Dietary Intake of Naturally Occurring Plant Sterols Is Related to a Lower Risk of a First Myocardial Infarction in Men but Not in Women in Northern Sweden

Sofia Klingberg, Lars Ellegård, Ingegerd Johansson, Jan-Håkan Jansson, Göran Hallmans, and Anna Winkvist

Department of Internal Medicine and Clinical Nutrition, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; Department of Public Health and Clinical Medicine/Nutritional Research, Department of Odontology/Cariology, and Department of Public Health and Clinical Medicine/Medicine, University of Umeå, Umeå, Sweden

Abstract

Dietary intake of naturally occurring plant sterols is inversely related to serum cholesterol concentrations. Elevated serum cholesterol increases the risk of myocardial infarction (MI), but it is unknown if this can be reduced by dietary intake of naturally occurring plant sterols. Our aim was to investigate if a high intake of naturally occurring plant sterols is related to a lower risk of contracting a first MI. The analysis included 1005 prospective cases (219 women, 786 men) and 3148 matched referents (723 women, 2425 men), aged 29–73 y at baseline, from the population-based Northern Sweden Health and Disease Study. A food frequency questionnaire (FFQ) was completed at baseline. Absolute plant sterol intake was inversely related to the risk of a first MI in men (OR highest vs. lowest quartile = 0.70; 95% CI: 0.53, 0.85; P-trend = 0.006) but not in women. After adjustment for confounders, the estimated risk was somewhat attenuated (OR highest vs. lowest quartile = 0.71; 95% CI: 0.55, 0.92; P-trend = 0.067), suggesting that increasing sterol intake from 150 to 340 mg/d reduces the risk of a first MI by 29%. Energy-adjusted plant sterol intake was not related to the risk of a first MI in either men or women. In conclusion, the findings of this observational study show that a high absolute intake of naturally occurring plant sterols is significantly related to a lower risk of a first MI in men in northern Sweden, whereas no significant relation was seen for energy-adjusted plant sterol intake. In women, no significant associations were found. The results from this study show that intake of plant sterols may be important in prevention of MI. J. Nutr. 143: 1630–1635, 2013.

Introduction

It is estimated that >17 million people died of cardiovascular disease (CVD) worldwide in 2008, representing 30% of all deaths (1). In Europe, the proportion is even higher; almost one-half of all deaths are caused by CVD (2). Although the incidence of myocardial infarction (MI) has decreased by 1–2%/y during the past decade, it still affects ~40,000 people/y in Sweden and is the leading cause of death (3). However, many CVDs can be treated or prevented.

There are several established risk factors for CVD, including both behavioral risk factors such as smoking, physical inactivity, and poor diet as well as medical conditions such as overweight, hypertension, elevated blood glucose, and dyslipidemia (4,5). Serum cholesterol concentrations are affected by diet and it is established that intake of saturated fat raises serum cholesterol concentrations, whereas intake of unsaturated fat and soluble dietary fiber lowers serum cholesterol concentrations (6,7).

Plant sterols are bioactive compounds found in varying concentrations in vegetable foods. It has long been known that plant sterols lower serum cholesterol when consumed in large doses, i.e., 1–2 g/d from foods enriched with plant sterols (8). The mean dietary intake of naturally occurring plant sterols in European populations is only ~200–300 mg/d (9–14), an amount previously considered too low to affect serum cholesterol. However, it has been shown in small experimental studies that a plant sterol intake of 150–584 mg/d alters whole-body...
cholesterol metabolism and might therefore also affect serum cholesterol concentrations (15–20). We recently showed in 2 epidemiological studies that intake of naturally occurring plant sterols is inversely related to serum cholesterol concentrations (10,13). Hence, it might be hypothesized that this effect on serum cholesterol may result in a lower risk of MI.

The aim of the study was to investigate if a high intake of naturally occurring plant sterols is related to a lower risk of contracting a first MI.

