Vitamins, selenium, iron, and coronary heart disease risk in Indians, Malays, and Chinese in Singapore

Kenneth Hughes, Choon-Nam Ong

Abstract

Study objective—To examine the hypothesis that the higher rates of coronary heart disease (CHD) in Indians (South Asians) compared with Malays and Chinese is partly because of differences in anti-oxidants (vitamins A, C, and E, and selenium) and pro-oxidants (iron).

Design—Cross sectional study of the general population.

Setting—Singapore.

Participants—Random sample of 941 persons aged 30 to 69 years.

Main results—There were moderate correlations between vitamin A and vitamin E, and between these vitamins and selenium. Mean plasma vitamins A and E were similar by ethnic group. Vitamin A concentration for Indians were (men 0.66 and women 0.51 mg/l), Malays (men 0.67 and women 0.54 mg/l), and Chinese (men 0.68 and women 0.52 mg/l). Vitamin E concentrations for Indians were (men 12.9 and women 12.8 mg/l), Malays (men 13.6 and women 13.3 mg/l), and Chinese (men 12.6 and women 12.6 mg/l). In contrast, mean plasma vitamin C concentrations were lower in Indians (men 5.7 and women 6.9 mg/l) and Malays (men 5.1 and women 6.4 mg/l) than Chinese (men 6.3 and women 8.4 mg/l). Mean serum selenium was lower in Indians (men 11.7 and women 115 µg/l) than Malays (men 122 and women 122 µg/l) and Chinese (men 126 and women 119 µg/l). Mean serum ferritin was much lower in Indians (men 132 and women 50 µg/l) than Malays (men 175 and women 85 µg/l) and Chinese (men 236 and women 92 µg/l).

Main conclusions—Lower vitamin C and selenium in Indians, particularly in combination, could play a part in their increased risk of CHD. Vitamins A and E, and ferritin (iron) have no such role. Lower vitamin C in Indians and Malays is probably because of its destruction by more prolonged cooking. In Indians, lower selenium is probably because of a lower dietary intake and the much lower ferritin to a lower dietary intake of iron and its binding by phytates.

Indians or South Asians (that is, people from the Indian subcontinent) have been found in a number of countries to be particularly susceptible to coronary heart disease (CHD). This is not because of the classic risk factors of cigarette smoking, hypertension, and hypercholesterolaemia. Abdominal obesity, insulin resistance with hyperinsulinaemia, and Syndrome X may be part of the explanation. However, there may be other risk factors that need to be identified. Finding the reasons for the increased susceptibility of Indians to CHD is not only of importance to Indians themselves but will provide important information on the aetiology of the disease.

There is strong evidence that oxidative free radicals have a role in the development of degenerative diseases including CHD. Oxidative free radicals increase the peroxidation of low density lipoprotein thereby increasing its uptake by macrophages with increased foam cell formation and atherosclerosis, though other mechanisms may exist. Anti-oxidants in the diet include vitamin A (carotenoids, which are metabolised to retinol), vitamin C (ascorbate), vitamin E (tocopherol), and selenium, which is an integral part of the antioxidant enzyme glutathione peroxidase.

There is evidence that anti-oxidant vitamins are protective against CHD from both laboratory and observational epidemiological studies, with strong evidence for the benefits of fresh fruits and vegetables. However, the evidence for the beneficial effects of anti-oxidants is considered inconclusive. No benefits have been found for vitamins A and E supplementation on cardiovascular disease or cancer in the Alpha-Tocopherol, Beta Carotene (ATBC) Cancer Prevention Study, the Physicians’ Health Study, and the Beta-Carotene and Retinol Efficacy Trial (CARET). These trials were of short duration, however, and examined the possible benefits of vitamin supplementation rather than the possible harmful effects of low vitamin intake. There is epidemiological evidence for the beneficial effect of selenium particularly from Finland, though again it is considered inconclusive.

Iron, another dietary constituent, is a pro-oxidant and high concentrations of blood ferritin, which measures stored iron, is a possible risk factor for CHD. It has been proposed that the sex difference in CHD is a result of differences in ferritin values. It has been concluded on present evidence, however, that the role of iron on CHD is undecided.

