Cognitive Function in Elderly People Is Influenced by Vitamin E Status


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ABSTRACT The aim of this study was to examine associations between vitamin E status and cognitive performance in elderly people. The study subjects were a group of 34 men and 86 women, aged 65–91 y, who were free of significant cognitive impairment. Dietary intake was monitored using a “weighed food record” for 5 consecutive days including a Sunday. Serum levels of α-tocopherol and cholesterol were determined by HPLC and colorimetric methods, respectively. The cognitive capacity of subjects was tested using the Pfeiffer’s Mental Status Questionnaire (PMSQ). Subjects with vitamin E intakes lower than 50% of those recommended had higher PMSQ scores, demonstrating a greater number of errors in comparison to participants with a greater intake of the vitamin (0.91 ± 1.22 vs. 0.47 ± 0.60, respectively, P < 0.05). Subjects who made no errors in the PMSQ test had significantly higher serum α-tocopherol concentrations (19.7 ± 8.6 μmol/L in men and 20.0 ± 8.4 μmol/L in women) and α-tocopherol/cholesterol ratios (3.5 ± 2.0 μmol/mmol in men 2.9 ± 1.4 μmol/mmol in women) compared with those who made errors (α-tocopherol 15.1 ± 5.6 μmol/L in men and 14.9 ± 6.1 μmol/L in women; α-tocopherol/cholesterol ratio 2.4 ± 0.8 and 2.3 ± 1.3 μmol/mmol in men and women, respectively). This study shows there to be a relationship between vitamin E status and cognitive function, and that vitamin E status could be improved in this population of elderly individuals. J. Nutr. 132: 2065–2068, 2002.

KEY WORDS: • vitamin E • elderly people • α-tocopherol • intake • cognitive function

Long-term oxidative stress is believed to be one of the major factors contributing to the decline of cognitive function observed with aging (1,2). Oxidative stress due to the generation of free radicals resulting from normal metabolism (3) causes accumulated oxidative damage to critical biomolecules, especially when coupled with insufficient endogenous antioxidant defense mechanisms (2,4).

Brain tissue, which has relatively little antioxidant protection (1), also contains high levels of polyunsaturated fatty acids (PUFA) (1), making it more vulnerable to oxidative insult (2). Interventions to increase antioxidant capacity and reduce oxidative damage have been suggested as a potentially useful strategy to prevent or retard this process (2). Due to its antioxidant properties, vitamin E plays a role in the prevention of certain diseases, including cancer, diabetes, cataracts, and cardio- and cerebrovascular disease (2), and has been related to the prevention or slowing of cognitive decline (2,5,6).

The incidence of low cognitive capacity in elderly people is expected to increase concomitantly with the rise in the elderly population (2). Devising strategies to prevent age-related cognitive decline and to maintain an independent elderly population is a priority.

The aim of this study was to evaluate vitamin E status in a group of noninstitutionalized elderly individuals, and to analyze its relationship with cognitive capacity.

SUBJECTS AND METHODS

The study subjects were a group of 120 noninstitutionalized elderly individuals between the ages of 65 and 91 y. All subjects resided in Madrid, Spain, and were recruited at two elderly persons’ clubs frequented by healthy, elderly people who returned to their own homes to sleep. The clubs were chosen randomly from the day centers in Madrid with >200 members. The characteristics of the sample are given in Table 1 and were described in a previous paper (7).

Subjects were excluded if they had a major underlying illness (e.g., neoplasm), an abnormal hepatic function test, diabetes mellitus or other endocrine disorders, if they suffered serious mental deterioration, or were taking medication that might modify the results. Also excluded were those who were modifying their diets to lose or gain weight, those who did not provide all of the required information, and those who were absent at the time of study or who showed a lack of consistency in their answers in the different tests performed. After the presentation of the study protocol, written consent of inclusion was obtained from interested subjects. This study was approved by the Comité de Investigación de la Facultad de Farmacia, Universidad Complutense de Madrid.