Subjects and Methods

Study design. This study was designed as a nested case-referent study within 2 cohorts of the Northern Sweden Health and Disease Study, i.e., the Västerbotten Intervention Program (VIP) and the Northern Sweden WHO Monitoring Trends and Cardiovascular Disease study (MONICA), both of which were started in 1985 (21).

The VIP is ongoing; all inhabitants of Västerbotten county in northern Sweden (population ~260,000) are invited to a health examination at their primary health center the year they turn 40, 50, and 60 y of age (until 1995, those turning 30 were also included) (22,23). The health examination includes an extensive diet and lifestyle questionnaire, measurement of important CVD-related risk factors, and a blood sample. On average, ~60% of the invited population participated each year and no systematic differences were found between participants and nonparticipants (22).

In the MONICA study, health examinations similar to those in the VIP were performed in a population-based random sample in 1986, 1990, 1994, and 1999. Between 2000 and 2500 individuals were examined each year; the average participation rate in MONICA is 77% (24).

The Regional Ethical Review Board in Göteborg, Sweden, approved the study (registration no. 622-05).

Study population. All MI events in northern Sweden are registered in the population-based MONICA registry according to standardized WHO and MONICA criteria and based on reports from hospitals or general practitioners as well as hospital discharge records and death certificates (24). All prospective cases of first MI in VIP and MONICA participants occurring between 1986 and 2006 were identified via the MONICA registry.

Individuals with a history of MI were excluded from this case-referent study. Up to 4 referents, matched by sex, age (±2 y), year of health examination, and cohort, were selected for each case. In total, 1367 cases of first MI and 4818 referents were identified. Participants having responded to a FFQ (see details below) with only 49 questions within MONICA 1990 (71 cases, 284 referents) were excluded, because the few questions were judged not to be representative of the whole diet. Participants who at baseline reported current medication for hyperlipidemia, high blood pressure, and/or angina/other cardiac conditions and/or had ever been diagnosed with diabetes prior to the health examination (291 cases, 1386 referents) were excluded to avoid bias according to Hornell et al. (25). Hence, the dataset consisted of 1005 cases (219 female, 786 male) and 3148 referents (723 female, 2425 male).

Blood samples and laboratory procedures. Blood samples were taken after a minimum 4-h fast and were analyzed for total cholesterol, TGs, and plasma glucose by using a bench-top analyzer (Reflotron, Boehringer Mannheim). Since 2005, a HemoCue bench-top analyzer (Quest Diagnostics) has been used for glucose values. An oral glucose tolerance test was performed with a 75-g oral glucose load according to WHO standards.

Anthropometric measurements. Height was measured without shoes to the nearest centimeter. Weight was measured in light clothing without shoes to the nearest kilogram. BMI was calculated as weight (kg) divided by height squared (m²).

Lifestyle variables, medication, and disease. Physical activity level was estimated based on a combination of 2 questions from the lifestyle questionnaire, one on physical activity at work and one on leisure physical activity, as described and validated by Johansson and Westerterp (26).

Participants were classified as smokers if they smoked at least one cigarette per day, as ex-smokers if they had previously smoked, and as never-smokers in all other cases.

Participants were regarded as diabetic if fasting capillary plasma glucose was ≥7.0 mmol/L and/or 2-h plasma glucose was ≥12.2 mmol/L. Participants were regarded as hypertensive if systolic blood pressure was ≥140 mm Hg and/or diastolic blood pressure was ≥90 mm Hg.

Dietary assessment. Dietary assessments were obtained from a semi-quantitative FFQ containing either 84 or 64 questions. In the 64-question FFQ, some foods were deleted and some were merged, but it covered essentially the same food items as the 84-question FFQ. After validation and calibration with 10 repeated 24-h diet recalls, the 84-question FFQ was concluded to have a validity similar to other FFQs used in prospective cohort studies (27). The FFQ has also been evaluated with regard to the ability to estimate plant sterol intake (28). Calculation of nutrient intake from the FFQ has been described elsewhere (29), as have the criteria for incomplete dietary data (27), including missing responses to >10% of the FFQ questions or one or more missing portion size response.

