Brief Report

Intakes of Potassium, Magnesium, and Calcium and Risk of Stroke

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Background and Purpose—We aimed to investigate the associations of dietary and total potassium, magnesium, and calcium intakes with stroke occurrence.

Methods—A prospective cohort study was conducted among 36094 participants aged 21 to 70 years. Dietary intake was assessed with a food frequency questionnaire.

Results—During 12 years of follow-up, 631 strokes occurred. After adjustment for confounders, magnesium intake was associated with reduced stroke risk (hazard ratio [95% confidence interval] per 100 mg/d, 0.80 [0.67–0.97] dietary magnesium; 0.78 [0.65–0.93] total magnesium). Potassium and calcium intakes were not associated with stroke.

Conclusions—This study supports an association between high magnesium intake and a reduced stroke risk. (Stroke. 2014;45:00-00.)

Key Words: calcium ■ magnesium ■ potassium ■ stroke

Stroke remains a major cause of morbidity and mortality. Blood pressure (BP) is a major stroke risk factor. Since previous studies showed inverse relationships of potassium, magnesium, and calcium with BP, these electrolytes may also be useful in reducing stroke risk. Meta-analyses of prospective studies pointed toward inverse associations of dietary potassium, magnesium, and calcium with stroke. For calcium, inverse associations have only been reported in populations with low dietary calcium intakes. Few studies included supplements in their estimates of electrolyte intakes.

We investigated whether higher dietary and total (diet plus supplements) potassium, magnesium, and calcium intake is associated with reduced stroke occurrence.

Subjects and Methods

European Prospective Investigation into Cancer and Nutrition-Netherlands (EPIC-NL) consists of 2 Dutch contributing cohorts to EPIC. Participants signed informed consent before study inclusion. Both cohorts comply with the Declaration of Helsinki and were approved by local medical ethics committees.

Food intake was assessed using a food frequency questionnaire. Total calcium and magnesium intakes were calculated by summing up intakes from diet and supplements. Relative validity was moderate for fruits and vegetables (r=0.31–0.68) and high for milk and milk products (r=0.71–0.79).

Diagnoses of stroke, defined according to national guidelines, were obtained from the Dutch Centre for Health Care Information and Statistics Netherlands. For the present analyses, we used International Classification of Diseases, Ninth Revision (ICD-9), Clinical Modification codes 430 to 434 and 436. High validity was previously reported for stroke ICD-9 coding in hospital discharge registries.

We used multivariable Cox regression to quantify associations.

Results

The study population (n=36094) had a mean (SD) age of 49 (12) years, systolic BP of 126 (19) mmHg, and 25% were male. Mean intakes of dietary potassium, total magnesium, and total calcium (mg/d) were 3672 (903), 348 (93), and 1138 (508), respectively. Table I in the online-only Data Supplement shows baseline characteristics according to quartiles of total magnesium intake.

During a mean (SD) follow-up of 12 (2) years, 631 strokes occurred (360 ischemic, 170 hemorrhagic, 101 unspecified). In adjusted analysis, magnesium associated inversely with stroke (hazard ratio [95% confidence interval] per 100 mg/d, 0.80 [0.67–0.97] dietary; 0.78 [0.65–0.93] total), whereas calcium and potassium intakes were not associated with stroke (Table). Associations did not materially change after adjustment for sodium intake or BP classified according to the European guideline of hypertension. No interactions with sex and age were observed (P≥0.15), except for calcium (P≤0.04 with age). However, age-stratified associations of calcium and stroke were all nonsignificant.
Of the main electrolyte providing food groups, nuts associated inversely with stroke (hazard ratio quartile 4 versus 1, 0.76 [95% confidence interval, 0.59–0.99]). Grain products were only associated with reduced stroke in univariable analysis. Fruits plus vegetables and dairy products showed no association with stroke occurrence.

**Discussion**

In this large cohort, high magnesium intakes associated with reduced stroke, whereas calcium and potassium intakes were not associated with stroke.

