News in Brief

DOES VITAMIN D INCREASE MORTALITY?

Vitamin D may reduce all causes of mortality by a small but statistically significant degree.

This finding emerged from a meta-analysis of 18 randomised trials, which found that daily vitamin D in doses ranging from 300 to 2,000 IUs reduced all cause mortality by 7% (95% CI 0.87-0.99). The benefit was slightly greater (8% reduction) when vitamin D was taken daily for three years or longer.

The mechanisms by which vitamin D might decrease mortality are unclear. Possible effects suggested by the authors include "… inhibition of cellular proliferation and activation of cellular differentiation, (which) could reduce aggressiveness of cancerous processes and expansion of atheromatous lesions".

The 18 trials consisted of 12 placebo-controlled trials and six open-label trials. The total number of participants was 57,311 (range 55 to 36,282, mean follow-up 5.7 years). The daily dose of vitamin D was very wide, with a mean of 528 IU. Compliance ranged from 48-95%. There were 4,777 deaths (from any cause).

Vitamin D and calcium supplementation was part of active treatment in 13 trials. But the authors believe that the benefit was probably not due to the calcium supplements, because five trials that did not include calcium supplements had similar relative risk to those that included calcium.

The mortality benefit is not explained by the effect of vitamin D in reducing the fracture risk in the frail elderly. 15 frail elderly patients need to be treated with vitamin D to prevent one fall, and such an effect does not translate into a 7% decrease in total mortality.

An editorial in the same issue suggests that since there is a high probability of benefit for some conditions associated with vitamin D deficiency, and that there is a low likelihood of harm, a proactive attitude to identify, prevent, and treat vitamin D deficiency should be part of standard medical care. However, the role of vitamin D supplements is not yet clear and needs further research. It was suggested that more population-based, placebo-controlled randomised trials in people 50 years or older for at least six years with total mortality as the main endpoint are required.

Doctors may have to explain to interested patients that: (a) the finding from the meta-analysis needs to be confirmed in a randomised controlled trial; (b) vitamin D has a number of benefits and is generally well tolerated; and (c) there is no evidence that increasing the dose of vitamin D would increase the benefit.

(Source: Autier P. and Gandini S. Vitamin D. Supplementation and total mortality: a meta-analysis of randomised controlled trials. Archives of Internal Medicine 2007; 167:1730-7.)

RISK OF STOPPING STATIN THERAPY

According to an Italian study, stroke survivors who stop statin therapy within a year of hospital discharge almost triple their mortality risk.

Discontinuation of lipid-modifying therapy was the strongest predictor of one-year mortality, with a hazard ratio of 2.78 compared with stroke survivors who continued statin-based therapy. The earlier a patient discontinued therapy, the greater the mortality risk.

The study prospectively followed 631 consecutive stroke survivors without clinical coronary artery disease, discharged from the hospital over a 4.5 year period. All the patients were on statin therapy at discharge and were followed for 12 months. The primary endpoint was death from all causes 12 months after discharge. Statin therapy was in the form of atorvastatin 10-20 mg/d (N=409, 77.6%) or simvastatin 20-40 mg/d (N=222, 22.4%).

The presence of concurrent cardiovascular disease was ruled out during the index admission in all cases by a comprehensive clinical evaluation (history, physical examination, 12-lead ECG, and echocardiography). Patients with any evidence of CHD were excluded, as were patients with a past history of a cardiovascular event (history of myocardial infarction, angina pectoris, myocardial ischaemia by stress testing, prior coronary artery bypass grafting, prior percutaneous coronary angioplasty, abnormal coronary angiography).

During the 12 months of follow-up, 246 patients (38.9%) discontinued statin therapy, and 87 patients (13.7%) switched from their initial statin to a different drug in the same class. The discontinuation rate was

Page 27 ▶

◀ Page 26 – News in Brief

similar with atorvastatin and simvastatin. The main known reason for discontinuation was side effects (71 of 246). Much of the blame for early discontinuation of statin therapy was also placed on a lack of continuity in patient care. In 175 cases, there was no known specific reason for discontinuation.