Plant sterol analysis and database. Analyses of the plant sterol content in food items were performed at the Department of Internal Medicine and Clinical Nutrition, University of Gothenburg, Sweden, using a GLC procedure as modified by Jonker et al. (30) and validated with GC-MS (31). The method is further described in Klingberg et al. (13).

More than 330 food items were analyzed and the results were collected in a plant sterol database, which was used to estimate dietary plant sterol intake in this study. The database includes different food groups, i.e., vegetables, fruits, cereals, bread, fats, nuts, confectionery, and beverages. A large part of the database has been published (32–34). In this analysis, each food item in the FFQ was assigned a plant sterol value as described in detail in Klingberg et al. (13).

Statistical analysis. Statistical calculations were performed using PASW Statistics 18 for Windows (SPSS). The significance level was set to 0.05 in 2-sided tests. The numbers presented are either medians (25th, 75th percentiles) for continuous variables, frequency (%) for categorical variables, or ORs with 95% CIs.

Cases and referents were compared by Mann-Whitney U-test for continuous variables and chi-squared test for categorical variables.

Plant sterol intake was energy-adjusted by the residual method (35). Plant sterol intake quartiles, both absolute (mg/d) and energy-adjusted (mg/d), were constructed separately for men and women and FFQ version and were based on the intake distribution among the referents. ORs with 95% CIs for a first MI were calculated by multivariable conditional logistic regression, with plant sterol intake quartile as the main predictor of a first MI after adjustment for known confounders. Confounders included in the analyses were: BMI (continuous), dietary fiber intake (g/MJ), saturated and unsaturated fat intake (percentage of energy intake; categorical: 8 values), alcohol intake (percentage of energy intake) (continuous: quartiles), education (categorical: corresponding to elementary school, junior high school, senior high school, college/university, missing), smoking (categorical: current, ex, never, missing), physical activity level (continuous), diabetes (categorical: yes, no, missing), hypertension (categorical: yes, no, missing), and TGs (continuous). Intakes of saturated fat, unsaturated fat, and fiber exhibited strong colinearity and a new composite categorical variable was constructed to address this, as previously described (13). Briefly, intakes of saturated fat, unsaturated fat, and fiber were divided into high or low intake, with cutoffs according to the Nordic Nutrition Recommendations (36), and combined into 1 of 8 possible categories for each individual.

To correct for measurement error in the FFQ, the risk estimates were adjusted using regression calibration (37). The calibration coefficients were calculated by linear regression of the plant sterol intake estimated with repeated 24-h recalls on the plant sterol intake estimated with the 84-item FFQ (28).
Results

The baseline characteristics of the study population are presented in Table 1. Compared with referents, both the female and male cases had higher BMI, higher total serum cholesterol, and higher serum TGs and were more likely to be current smokers or hypertensive. Male cases were also more likely to be diabetic. Among cases, the interval from screening to diagnosis of first MI varied between 0.01 and 20.6 y, with a median of 6.9 y.

Differences in energy and nutrient intake between cases and referents were generally minor, but some were significant (Table 2). The female cases had lower intakes of energy compared with referents. The male cases had lower energy, plant sterol, alcohol, and dietary fiber intakes as well as lower energy intake from fat compared with referents.

Table 3 shows the absolute and energy-adjusted plant sterol intake by quartiles. Absolute plant sterol intake was about twice as high in the highest quartile compared with the lowest quartile for both women and men. The energy-adjusted plant sterol intake was ~50% higher in the highest quartile compared with the lowest quartile in both women and men.

Table 3 also displays crude and multivariable ORs for a first MI by quartiles of absolute plant sterol intake and energy-adjusted plant sterol intake. Among women, absolute plant sterol intake was not associated with risk of a first MI. Among men, crude analysis showed that absolute plant sterol intake was inversely related to the risk of a first MI [OR highest vs. lowest quartile = 0.70 (95% CI: 0.53, 0.85); P-trend = 0.006]. Adjustment for BMI and fat and fiber intake did not influence the risk estimates. In the fully adjusted model, the risk estimates were essentially the same, but the trend was no longer significant. However, the OR for the highest quartile compared with the lowest quartile was still significant [OR highest vs. lowest = 0.71 (95% CI: 0.55, 0.92)], indicating a reduced risk of a first MI of 29% in the former group. Correction of this risk estimate for measurement error in the FFQ by regression calibration resulted in an OR of 0.48. No significant trends or risk estimates were found for energy-adjusted plant sterol intake in women or men.