Strengths of our study include its long follow-up, large number of stroke cases, and prospective design. Limitations include that we assessed dietary intake with a food frequency questionnaire, which is prone to imprecision and reporting bias. Our food frequency questionnaire was not validated for electrolytes. However, the main electrolyte sources had moderate to high validity, and their associations with stroke risk support our findings. Furthermore, (older) women were over-represented. Because results were similar by sex and age groups, this suggests our findings are generalizable to (older) men. Finally, by using registered ICD-9 codes for stroke ascertainment, we may have missed participants who experienced a minor stroke. However, this can only have attenuated our findings.

The inverse association of magnesium intake and stroke is consistent with a meta-analysis of 7 prospective studies. They reported an 8% reduced stroke risk per 100 mg/d dietary magnesium increment.6 We found a greater reduction, 20% per 100 mg/d, which may be attributable to differences in study.
population or covariables taken into account, such as hypertension and hypertriglyceridemia. We did not adjust for such factors because we consider these parts of the causal pathway to stroke. Our findings are supported by a large-scale trial that showed reduced stroke when a Mediterranean diet is supplemented with nuts, which are rich in magnesium. Next to BP-lowering effects, mechanisms by which magnesium may protect against stroke include beneficial effects on cholesterol synthesis and inflammation.14

Our and previous studies suggest that a diet rich in sources of magnesium, such as with leafy vegetables, grain, and dairy products, may be useful in stroke prevention. However, the effect of magnesium seems marginal, and we cannot exclude that residual confounding by healthy lifestyle (partly) explains our results. Large-scale intervention studies are needed to confirm our findings.

We found no association of potassium with stroke, and others have reported inconsistent findings.7 Regarding the lack of association between calcium and stroke, our report is in line with what was generally observed in previous cohorts.5 The relatively high potassium and calcium intakes in our study may have contributed to our inability to detect associations.

In conclusion, there is a strong association between higher magnesium intake and a reduced stroke risk.

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Disclosures
None.

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### Supplementary table I. Baseline characteristics according to quartiles of total magnesium intakes*

<table>
<thead>
<tr>
<th>Range of intake (mg/d)</th>
<th>Quartile 1 ≤285</th>
<th>Quartile 2 286-336</th>
<th>Quartile 3 337-397</th>
<th>Quartile 4 ≥398</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52 (12)</td>
<td>51 (11)</td>
<td>50 (11)</td>
<td>45 (12)</td>
</tr>
<tr>
<td>Male</td>
<td>10</td>
<td>15</td>
<td>24</td>
<td>53</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.9 (4.2)</td>
<td>25.8 (4.0)</td>
<td>25.6 (3.9)</td>
<td>25.4 (3.8)</td>
</tr>
<tr>
<td>SBP† (mmHg)</td>
<td>129 (21)</td>
<td>128 (19)</td>
<td>126 (19)</td>
<td>124 (17)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>42</td>
<td>40</td>
<td>36</td>
<td>31</td>
</tr>
<tr>
<td>Current smoking</td>
<td>30</td>
<td>28</td>
<td>29</td>
<td>34</td>
</tr>
<tr>
<td>Physically (moderately) inactive</td>
<td>40</td>
<td>33</td>
<td>30</td>
<td>24</td>
</tr>
<tr>
<td>Low education</td>
<td>14</td>
<td>18</td>
<td>22</td>
<td>27</td>
</tr>
<tr>
<td>Moderate alcohol</td>
<td>18</td>
<td>21</td>
<td>24</td>
<td>28</td>
</tr>
</tbody>
</table>

*Values are means (SD) or percentages; total magnesium is defined dietary plus supplementary intakes of magnesium; N=36,094, with 9,024 participants in the first and third quartile, and 9,023 in the second and fourth quartile; †SBP: systolic blood pressure; ‡Defined as 11-25 g alcohol/d.