Patients who discontinued statin therapy were older (71.4 versus 69.5 years, p=0.002) and more often female (56% versus 44% of male patients, p=0.004). Also, those with diabetes or a history of stroke were more likely to remain on statin therapy. Overall, 116 of 631 patients (18.3%) died within 12 months of discharge (with 93 deaths or 80.1% being due to a cardiovascular event).

Besides discontinued statin therapy, other significant predictors of one-year mortality were: (a) discontinuation of anti-platelet therapy (HR 1.81, p=0.008); (b) stroke severity at admission (HR 1.11, p=0.002); and (c) older age (HR 1.08 per year, p=0.001). Discontinuation of anti-hypertensive medication (regardless of class) did not predict one-year mortality.

These other significant predictors (and unmeasured confounders) raised questions about the benefits of post-stroke statin therapy. Additional research should be carried out.

(Source: Colivicchi F et al. Discontinuation of statin therapy and clinical outcome after ischemic stroke. Stroke 2007; 38: doi: 10.1161/STROKEAHA.107.487017.)

EXCESS WEIGHT EXCESS RISK

According to a meta-analysis, excess weight alone increases the risk of developing coronary heart disease (CHD), partly independent of traditional risk factors. The risk is increased by 17% to 49%, depending on the weight. The extent to which being moderately overweight (BMI 15.0-29.9) or obese (≥ 30.0) is associated with the increased risk through adverse effects on blood pressure (BP) and cholesterol levels is unclear.

21 studies of being overweight and heart disease, involving 302,296 mainly white, healthy persons, were looked at. A total of 18,000 cardiac events or deaths occurred during follow-up.

The relative risks (RRs) of CHD associated with being moderately overweight or obese, with and without adjustment for BP and cholesterol levels, were calculated.

After adjustments for age, sex, physical activity, and smoking: (a) moderately overweight individuals had a 32% increased risk of CHD compared with normal-weight individuals (adjusted RR 1.32, 95% confidence intervals 1.24-1.40); and (b) obese individuals had an 81% increased risk compared with normal weight individuals (RR 1.81, 1.56 - 2.10).

An additional adjustment for BP and cholesterol levels shows: (a) the excess risk associated with being moderately overweight was reduced by nearly half to 17% (RR 1.17, 1.11-1.23); and (b) the excess risk associated with being obese was 49% (RR, 1.49, 1.32-1.67). Furthermore, a 5-unit increase in BMI amounted to a 16% increased risk (RR 1.16, 1.11-1.21). The RR relative before adjustment was 29% (RR 1.29, 1.22- 1.35).

Several mechanisms may explain the independent effect of being overweight on CHD – low-grade inflammation, endothelial dysfunction, haemostatic imbalance favouring coagulation, impaired endothelial vasodilatory responses, left ventricular hypertrophy and reduced heart rate variability. The association of being overweight with diabetes probably aggravated these mechanisms.

The main weaknesses of the meta-analysis are: (a) it did not control for diet as data on this was not included in the studies reviewed; and (b) the study population was mainly white, healthy persons.

Even with optimal treatment for hypertension and hypercholesterolaemia, overweight persons would have an elevated risk of CHD. Some alternative explanations for the findings should be noted.

Doctors may also have to explain to interested patients that: (a) being overweight or obese not only increases traditional heart disease risks (hypertension and high cholesterol levels), but that excess weight is in itself a risk factor; (b) the meta-analysis does not prove causality; and (c) there is a possibility of unknown confounders in the meta-analysis. ■

(Source: Bogers, R, et al. Association of overweight with increased risk of coronary heart disease partly independent of blood pressure and cholesterol levels. Archives of Internal Medicine 2007; 167:1720-8.)