Sensitivity analyses were performed by exclusion of cases diagnosed within 1 y (n = 50) from baseline. The results of these analyses (data not shown) did not differ essentially from the results of the analysis of the whole study population. Risk estimates for absolute plant sterol intake were nearly unchanged, whereas risk estimates for energy-adjusted plant sterol intake increased marginally. The significance levels for trends in the analyses were not altered.

Discussion

This is, to our knowledge, the first study investigating the effect of dietary intake of naturally occurring plant sterols on the risk of a first MI. Previous cross-sectional studies have shown that dietary intake of naturally occurring plant sterols is inversely related to serum cholesterol (10, 13, 38) and carotid intima media thickness (38). In multivariable regression analyses, LDL cholesterol was 0.13 mmol/L lower in the highest quintile compared with the lowest quintile of plant sterol intake in both men and women in the VIP population (13) and was 0.12 and 0.14 mmol/L lower in women and men, respectively, in the European Prospective Investigation into Cancer and Nutrition Norfolk population (10). In a Chinese population, LDL cholesterol was 0.23 and 0.26 mmol/L lower in women and men, respectively, when the highest plant sterol intake quartile was compared with the lowest quartile (38). These differences in LDL cholesterol might correspond to a decreased incidence in ischemic heart disease by 10–22% at age 40 y, by 8–17% at age 50 y, and by 6–13% at age 60 y (39).

The results of our nested case-referent study show that absolute intake of naturally occurring plant sterols is significantly inversely related to the risk of a first MI in men. The analyses indicated a 29% decreased risk of a first MI for men in the highest compared with the lowest absolute plant sterol intake quartile. This 29% risk reduction is somewhat higher than could be expected, considering the observed effect of plant sterol intake on LDL cholesterol in the VIP population and the fact that the median age was >50 y for male cases and referents. One possible explanation is that the effect of plant sterol intake on LDL cholesterol may have been underestimated in the VIP population. After correction for measurement error by regression calibration, the OR of the highest compared with the lowest quartile in the fully adjusted model decreased to 0.48 compared to 0.71 in the original model. This indicates that if the intake of naturally occurring plant sterols could be measured without error, the risk reduction might be expected to be even greater than the 29% demonstrated in the original model. In women, we found no significant effect of plant sterol intake on the risk of a first MI. This may simply reflect the smaller female sample size but also the decreasing effect of cholesterol as a risk factor for CVD and MI with age, especially in women (40, 41).

TABLE 1 Descriptive characteristics at baseline in first-time MI cases and their matched referents within the Northern Sweden Health and Disease Study

<table>
<thead>
<tr>
<th>Age at baseline, y</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Cases</td>
<td>n</td>
</tr>
<tr>
<td>219</td>
<td>60 (50, 60)</td>
<td>723</td>
</tr>
</tbody>
</table>

