COCHRANE CORNER

Vitamin and mineral supplementation for maintaining cognitive function in cognitively healthy people in mid and late life: a Cochrane Review†

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† This review is the abstract of a Cochrane review previously published in the *Cochrane Database of Systematic Reviews*, 2018, December 17, Issue 12: CD011906 (doi: 10.1002/14651858.CD011906.pub2) (see www.cochranelibrary.com for information). Cochrane reviews are regularly updated as new evidence emerges and in response to feedback, and the Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review.

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See commentary in this issue.

Background

Vitamins and minerals play multiple functions in the central nervous system which may help to maintain brain health and optimal cognitive functioning. Supplementation of the diet with various vitamins and minerals has been suggested as a means of maintaining cognitive function, or even of preventing dementia, in later life.

Objectives

To evaluate the effects of vitamin and mineral supplementation on cognitive function in cognitively healthy people aged 40 years or more.

Search methods

We searched ALOIS, the Cochrane Dementia and Cognitive Improvement Group's specialised register, as well as MEDLINE, Embase, PsycINFO, CINAHL, ClinicalTrials.gov and the WHO Portal/ICTRP from inception to 26 January 2018.

Selection criteria

We included randomised controlled trials that evaluated the cognitive effects on people aged 40 years or more of any vitamin or mineral supplements taken by mouth for at least 3 months.

Data collection and analysis

Study selection, data extraction and quality assessments were done in duplicate. Vitamins were considered broadly in the categories of B vitamins, antioxidant vitamins and combinations of both. Minerals were considered separately, where possible. If interventions and outcomes were considered sufficiently similar, then data were pooled. To separate short-term cognitive effects from possible longer-term effects on the trajectory of cognitive decline, data were pooled for various treatment durations from 3 to 12 months and up to 10 years or more.

Main results

We included 28 studies with a total of more than 83 000 participants. The evidence had some general limitations. Most participants were enrolled in studies that were not designed primarily to assess cognition. These studies often had no baseline cognitive assessment and used only brief cognitive assessments at follow-up. Very few studies assessed the incidence of dementia. Most study reports did not mention adverse events or made only very general statements about them. Only 10 studies had a mean follow-up >5 years. Only two studies had participants whose mean age was <60 years at baseline. The risk of bias in the included studies was generally low, other than a risk of attrition bias for longer-term outcomes. We considered the certainty of the evidence behind almost all results to be moderate or low.

We included 14 studies (27 882 participants) that compared folic acid, vitamin B_{12}, vitamin B_6 or a combination of these, with placebo. The majority of participants were aged over 60 years and had a history of cardio- or cerebrovascular disease. We found that giving B vitamin supplements to cognitively healthy adults, mainly in their 60s and 70s, probably has little or no effect on global cognitive function at any time point up to 5 years (SMD values from –0.03 to 0.06) and may also have no effect after 5–10 years (SMD = –0.01). There were very sparse data on adverse effects or on incidence of cognitive impairment or dementia.

We included eight studies (47 840 participants) in which the active intervention was one or more of the antioxidant vitamins: ß-carotene, vitamin C or vitamin E. Results were mixed. For overall cognitive function, there was low-certainty evidence of benefit associated with ß-carotene after a mean of 18 years of treatment (MD = 0.18 TICS points, 95% CI 0.01–0.35) and of vitamin C after 5–10 years (MD = 0.46 TICS points, 95% CI 0.14–0.78), but not at earlier time points. From two studies that reported on dementia incidence, there was low-certainty evidence of no effect of an antioxidant vitamin combination or of vitamin E, either alone or combined with selenium. One of the studies had been designed to look for effects on the incidence of prostate cancer; it found a statistically significant increase in prostate cancer diagnoses among men taking vitamin E.

One trial (4143 participants) compared vitamin D_3 (400 IU/day) and calcium supplements with placebo. We found low- to moderate-certainty evidence of no effect of vitamin D_3 and calcium supplements at any time point up to 10 years on overall cognitive function (after a mean of 7.8 years, MD = –0.1 MMSE points, 95% CI –0.81 to 0.61) or the incidence of dementia (HR = 0.94, 95% CI 0.72–1.24). A pilot study (60 participants) used a higher dose of vitamin D_3 (4000 IU on alternate days) and found preliminary evidence that this dose probably has no effect on cognitive function over 6 months.

We included data from one trial of zinc and copper supplementation (1072 participants). There was moderate-certainty evidence of little or no effect on overall cognitive function (MD = 0.6 MMSE points, 95% CI –0.19 to 1.39) or on the incidence of cognitive impairment after 5–10 years. A second smaller trial provided no usable data, but reported no cognitive effects of 6 months of supplementation with zinc gluconate.

From one study (3711 participants) there was low-certainty evidence of no effect of about 5 years of selenium supplementation on the incidence of dementia (HR = 0.83, 95% CI 0.61–1.13).

Finally, we included three trials (6306 participants) of complex supplements (combinations of B vitamins, antioxidant vitamins and minerals). From the one trial that assessed overall cognitive function, there was low-certainty evidence of little or no effect on the TICS (after a mean of 8.5 years, MD = 0.12, 95% CI –0.14 to 0.38).

Authors' conclusions

We did not find evidence that any vitamin or mineral supplementation strategy for cognitively healthy adults in mid- or late-life has a meaningful effect on cognitive decline or dementia, although the evidence does not permit definitive conclusions. There were very few data on supplementation starting in mid-life (<60 years); studies designed to assess cognitive outcomes tended to be too short to assess maintenance of cognitive function; longer studies often had other primary outcomes and used cognitive measures that may have lacked sensitivity. The only positive signals of effect came from studies of long-term supplementation with antioxidant vitamins. These may be the most promising for further research.

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