Dietary survey. A prospective method utilizing a weighed-food record was followed over 5 consecutive days including a Sunday. All subjects were given kitchen scales for weighing food. When the record was complete, subjects returned their booklets in person. A qualified nutritionist inspected all records to ensure that they were completed and that sufficient detail had been recorded. The energy and nutrient contents of all foods ingested were determined using the Spanish food-composition tables (8). Fatty acid contents were determined using the tables of Moreiras et al. (9). The Tables of Recommended Intakes of Energy and Nutrients for the Spanish Population, issued by the Department of Nutrition (10) were used to calculate the recommended dietary intakes (RDI) for this population group. Com-

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2 Abbreviations used: PMSQ, Pfeiffer’s Mental Status Questionnaire; PUFA, polyunsaturated fatty acid; RDI, recommended dietary intakes.
levels of those of different lipid components of serum (6). Triacylglycerol was determined by enzymatic hydrolysis (method GPO/PAP) (Merk 19706, CV = 3.2%) (17) and total cholesterol by the same method as the esterase cholesterol (Merk 19705, CV = 2.1%) (18).

The vitamin E/cholesterol ratio was then determined. Statistical analyses. Blood samples were taken from the antecubital vein first thing in the morning from subjects who had fasted overnight. Samples were placed in vacutainers without anticoagulant. Serum vitamin E concentration was determined by reverse-phase HPLC, following the method of Cuesta and Castro (16). Reagents included HPLC-grade ethanol, methanol and hexane (E. Merck, Darmstadt, Germany), and tocopheryl acetate (Sigma Chemical, St. Louis, MO). Serum (300 μL) was treated with an equal volume of methanol:methylene dichloride (3:1, v/v), and 100 μL was then injected into an HPLC system using a Rheodyne manual injector (model 7125; Cottati, CA). An ODS-C2 Spherisorb column was used (250 × 4 mm with 5-μm particle size).

Differences were considered significant at P < 0.05 (21).

RESULTS

Subjects’ personal and anthropometric data did not differ with respect to PMSQ scores. Subjects with the worst scores had only 1.65 ± 1.07 errors (1.44 ± 0.11 errors in men and 1.72 ± 1.10 in women), showing that this group suffered only slight cognitive decline (Table 1).

Most (95.2%) of subjects had vitamin E intakes below those recommended (86.7% had intakes < 66% of RDI), and none took vitamin E supplements during the study period.

### TABLE 1

Personal, anthropometric and cognitive function data of elderly people categorized by gender and their Pfeiffer’s Mental Status Questionnaire (PMSQ) scores

<table>
<thead>
<tr>
<th></th>
<th>PMSQ = 0 (No errors)</th>
<th>PMSQ &gt; 0 (Some errors)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>n</td>
<td>20</td>
<td>42</td>
</tr>
<tr>
<td>Age, y</td>
<td>73.8 ± 5.9</td>
<td>70.8 ± 6.8</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>17.9 ± 8.2</td>
<td>7.9 ± 9.5</td>
</tr>
<tr>
<td>Height, cm</td>
<td>167.5 ± 2.7</td>
<td>150.8 ± 6.3</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.7 ± 2.9</td>
<td>29.9 ± 3.8</td>
</tr>
<tr>
<td>BMI &gt; 25 kg/m², %</td>
<td>53.8</td>
<td>89.3</td>
</tr>
<tr>
<td>Smokers, %</td>
<td>80</td>
<td>7.1</td>
</tr>
<tr>
<td>Supplements taken sporadically, %</td>
<td>5</td>
<td>7.1</td>
</tr>
<tr>
<td>PMSQ resultsb</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

1 Values are means ± sd. Significant differences (P < 0.05) in two-way ANOVA for sex (a) and PMSQ score (b).

2 BMI, body mass index.

parisons between observed intakes and RDI were used to assess the adequacy of the diets.

Estimates of 24-h energy expenditure were made using equations proposed by the WHO (11) multiplied by an activity ratio in accordance with the criteria of several expert groups (10,11). To establish activity coefficients necessary for the calculation of energy expenditure, subjects completed a questionnaire on their physical activity for what they considered to be a typical day during the experimental period. The questionnaire was a modified version of that previously published by Dalloso et al. (12), based on the self-assessment of time spent walking, sleeping, eating, standing or in physically active leisure, for example. The percentage of discrepancy in reporting was established in accordance with Johnson et al. (13) using the following formula: (energy expenditure – energy intake) × 100/energy expenditure. When this method is used, a negative value indicates a reported energy intake greater than the predicted total energy expenditure (probable overreporting) and a positive value denotes a reported energy intake less than the predicted total energy expenditure (underreporting) (13,14).

