lower rate of progression in the shorter term.

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