

## Vitamin E, donepezil ineffective for mild cognitive impairment

**Clinical question** Does Vitamin E or donepezil (Aricept) prevent progression from mild cognitive impairment to Alzheimer's disease?

**Bottom line** Vitamin E does not slow progression of mild cognitive impairment to full-fledged Alzheimer's disease. Donepezil provides an early benefit that is gone by 3 years. A secondary analysis found that donepezil appeared more beneficial for patients with the apolipoprotein E4 (apo E) gene. This finding requires prospective confirmation before we begin to test all patients with mild cognitive impairment for apo E and use it to guide therapy. (Level of evidence = 1b)

Petersen RC, Thomas RG, Grundman M, et al. Vitamin E and donepezil for the treatment of mild cognitive impairment. *N Engl J Med*. 2005;352:2379-2388.

**Synopsis** Mild cognitive impairment (MCI) is an intermediate stage between normal cognition and Alzheimer's disease often characterized by deficits of memory. In this study, researchers identified 769 patients with MCI, defined as impaired memory on standardized tests, a Mini-Mental State (MMS) test score between 24 and 30, and age 55 years to 90 years. These patients were randomly assigned to receive either 2,000 IU vitamin E, 10 mg donepezil (Aricept), or placebo daily; all patients received a multivitamin containing 15 IU vitamin E. MMS scores, age, and apo E gene status were considered when patients were allocated to treatment groups but appear to have been concealed from the investigators. Analysis was by intention to treat, and outcomes were blindly assessed. At the end of the 3-year study, 212 of the 769 patients who began the study had progressed to Alzheimer's disease (a rate of 16% per year). Taking vitamin E or donepezil did not have any effect on the likelihood of progression to Alzheimer's at 3 years. There was a decreased risk of progression to Alzheimer's in the donepezil group at 12 months compared with placebo (14.7% versus 6.3%;  $P=.04$ ; number needed to treat [NNT]=12), but this did not persist at 36 months. There was also no significant difference in MMS scores or other measures of cognition at 3 years. Patients with the apo E gene were much more likely to progress to Alzheimer's disease, and if you consider only that group, the benefit of donepezil persists for the full 3 years of the study.

## Statins associated with reduced risk of colorectal cancer

**Clinical question** Is statin use associated with a reduced risk of colorectal cancer?

**Bottom line** This observational study found an association between statin use and a reduced risk of colorectal cancer. Large randomized controlled trials are needed to confirm this potential benefit before we begin recommending statins to our patients for this indication, given the relatively small absolute magnitude of benefit, the cost, and the findings of increased risk of cancer in some previous clinical trials. (Level of evidence = 3b)

Poynter JN, Gruber SB, Higgins PDR, et al. Statins and the risk of colorectal cancer. *N Engl J Med*. 2005;352:2184-2192.

**Synopsis** Clinical trials designed to examine the effect of statins on heart disease have also looked at the incidence of cancer. They have had mixed results—some results show a benefit and some indicate harm. This case-control study identified colorectal cancer patients in a part of Israel between 1998 and 2004. They were matched according to age, sex, and ethnic group with a group of control patients without any history of colorectal cancer from the same population. Statin use was confirmed by a review of pharmacy records, and all participants completed a careful dietary and medical history. Case patients were similar regarding age and sex but were more like-

ly to be Ashkenazi Jews, more likely to have a family history of colorectal cancer, and less likely to exercise than control patients. They were also more likely to have a low vegetable consumption. Colorectal cancer was less likely to occur in patients who took a statin for at least 5 years (adjusted odds ratio [aOR]=0.57; 95% CI 0.44-0.73). Use of aspirin or other nonsteroidal anti-inflammatory drugs for at least 5 years was also associated with a reduced risk of colorectal cancer (aOR=0.70; 0.55-0.90). The association occurred in a variety of different types of patients.

## Parents satisfied with no treatment of otitis

**Clinical question** Are parents whose children do not receive treatment for acute otitis media less satisfied with their child's care?

**Bottom line** Parents don't seem to mind if their children are not treated with antibiotics. In this study comparing no treatment to immediate antibiotic treatment of acute otitis media, parent satisfaction scores were similar between the 2 groups, even though 21% of the no-treatment children eventually needed antibiotics. (Level of evidence = 1b)

McCormick DP, Chonmaitree T, Pittman C, et al. Nonsevere acute otitis media: a clinical trial comparing outcomes of watchful waiting versus immediate antibiotic treatment. *Pediatrics*. 2005;115:1455-1465.

**Synopsis** Several studies have shown that not treating children initially with antibiotics for acute otitis media results in fewer eventual prescriptions and fewer adverse effects. This study again evaluated watchful waiting versus immediate antibiotic treatment and also surveyed parents regarding their satisfaction with care. The researchers enrolled 223 infants and children with symptoms and otoscopic evidence of acute otitis media rated as not severe. Approximately 30% of the children were younger than 1 year, 25% were between the ages of 1 year and 2 years, and the rest were between the ages of 2 years and 13 years. The children were randomized (allocation concealment uncertain) to receive either high-dose amoxicillin, 90 mg per kg per day for 10 days, or no treatment. Children were concurrently treated with ibuprofen, a decongestant, and saline nose drops. They were also given an antihistamine, although this class of drugs was shown to be ineffective more than 20 years ago and was recently shown to extend the duration of middle ear effusion.

Parents were instructed to return to the clinic if symptoms failed to improve or worsened, which occurred in 5% of antibiotic-treated children and 21% of no-antibiotic children ( $P=.001$ ; number needed to treat with antibiotic to prevent one failure=7). Treatment failure occurred significantly more often in children who had received antibiotics in the previous 30 days. On a questionnaire of satisfaction, which included questions regarding the parents' feelings toward medication side effects, extra time spent receiving care for the infection, difficulty giving the antibiotic, work absences, and overall satisfaction, the average score was not significantly different between the 2 groups of parents when measured on day 12 and day 30 of the study, with scores in both groups averaging about 44 of a possible 48. The study has many limitations: there is no mention whether the parent questionnaires were written in Spanish, which is important since the study was conducted in a predominantly Spanish-speaking area of the United States; the questionnaire was not validated; and there was unblinding of the investigators in a number of instances. Parents were also not given a delayed prescription to fill if symptoms didn't resolve but were asked to return to the clinic for further evaluation.

Levels of evidence are explained at <http://www.infopeoms.com/levels.html>.

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