1 Values are medians (25th, 75th percentiles) for continuous variables and frequency (%) for categorical variables. Cases and referents were compared by Mann-Whitney U-test for continuous variables and chi-squared test for categorical variables. MI, myocardial infarction.
2 Hypertension defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg.
3 Diabetes defined as fasting plasma glucose ≥7.0 mmol/L and/or 2-h post-glucose load plasma glucose ≥12.2 mmol/L and/or self-reported diabetes.
In the analyses presented in this paper, we also studied the effect of energy-adjusted plant sterol intake. For energy-adjusted plant sterol intake, no significant associations with the risk of a first MI were found. One explanation could be that plant sterol intake and energy intake are strongly correlated (Spearman correlation coefficient: women 0.82, men 0.75; both $P < 0.001$), meaning that a person with a high absolute plant sterol intake could have a low energy-adjusted plant sterol intake due to a high energy intake. Energy adjustment makes the intake distribution narrower, which could make it more difficult to find an association between intake and outcome. It could also be speculated that the unwanted effect of possible misreporting is strengthened by energy-adjustment, because a low reported energy intake is associated with selective reporting of healthy foods (42) in which plant sterols are found. It must also be taken into consideration if it is the absolute plant sterol intake or the energy-adjusted plant sterol intake that is of highest biological importance. As plant sterols act on both endogenous, bilary-secreted cholesterol and exogenous, dietary cholesterol, it could be speculated that the absolute intake is the most important exposure information.

### TABLE 2
Energy and nutrient intake at baseline in first-time MI cases and their matched referents within the Northern Sweden Health and Disease Study

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th></th>
<th>Men</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases ($n = 219$)</td>
<td>Referents ($n = 723$)</td>
<td></td>
<td>Cases ($n = 786$)</td>
</tr>
<tr>
<td>Energy, MJ/d</td>
<td>5.8 (4.9, 7.1)</td>
<td>6.1 (5.1, 7.3)</td>
<td>0.042</td>
<td>8.1 (6.6, 9.7)</td>
</tr>
<tr>
<td>Plant sterols, mg/d</td>
<td>176 (142, 225)</td>
<td>183 (150, 229)</td>
<td>0.27</td>
<td>218 (171, 280)</td>
</tr>
<tr>
<td>Energy-adjusted plant sterols, mg/d</td>
<td>192 (171, 216)</td>
<td>190 (168, 212)</td>
<td>0.23</td>
<td>230 (201, 266)</td>
</tr>
<tr>
<td>Total fat, g/d</td>
<td>48 (38, 60)</td>
<td>50 (40, 62)</td>
<td>0.11</td>
<td>75 (60, 92)</td>
</tr>
<tr>
<td>Total fat, % energy</td>
<td>31 (27, 35)</td>
<td>31 (28, 35)</td>
<td>0.96</td>
<td>35 (21, 39)</td>
</tr>
<tr>
<td>Alcohol, g/d</td>
<td>0.34 (0.067, 2.22)</td>
<td>0.53 (0.078, 3.1)</td>
<td>0.052</td>
<td>3.5 (0.63, 6.86)</td>
</tr>
<tr>
<td>Alcohol, % energy</td>
<td>0.17 (0.030, 1.2)</td>
<td>0.28 (0.035, 1.4)</td>
<td>0.11</td>
<td>1.2 (0.22, 2.5)</td>
</tr>
<tr>
<td>Fiber, g/d</td>
<td>17 (13, 21)</td>
<td>18 (14, 22)</td>
<td>0.14</td>
<td>19 (14, 25)</td>
</tr>
<tr>
<td>Fiber, g/MJ</td>
<td>2.9 (2.4, 3.4)</td>
<td>2.8 (2.4, 3.3)</td>
<td>0.51</td>
<td>2.3 (2.0, 2.8)</td>
</tr>
</tbody>
</table>

1 Values are medians (25th, 75th percentiles). Cases and referents were compared by Mann-Whitney U-test. MI, myocardial infarction.

### TABLE 3
OR and 95% CI of a first MI by plant sterol intake quartile within the Northern Sweden Health and Disease Study

