Selenium and Cardiovascular Disease

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Below we outline a study on the effects of low selenium (Se) status on cardiovascular mortality, incidence of myocardial infarction, and atherosclerosis, which will take place in the Netherlands from 1985 to 1988. As serum Se levels in the Netherlands vary from 60 to 130 μg/l in healthy subjects, this study may provide insight into the shape of the 'selenium-cardiovascular disease' risk curve.

The objectives of the study are:

1. To assess the association between level of serum Se and cardiovascular mortality in a population-based follow-up study.
2. To study the acute and chronic effect of Se status on cardiovascular morbidity, by comparing (short-term) serum Se and (long-term) toenail Se levels among patients with a first myocardial infarction and population controls.
3. To study the effect of Se status on atherosclerosis by comparing serum and toenail Se levels of patients with varying degrees of angiographically determined coronary sclerosis.

The first study is designed as a case-control study within a prospective cohort study. From a cohort of 10,500 persons, examined between 1975 and 1978, follow-up data on mortality and cause of death, as well as frozen serum samples are available. Cases are people who died of cardiovascular disease since 1978 (about 100). A referent series comprises 100 healthy cohort members, still alive by 1984.

The other two studies are case-control studies which will be jointly carried out at the Zuiderziekenhuis hospital in Rotterdam. Of all patients admitted to the cardiology unit in the study period, medical records, angiogram, toenails and serum samples will be taken and stored, and information on risk factors and dietary habits will be gathered by personal interview. Not eligible will be patients who changed dietary habits and/or had physical complaints half a year prior to entry into the study.

In the second study 100 incident cases with a first myocardial infarction and 100 community controls, drawn as a random sample of the catchment population of the Zuiderziekenhuis hospital, will be selected. The study population of the third study will comprise 100 incident cases with severe generalized coronary atherosclerosis, and 100 incident controls with no or little coronary sclerosis. Since the samples will be taken before angiography we will afterwards select groups of patients at both extremes. Patients with either congenital or valvular heart disease will be excluded.

Matching will be performed for age and gender. Other potential confounders are cardiovascular and dietary risk factors. In the first study we will use baseline data for smoking, serum cholesterol, and blood pressure to adjust for possible confounding in the analysis.

In the other two studies respondent’s recall data on smoking and alcohol consumption will be sought. Blood pressure and serum cholesterol data are available, but may not be valid directly after myocardial infarction. Other studies on Se and chronic disease, however, have shown that confounding by major risk factors is not an important issue, since there is no association with Se except for smoking and alcohol. In order to check whether the study base from which our study population is selected, was unbiased, we will verify the associations of Se and blood pressure, and Se and serum cholesterol in the population controls.

Potential dietary confounders are antioxidants (vitamin E, vitamin A, vitamin C) and polyunsaturated fatty acids, especially eicosapentanoic acid, mainly in fish. Serum concentration of these parameters will be determined by high pressure liquid—and gas liquid chromatography, respectively. Neutron activation analysis will be used to measure serum and toenail Se levels.

In a logistic model we will assess the effect of Se on the outcome variables (cardiovascular mortality, myocardial infarction, coronary sclerosis), adjusting simultaneously for possible confounders.

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