Singapore is an island state with a population of 3.3 million people composed of Chinese 76%, Malays 14%, Indians 7%, and others 3%.
whose origins have been described, with 80% of Indians originating from the southern states of India (Tamil Nadu or Kerala) and Sri Lanka. Indians have much more CHD (but not more cerebrovascular disease) than Malays and Chinese especially in the younger age groups, with Malays having more than Chinese. The Singapore Thyroid and Heart Study found that the greater susceptibility of Indians to CHD could not be explained by cigarette smoking, hypertension, and hypercholesterolaemia, physical activity, or general obesity, although Indians did have more diabetes and lower HDL-cholesterol, with the latter not explained by alcohol consumption. In Singapore the ethnic groups live in the same environment with the only difference in lifestyles being their diets, suggesting that the cause of the increased susceptibility of Indians to CHD is in their genetic make up or diet, or both.

The National University of Singapore Heart Study is a further cross sectional survey on the general population, carried out to examine cardiovascular risk factors, in particular the newer ones not studied in the Singapore Thyroid and Heart Study. A previous paper from the former study reported that Indians compared with Malays and Chinese had more abdominal obesity, insulin resistance with hyperinsulinaemia, and certain components of Syndrome X, together with higher serum concentration of lipoprotein (a), which could partly explain their increased susceptibility to CHD. However, other mechanisms may exist. The Indian diet is distinctive, entailing prolonged cooking at high temperatures, and could be different in its content of anti-oxidants and pro-oxidants. This paper examines ethnic differences in blood vitamins (A, C, and E), selenium, and ferritin.

Methods

SAMPLE

The National University of Singapore Heart Study was a cross sectional survey of a random sample of persons aged 30 to 69 years from the general population of Singapore. The sampling has been described in detail. There was a response rate of 71.2%, with 961 responders aged between 30 and 69 years. Of these, 20 persons did not have vitamin and mineral measurements because of the unavailability of the technician on their clinic days, but this was in a purely random way. Hence measurements were performed on 941 persons aged between 30 and 69 years.

PROCEDURES

All clinics were held on weekday mornings between 0900 and 1200 hours (from June 1993 to December 1995) with both sexes and three ethnic groups seen concurrently. The subjects were asked to fast from 2100 hours the previous evening. A questionnaire was administered by the same investigator trained in interview techniques and included questions on age, sex, and ethnic group (classification previously described).

Venous blood specimens were taken with the subject in a sitting position using venoject vacuum containers with minimum venous stasis. Specimens of 4.0 ml of blood were each taken in vacutainers containing EDTA and heparin as anticoagulants and covered with aluminium foil to prevent admission of light, and these were transported on ice to the laboratory where the blood was centrifuged and measurements made on plasma by automated high performance liquid chromatography. On the EDTA tube, measurement of plasma vitamin C (ascorbic acid) was performed immediately, while on the heparinised tube, measurements of plasma vitamin A (retinol), and plasma vitamin E (α tocopherol), were performed in batches within two weeks after storing at −70°C. On specimens collected in plain vacutainers serum ferritin was measured in batches weekly after storing at −20°C by microparticle enzyme immunoassay using Abbott IMX, while serum selenium was measured by Zeeman atomic absorption spectrophotometry in batches within two weeks after storing at −70°C.

ANALYSIS

The mean ages were similar by sex and ethnic group; nevertheless age adjustment was performed. Pearson product moment partial correlation coefficients adjusted for age between the vitamins and minerals were calculated on SPSS. Means were age adjusted by analysis of covariance using the GLM Procedure of SAS. As cigarette smoking is known to reduce vitamin C, this vitamin was also compared by ethnic group in non-smokers. Ferritin was also examined in pre-menopausal and post-menopausal women, as there is iron loss with menstruation. All significance testing was two tailed.

Results

Table 1 shows the correlations in the subjects of the vitamins and minerals. The only consistent, statistically significant, and reasonably strong correlations were moderate ones between vitamin A and vitamin E and slight/moderate ones between these two vitamins and selenium.

Table 2 shows the mean concentrations of vitamins and minerals in the three ethnic groups. Vitamin A values (higher in men than women) were very similar by ethnic group. Vitamin E values (similar in the two sexes)
increased susceptibility of Indians to CHD. These as a possible contributory cause of the differential risk from CHD between Indians, Malays, and Chinese and is the first to examine this as a possible contributory cause of the increased susceptibility of Indians to CHD. The blood concentrations of vitamins and minerals in people will vary with changes in their dietary intake, though it should be noted that the subjects in this study had been fasting for at least 12 hours. Despite any individual variation, on a population basis blood concentrations of these vitamins and minerals will measure ethnic differences in blood levels and dietary intake.