<table>
<thead>
<tr>
<th>Quartiles</th>
<th>Women</th>
<th></th>
<th>Men</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases/referents, n</td>
<td></td>
<td></td>
<td>Cases/referents, n</td>
</tr>
<tr>
<td>1</td>
<td>67/181</td>
<td>47/181</td>
<td>57/181</td>
<td>48/180</td>
</tr>
<tr>
<td>Absolute plant sterol intake, g/d</td>
<td>128 (108, 140)</td>
<td>164 (157, 175)</td>
<td>205 (192, 217)</td>
<td>266 (242, 312)</td>
</tr>
<tr>
<td>Crude OR (95% CI)</td>
<td>1.0</td>
<td>0.70 (0.45, 1.10)</td>
<td>0.89 (0.56, 1.35)</td>
<td>0.75 (0.48, 1.17)</td>
</tr>
<tr>
<td>Adjusted OR (95% CI)</td>
<td>1.0</td>
<td>0.68 (0.43, 1.07)</td>
<td>0.82 (0.54, 1.27)</td>
<td>0.68 (0.43, 1.09)</td>
</tr>
<tr>
<td>Adjusted OR (95% CI)</td>
<td>1.0</td>
<td>0.75 (0.46, 1.23)</td>
<td>1.01 (0.63, 1.62)</td>
<td>0.87 (0.52, 1.45)</td>
</tr>
<tr>
<td>2</td>
<td>154/133, 169</td>
<td>207 (196, 219)</td>
<td>259 (245, 273)</td>
<td>341 (312, 381)</td>
</tr>
<tr>
<td>Crude OR (95% CI)</td>
<td>1.0</td>
<td>0.78 (0.63, 0.98)</td>
<td>0.75 (0.60, 0.94)</td>
<td>0.70 (0.53, 0.85)</td>
</tr>
<tr>
<td>Adjusted OR (95% CI)</td>
<td>1.0</td>
<td>0.79 (0.63, 0.99)</td>
<td>0.76 (0.60, 0.96)</td>
<td>0.69 (0.54, 0.88)</td>
</tr>
<tr>
<td>Adjusted OR (95% CI)</td>
<td>1.0</td>
<td>0.81 (0.64, 1.02)</td>
<td>0.82 (0.64, 1.05)</td>
<td>0.71 (0.55, 0.92)</td>
</tr>
<tr>
<td>3</td>
<td>155/134, 161</td>
<td>178 (172, 185)</td>
<td>199 (194, 206)</td>
<td>228 (217, 248)</td>
</tr>
<tr>
<td>Crude OR (95% CI)</td>
<td>1.0</td>
<td>1.07 (0.68, 1.67)</td>
<td>1.27 (0.81, 1.97)</td>
<td>1.36 (0.88, 2.10)</td>
</tr>
<tr>
<td>Adjusted OR (95% CI)</td>
<td>1.0</td>
<td>1.00 (0.63, 1.60)</td>
<td>1.11 (0.68, 1.80)</td>
<td>1.21 (0.71, 2.05)</td>
</tr>
<tr>
<td>Adjusted OR (95% CI)</td>
<td>1.0</td>
<td>0.89 (0.53, 1.51)</td>
<td>1.19 (0.69, 2.04)</td>
<td>1.32 (0.73, 2.38)</td>
</tr>
<tr>
<td>4</td>
<td>221/210, 229</td>
<td>231 (214, 229)</td>
<td>253 (245, 262)</td>
<td>300 (284, 326)</td>
</tr>
<tr>
<td>Crude OR (95% CI)</td>
<td>1.0</td>
<td>1.00 (0.80, 1.24)</td>
<td>0.83 (0.66, 1.05)</td>
<td>0.81 (0.63, 1.05)</td>
</tr>
<tr>
<td>Adjusted OR (95% CI)</td>
<td>1.0</td>
<td>0.97 (0.77, 1.22)</td>
<td>0.83 (0.64, 1.07)</td>
<td>0.82 (0.62, 1.08)</td>
</tr>
<tr>
<td>Adjusted OR (95% CI)</td>
<td>1.0</td>
<td>1.04 (0.82, 1.32)</td>
<td>0.89 (0.68, 1.17)</td>
<td>0.91 (0.68, 1.22)</td>
</tr>
</tbody>
</table>

