Review: high dose vitamin E supplementation is associated with increased all cause mortality


Does vitamin E supplementation increase all cause mortality? Does a dose-response relation exist between vitamin E and all cause mortality?

**METHODS**

Data sources: Medline (1966 to August 2004), Cochrane Central Register of Controlled Trials, bibliographies of relevant studies and reviews, and personal files of the investigators.

Study selection and assessment: randomised controlled trials (RCTs) that compared vitamin E supplementation (alone or combined with other vitamins or minerals) with a control or placebo group in men or non-pregnant women. Study duration and follow up were >1 year, and >10 deaths occurred.

Outcomes: all cause mortality.

**MAIN RESULTS**

19 RCTs (n = 135 967, mean age range 47–84 y) met the selection criteria. 9 RCTs evaluated vitamin E alone, and 10 combined vitamin E with other vitamins or minerals. 16 RCTs were placebo controlled. Vitamin E dose varied between 16.5 and 2000 IU/d. Overall, vitamin E supplementation did not affect all cause mortality (table). However, although mortality was not increased in 8 RCTs evaluating low dose vitamin E, high dose vitamin E was associated with increased mortality (11 RCTs) (table). A dose-response analysis showed that all cause mortality increased as vitamin E dose increased to >150 IU/d. The effect of vitamin E did not change after adjustment for differences in sex, mean age, or mean follow up. The association of high dose vitamin E and mortality was stronger after adjustment for simultaneous use of other vitamins and minerals (pooled relative risk adjusted for differences in sex, mean age, or mean follow up were 1.06, 95% CI 1.01 to 1.11; risk difference 63 per 10 000 persons, CI 6 to 119).

**CONCLUSIONS**

High dose (>400 IU/d) vitamin E supplementation is associated with increased risk of all cause mortality. A dose-response relation exists between vitamin E doses >150 IU/d and mortality.

For correspondence: Dr E R Miller 3rd, Johns Hopkins Medical Institutions, Baltimore, MD, USA. ermiller@jhmi.edu

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**TREATMENT**

<table>
<thead>
<tr>
<th>Number of trials (n)</th>
<th>Vitamin E dose</th>
<th>RRI (95% CI)</th>
<th>Risk difference per 10 000 persons (CI)</th>
<th>NNH (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>19 (135 967)</td>
<td>High and low</td>
<td>1% (–2 to 4)</td>
<td>10 (–18 to 38)</td>
<td>Not significant</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>4% (1 to 7)</td>
<td>39 (3 to 74)†</td>
<td>257 (136 to 3334)</td>
</tr>
<tr>
<td>RRR (CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>18 to 38</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 (40 950)</td>
<td>Low</td>
<td>2% (–1 to 4)</td>
<td>–16 (–41 to 10)</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary; RRI, RRR, NNH NNT, and CI calculated from data in article. Follow up ranged from 1.4 to 8.2 years. A dose-response regression model was used.

†Favours placebo or no vitamin E.

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