The intake of supplements was also monitored. Subjects were asked which supplements they took (nutrients supplied) and the frequency of intake: habitually, 6–11 times/y, 2–5 times/y, < 2 times y, or never.

**Anthropometric survey.** Weight and height (without shoes) were determined using a digital electronic weighing scale (Seca Alpha, Rue Lavoisier 91430, Igmy, France) (range: 0.1–150 kg) and a digital stadiometer (Harpen, Carlstadt, NJ) (range: 70–205 cm). These data allowed the calculation of each subject’s body mass index (kg/m²). Anthropometric dimensions were taken by trained observers following norms set by the WHO (15).

**Biochemical analyses.** Blood samples were taken from the antecubital vein first thing in the morning from subjects who had fasted overnight. Samples were placed in vacutainers without anticoagulant. Serum vitamin E concentration was determined by reverse-phase HPLC, following the method of Cuesta and Castro (16). Reagents included HPLC-grade ethanol, methanol and hexane (E. Merck, Darmstadt, Germany), and tocopheryl acetate (Sigma Chemical, St. Louis, MO). Serum (300 μL) was treated with an equal volume of methanol:methylene dichloride (3:1, v/v), and 100 μL was then injected into an HPLC system using a Rheodyne manual injector (model 7125; Cottati, CA). An ODS-C2 Spherisorb column was used (250 × 4 mm with 5-μm particle size). Determinations were made using a Varian 500 chromatograph (Varian Analytical Instruments 505, Sugarland, TX). The mobile phase was a mixture of methanol and water (95:5, v/v) at a flow rate of 2 mL/min. Absorbance was monitored at 290 nm using a Kontron detector (Kontron AG Instruments, Zürich, Switzerland). A Varian 4290 integrator was used to calculate peak areas. Concentrations were calculated according to standards. The minimum detection level was 0.1 μmol/L for α-tocopherol. Before determinations, a quality control check was performed using pooled serum divided into 50 aliquots. Tocopherol levels were determined in these 50 samples at a rate of 10% over 5 consecutive days. The assay CV was 2.6%.

For the evaluation of nutritional vitamin E status, several indices have been proposed that establish relationships between plasma levels and of those of different lipid components of serum (6). Triacylglycerol was determined by enzymatic hydrolysis (method GPO/PAP) (Merk 19706, CV = 3.2%) (17) and total cholesterol by the same method as the esterase cholesterol (Merk 19705, CV = 2.1%) (18).

The vitamin E/cholesterol ratio was then determined.

Studies on cognitive capacity. Cognitive function was evaluated by Pfeiffer’s Mental Status Questionnaire (PMSQ) (19), as translated and validated for the Spanish population by González et al. (20). This establishes three groups in relation to the number of errors made by subjects, i.e., intellectual function intact (0–2 errors), slight intellectual deterioration (3–4 errors), and moderate intellectual deterioration (5–7 errors). This test is extremely useful when working with illiterate populations because it is simple and contains a correction factor for the level of education that different subjects might have received. The test was performed by a geriatrician experienced in this area.

Subjects were grouped by sex and according to their PMSQ scores (means and sd are shown). The degree of significance of the differences between mean values was calculated using two-way ANOVA, taking into account the influence of sex and the PMSQ results obtained. For nonhomogeneous distributions of results, the Kruskall-Wallis test was used. Differences between proportions were examined using the χ² test. Linear correlation coefficients between dietary, biochemical and functional data were calculated. Differences were considered significant at P < 0.05 (21).
α-Tocopherol concentrations were <18 μmol/L in 51.7% of the subjects and 17.5% (14.3% of men, 19.2% of women) had concentrations < 11.5 μmol/L. Subjects who made no errors on the PMSQ test had significantly higher serum α-tocopherol concentrations and α-tocopherol/cholesterol ratios than those who made errors (Table 2).

Significant inverse correlations were found between the number of errors in the PMSQ test and serum vitamin E concentration ($r = -0.3519$), and the vitamin E/cholesterol ratio ($r = -0.3014$). These correlations were maintained when only the women were considered ($r = -0.3894$ for serum α-tocopherol and $r = -0.3059$ for the α-tocopherol/cholesterol ratio).