In 1993 a food consumption survey on a number of dietary constituents (including vitamin A) was carried out in Singapore on a random sample of the general population aged 18 to 69 years using both the methods of 24-Hour Dietary Recall and 3-Day Food Intake Records. Plasma lipids influence tocopherol concentrations so that the vitamin E:cholesterol ratio is sometimes used. However, total cholesterol concentrations are similar in the three ethnic groups, so that this correction would make no difference to ethnic comparisons. Plasma concentrations of vitamins A and E were correlated, which is no doubt because of common dietary sources. The consumption survey in Singapore found that intakes of vitamin A were higher in men than women with no important ethnic differences. The finding of higher plasma concentrations of vitamin A in men than women and no ethnic differences are consistent with the findings on diet. Similar values of blood vitamins A and E by ethnic group indicate that these anti-oxidants have no role in the increased susceptibility of Indians to CHD compared with Malays and Chinese. Values of vitamins A and E in Singapore are comparable to those reported in US populations.

The lower plasma concentrations of vitamin C in smokers was shown in men by higher levels in non-smokers than all men. There was little difference for women because of the very small proportion of women who smoke in Singapore. Lower concentrations of vitamin C in smokers is both a result of lower intake and of a higher metabolic turnover. Plasma concentrations of vitamin C were higher in women than men, which is consistent with findings

Table 2: Means (95% confidence intervals), age adjusted by analysis of covariance, of vitamins and minerals for Indians (I), Malays (M), and Chinese (C), by sex, for age group 30 to 69 years

<table>
<thead>
<tr>
<th></th>
<th>Indians (men=166, women=166)</th>
<th>Malays (men=144, women=142)</th>
<th>Chinese (men=158, women=165)</th>
<th>Significance, p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plasma vitamin A (mg/l)</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Men</td>
<td>0.66 (0.60, 0.68)</td>
<td>0.67 (0.65, 0.69)</td>
<td>0.68 (0.66, 0.70)</td>
<td>0.58 0.34 0.70</td>
</tr>
<tr>
<td>Women</td>
<td>0.51 (0.49, 0.53)</td>
<td>0.54 (0.52, 0.56)</td>
<td>0.52 (0.50, 0.54)</td>
<td>0.19 0.63 0.39</td>
</tr>
<tr>
<td><strong>Plasma vitamin E (mg/l)</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>12.9 (12.4, 13.4)</td>
<td>13.6 (13.0, 14.2)</td>
<td>12.6 (12.0, 13.2)</td>
<td>0.11 0.46 0.02</td>
</tr>
<tr>
<td>Women</td>
<td>12.8 (12.3, 13.3)</td>
<td>13.3 (12.7, 13.9)</td>
<td>12.6 (12.0, 13.1)</td>
<td>0.18 0.67 &lt;0.08</td>
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<tr>
<td><strong>Plasma vitamin C (mg/l)</strong></td>
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</tr>
<tr>
<td>Men</td>
<td>5.7 (5.2, 6.2)</td>
<td>5.1 (4.6, 5.6)</td>
<td>6.3 (5.8, 6.8)</td>
<td>0.12 0.09 &lt;0.01</td>
</tr>
<tr>
<td>Women</td>
<td>6.9 (6.4, 7.4)</td>
<td>6.4 (5.8, 7.0)</td>
<td>8.4 (7.9, 8.9)</td>
<td>0.20 &lt;0.01 &lt;0.01</td>
</tr>
<tr>
<td>*Women</td>
<td>6.1 (5.6, 6.6)</td>
<td>5.6 (5.1, 5.7)</td>
<td>7.3 (6.8, 7.8)</td>
<td>0.35 &lt;0.01 &lt;0.01</td>
</tr>
<tr>
<td>*Women</td>
<td>6.8 (6.5, 7.1)</td>
<td>6.4 (6.1, 6.7)</td>
<td>8.4 (8.1, 8.7)</td>
<td>0.21 &lt;0.01 &lt;0.01</td>
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<tr>
<td><strong>Serum selenium (µg/l)</strong></td>
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<tr>
<td>Men</td>
<td>117 (115, 119)</td>
<td>122 (120, 124)</td>
<td>126 (124, 128)</td>
<td>&lt;0.01 0.01 0.18</td>
</tr>
<tr>
<td>Women</td>
<td>115 (113, 117)</td>
<td>122 (120, 124)</td>
<td>119 (117, 121)</td>
<td>&lt;0.01 0.01 0.18</td>
</tr>
<tr>
<td><strong>Plasma ferritin (µg/l)</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Men</td>
<td>132 (117, 147)</td>
<td>175 (158, 192)</td>
<td>236 (221, 251)</td>
<td>&lt;0.01 &lt;0.01 &lt;0.01</td>
</tr>
<tr>
<td>Women</td>
<td>50 (35, 65)</td>
<td>85 (68, 101)</td>
<td>92 (77, 107)</td>
<td>&lt;0.01 &lt;0.01 0.54</td>
</tr>
<tr>
<td>*Women</td>
<td>30 (24, 36)</td>
<td>65 (50, 82)</td>
<td>61 (44, 78)</td>
<td>0.04 0.01 0.05</td>
</tr>
<tr>
<td>*Women</td>
<td>83 (55, 111)</td>
<td>140 (109, 171)</td>
<td>141 (115, 167)</td>
<td>&lt;0.01 &lt;0.01 0.93</td>
</tr>
</tbody>
</table>