1 OR and 95% CI calculated by conditional logistic regression. MI, myocardial infarction.
2 Plant sterol intake (mg/d) is given as median (25th, 75th percentiles).
3 Adjusted for BMI, fat, and fiber intake.
4 Adjusted for BMI, fat and fiber intake, alcohol intake, PAL, smoking, hypertension, diabetes, education, and TGs.
In this study, we chose to investigate only participants without known health problems existing before the baseline examination. This rationale was chosen, because in a previous study investigating the relation between food patterns and existing health problems in the VIP population (25), we demonstrated that food patterns are associated with health problems prior to the health examination. It was concluded that it is important to be aware of these relations when studying associations between diet and disease. Furthermore, we suggested that appropriate exclusions should be made to avoid biases and attenuated associations between diet and disease (25). Sonestedt et al. (43) concluded in a study of another Swedish cohort that past food habit changes are related to obesity, lifestyle, and socioeconomic factors and that the most common reason for a diet change was health issues, including hypertension, hyperlipidemia, CVD, overweight, diabetes, high blood glucose, low physical activity, and the desire to control body weight. In the present study, we have no information on past food habit changes, but it is reasonable to assume that a considerable number of the individuals with known risk prior to baseline might have changed or intended to change their food habits as a consequence of their health status, either due to diet counseling by health professionals or at their own initiative. Moreover, we did not have information on participants developing hypertension or diabetes after the baseline examination. If these confounders are confounders and those who developed them during follow-up consumed lower amounts of plant sterols, then the lack of adjustment for them could have resulted in an overestimation of the association of plant sterol intake on the risk of a first MI.

Collinearity between different nutrients is a serious problem in all nutritional epidemiology, making it difficult to distinguish their respective effects on health outcomes. In a previous study of the effect of dietary intake of naturally occurring plant sterols on serum cholesterol concentrations in the VIP cohort (13), we found that intakes of saturated fat, unsaturated fat, and dietary fiber were strongly correlated with plant sterol intake and at the same time had a potential effect on serum cholesterol. In this study, saturated and unsaturated fat and fiber intakes might have had a potential effect on the risk of a first MI via their effect on the mediator serum cholesterol. To deal with the correlation among these 3 nutrients, we created a composite categorical variable including information from all 3 variables. Adjustment for this variable did not affect the risk estimates for the effect of plant sterol intake to any considerable extent, which implies that the effect of plant sterol intake on the risk of a first MI is separate from the effect of fat and fiber intake.

The reported consumption of plant sterols in the VIP population (13) was somewhat lower than in other European populations (9–12,14). This difference might be partly explained by differences in dietary assessment methods, but there may also be a real difference in intake. Nevertheless, dietary intake of plant sterols seems to be inversely related to the risk of a first MI in men in northern Sweden, even after adjustment for a range of confounders including fat and dietary fiber intake. In men, dietary intake of plant sterols in the lowest quartile was ~150 mg/d and intake was 340 mg/d in the highest quartile, suggesting that even moderate changes in the dietary intake of naturally occurring plant sterols could have an important effect on the risk of developing a first MI. Such a change could, e.g., be achieved by replacing 2 tablespoons of olive oil and 2 slices of white bread with the same amount of rapeseed oil and wholemeal bread.

Furthermore, the results from this study show that intake of plant sterols may be as important in preventing MI as daily consumption of fruits and vegetables (OR: 0.7), regular alcohol intake (OR: 0.91), and regular physical activity (OR: 0.86) seen in the INTERHEART study (5).

In conclusion, the findings of this observational study show that a high absolute intake of naturally occurring plant sterols is significantly related to a lower risk of a first MI in men in northern Sweden, whereas no significant relation was seen for energy-adjusted plant sterol intake. In women, no significant associations were found.

Acknowledgments

G.H. was principal investigator in the VIP study; J.-H.J. was responsible for the identification of MI cases and selection of referents; I.J. and A.W. were responsible for the VIP dietary database; L.E. and S.K. developed the plant sterol database; I.J. and S.K. prepared the plant sterol data in the VIP cohort; A.W. and L.E. designed the research; S.K. analyzed data; S.K., A.W., and L.E. wrote the paper; I.J., J.-H.J., and G.H. revised the manuscript; and S.K. had primary responsibility of the final content. All authors have read and approved the final manuscript.

Literature Cited