**DISCUSSION**

The intake of vitamin E by the elderly people in this study was similar to, or lower than that reported in other studies (14,22–24). This low intake could be influenced in part by the underestimation of intake by the subjects (Table 2). This possible underestimation, or discrepancy between energy intake and estimated energy expenditure (when theoretical expenditure is greater than that taken in), was larger ($P < 0.1$), and the energy intake smaller ($P < 0.05$) in those subjects with the worst PMSQ scores. This indicates that subjects with intact intellectual function might better remember the foods they have eaten or that because their overall diet is more adequate, their supply of nutrients is better and they therefore have better general and mental health. In fact, a significant inverse correlation was found between PMSQ results and the total number of foods consumed ($r = -0.3116$), as well as the consumption of vegetables ($r = -0.2785$), relationships that were maintained when only women were considered in the analysis ($r = -0.2965$, total food intake; $r = -0.3040$, vegetable consumption).

Subjects with vitamin E intakes < 50% of the RDI had more errors on the PMSQ than those with a greater intake of the vitamin. It would therefore appear that vitamin E influences cognitive function. Some investigators have found that vitamin E supplementation is beneficial to the elderly in terms of mental and functional capacities (25). However, Mendelsohn et al. (26) did not conclude that antioxidant supplementation is associated with better cognitive function in apparently healthy individuals, although they suggested that antioxidant supplementation might be effective in high risk populations.

The dietary vitamin E/PUFA ratio was lower than desired (0.6 mg/g) (27) in 44.2% of subjects, especially among men (Table 2). However, the comparison of subjects with this ratio < 0.6 mg/g with those above this figure, or those above and below the 25th (0.55 mg/g), 50th (0.64 mg/g) or 75th percentiles (0.78 mg/g), revealed no differences in PMSQ results.

There was a fairly large discrepancy in energy intake and expenditure (possible underreporting) that was higher than that found in other studies (23,24), particularly for subjects who had PMSQ errors (Table 2). This suggests that special attention should be paid to the biochemical evaluations of vitamin E status.

Serum metabolite concentrations were similar to or slightly lower than those found in other studies of elderly subjects (22,28). Participants with low dietary vitamin E intake (<50% RDI) had significantly lower serum α-tocopherol levels than those with intakes > 50% of the RDI. Furthermore, the participants with a lower dietary vitamin E/PUFA ratio had lower serum α-tocopherol concentrations, supporting the existence of an association between dietary and biochemical data (7).

The influence of vitamin E status on cognitive function has been noted in other studies. Perkins et al. (6) studied the data of 5000 elderly people in the Third National Health and Nutrition Examination Survey (NHANES III) and reported a lack of association between poor memory and plasma levels of vitamins C, A, β-carotene and selenium. However, they identified a significant relationship between poor memory performance and low plasma concentrations of vitamin E (as adjusted by plasma cholesterol level).

We found significant relationships between serum vitamin E concentration ($r = -0.3519$) and the vitamin E/cholesterol ratio ($r = -0.3014$) and PMSQ results. As the former increased, the number of errors made on the test was reduced. Further, vitamin E concentrations, as well as vitamin E/cho-

**TABLE 2**

Vitamin E status of elderly people categorized by gender and their Pfeiffer’s Mental Status Questionnaire (PMSQ) scores