*Non-smokers, † pre-menopausal (30-49 years), ‡ post-menopausal (50-69 years).
elsewhere with women having higher levels than men despite similar dietary intakes. Plasma concentrations of vitamin C were lower in Malays and Indians than Chinese for both sexes, both in all persons and in non-smokers. Most vitamin C in the diet comes from fruits and vegetables. It is unlikely that Indians and Malays have a lower dietary intake of these foods, particularly as dietary intake and plasma values of vitamin A and plasma values of vitamin E are similar by ethnic group. Unlike vitamins A and E, however, vitamin C is water soluble and easily destroyed by heat treatment. There is more prolonged cooking at higher temperatures with Indian and Malay dishes such as curries compared with the typical Chinese stir fried dishes, and furthermore in the latter cooking oil will protect vitamin C in food. Hence there will be more destruction of vitamin C in Indian and Malay cooking than Chinese cooking resulting in lower blood concentrations. Lower blood vitamin C in Indians and Malays may contribute to their higher rates of CHD compared with Chinese. It has been found that serum ascorbate concentration was inversely related to haemostatic factors fibrinogen and factor VIIc, suggesting that low vitamin C may also be a risk factor for CHD by increasing thrombosis. However, no important ethnic differences have been found in Singapore for fibrinogen or factor VIIc. Mean concentrations of vitamin C for all three ethnic groups in Singapore are lower than have been reported for US populations, and are at the lower end of the normal range of 4.0 to 15.0 mg/l.

Serum selenium concentrations showed little sex differences, with Indians having lower levels than Malays and Chinese in both sexes. The richest food sources of selenium are meats and seafoods, followed by cereals, and dairy products. Indians have a more vegetarian diet than the other two ethnic groups; the food consumption survey found that 7.8% of Indians but no Malays or Chinese were strict vegetarians. Vitamin A, vitamin E, selenium, and iron were each taken by less than 1% of the population. This suggests that average vitamin C from the normal diet is slightly less than indicated by plasma concentrations with the difference varying little by ethnic group. In conclusion, if vitamin C and selenium are established as being protective against CHD, lower blood concentrations of these dietary anti-oxidants, particularly in combination, could contribute to the increased risk of Indians for CHD compared with Malay and Chinese in Singapore. Lower blood vitamin C concentrations could contribute to the increased risk for CHD of Malays compared with Chinese. The differences in concentrations, however, suggest that these contributions are unlikely to be great. Vitamin A, vitamin E, and ferritin (a pro-oxidant) would seem to have no part to play in this differential ethnic risk of CHD. The only apparent explanation for the lower blood vitamin C in Indians and Malays is its destruction by the more prolonged cooking at higher temperatures in their cuisines. In Indians, their lower blood selenium is probably because of a lower intake and their much lower blood ferritin because of a lower iron intake and binding of nonhaem iron by phytates in their diet.

**KEY POINTS**

- Indians (South Asians) have more coronary heart disease (CHD) than Malays and Chinese in Singapore.
- Indians have lower blood concentrations of vitamin C and selenium (anti-oxidants), which may contribute to their increased risk of CHD.
- There are no ethnic differences for blood concentrations of vitamins A and E.
- Indians have lower blood concentrations of ferritin (a pro-oxidant) but this will not contribute to their increased risk of CHD.

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Conflicts of interest: none.
Vitamins, selenium, and iron in Singapore