<p>| Vitamin E status of elderly people categorized by gender and their Pfeiffer’s Mental Status Questionnaire (PMSQ) scores&lt;sup&gt;1&lt;/sup&gt; |
|---------------------------------|------------------|------------------|------------------|------------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>20</td>
<td>42</td>
<td>14</td>
<td>44</td>
</tr>
<tr>
<td>Energy, ab kJ/d</td>
<td>8017 ± 1928</td>
<td>6737 ± 1274</td>
<td>7014 ± 1490</td>
<td>6131 ± 1391</td>
</tr>
<tr>
<td>Underreporting, %</td>
<td>6.2 ± 24.9</td>
<td>11.9 ± 14.7</td>
<td>17.0 ± 20.0</td>
<td>19.1 ± 19.0</td>
</tr>
<tr>
<td>Vitamin E, mg/d</td>
<td>5.1 ± 2.0</td>
<td>5.4 ± 2.3</td>
<td>4.9 ± 3.2</td>
<td>4.8 ± 2.2</td>
</tr>
<tr>
<td>% of RDA</td>
<td>42.5 ± 16.4</td>
<td>42.0 ± 19.5</td>
<td>41.1 ± 26.5</td>
<td>39.6 ± 18.3</td>
</tr>
<tr>
<td>mg/mL</td>
<td>0.66 ± 0.24</td>
<td>0.82 ± 0.32</td>
<td>0.68 ± 0.32</td>
<td>0.78 ± 0.32</td>
</tr>
<tr>
<td>INQ</td>
<td>0.5 ± 0.2</td>
<td>0.5 ± 0.2</td>
<td>0.5 ± 0.2</td>
<td>0.5 ± 0.2</td>
</tr>
<tr>
<td>PUFA, g/d</td>
<td>10.4 ± 5.1</td>
<td>7.7 ± 2.7</td>
<td>8.8 ± 4.0</td>
<td>8.0 ± 3.4</td>
</tr>
<tr>
<td>Vitamin E/PUFA, ab mg/g</td>
<td>0.5 ± 0.2</td>
<td>0.7 ± 0.2</td>
<td>0.5 ± 0.1</td>
<td>0.6 ± 0.2</td>
</tr>
<tr>
<td>α-Tocopherol, b μmol/L</td>
<td>19.7 ± 8.6</td>
<td>20.0 ± 8.4</td>
<td>15.1 ± 5.6</td>
<td>14.9 ± 6.1</td>
</tr>
<tr>
<td>α-Tocopherol &lt; 18 μmol/L, %</td>
<td>5.0 ± 5.0</td>
<td>35.7</td>
<td>85.7 ± 50.0</td>
<td>56.8 ± 7.8</td>
</tr>
<tr>
<td>Triacylglycerol, mmol/L</td>
<td>1.7 ± 0.6</td>
<td>1.6 ± 1.6</td>
<td>1.9 ± 0.8</td>
<td>1.4 ± 0.6</td>
</tr>
<tr>
<td>Cholesterol, mmol/L</td>
<td>6.2 ± 1.0</td>
<td>7.0 ± 1.0</td>
<td>6.5 ± 1.0</td>
<td>6.5 ± 1.9</td>
</tr>
<tr>
<td>α-Tocopherol/cholesterol, b μmol/mmol</td>
<td>3.5 ± 2.0</td>
<td>2.9 ± 1.4</td>
<td>2.4 ± 0.8</td>
<td>2.3 ± 1.3</td>
</tr>
</tbody>
</table>

<sup>1</sup> Values are means ± sd. Significant differences ($P < 0.05$) in two-way ANOVA for sex (a) and PMSQ score (b). * Significant difference by χ² test.

<sup>2</sup> RDI, recommended dietary intake; INQ, index of nutritional quality (density in mg/mJ divided by density recommended); PUFA, polyunsaturated fatty acid.
listerol ratios, were lower in subjects who made PMSQ errors compared with those who did not (Table 2).

Several studies of patients with dementia (5) have found lower blood concentrations of vitamin E in these patients than in control subjects, but not at the level of nutritional deficiency. Thus, lower antioxidant status in patients with dementia may indicate an increased level of oxidative stress, an important factor in the impairment of cognitive function. Vitamin E might help in the prevention of cognitive decline through its powerful antioxidant action, which provides protection against nervous tissue damage (2), as well as through its role in the prevention of vascular dementia, a disorder responsible for cognitive decline in many people (2).

The association of vitamin E with reduced risk of vascular dementia can be attributed to its numerous effects on the vascular system, including its ability to prevent stroke by decreasing platelet aggregation and adhesion, and by slowing progression of carotid atherosclerosis (29). In addition, plasma vitamin E status is reported to be lower in patients with vascular dementia (30).

The evidence from experimental, clinical and epidemiologic studies supports the notion that consumption of foods containing high levels of dietary antioxidants, in addition to exerting several other health benefits, may prevent or reduce the risk of cognitive deterioration (2). The results of this study show that a relationship exists between vitamin E status and cognitive function, although they do not provide proof of a causative effect. This should be the subject of future research. However, it is clear that the vitamin E nutriture of this population of elderly people could be improved.

LITERATURE CITED