NEWS & VIEWS

Hole in the diet-heart hypothesis?

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Several common dietary saturated fatty acids raise total and low density lipoprotein cholesterol concentrations, whereas the omega-6 polyunsaturated fatty acid linoleic acid lowers them. Thus, linoleic acid would be expected to lower risk of mortality from coronary heart and cardiovascular diseases. Newly published data uncovered from a large randomised controlled trial conducted over four decades ago show no difference in mortality between a saturated fat and a linoleic acid rich diet, despite cholesterol lowering with the latter. These findings challenge the widely accepted diet-heart hypothesis.

Refers to Ramsden, C. E., et al. Re-evaluation of the traditional diet-heart hypothesis: analysis of recovered data from Minnesota Coronary Experiment (1968-73). BMJ 2016;353:i1246

The diet-heart hypothesis is based upon the assumptions that certain dietary components increase blood cholesterol concentrations and that, in turn, elevated blood cholesterol is causally linked to increased risk of coronary heart disease (CHD). Research conducted in the 1960s and 1970s suggested that several commonly occurring dietary saturated fatty acids raise total and low density lipoprotein (LDL) cholesterol concentrations, whereas the omega-6 polyunsaturated fatty acid (PUFA) linoleic acid lowers total and LDL cholesterol concentrations[1]. Linoleic acid is present in high amounts in vegetable oils such as corn,

sunflower, safflower, and soybean oils and in margarines made from these oils. It is the most prevalent PUFA and omega-6 PUFA in most Western diets. As a result of their opposing actions on blood cholesterol, decreasing intake of saturated fat and increasing intake of PUFAs has been a cornerstone of dietary advice for several decades, with the aim of reducing the risk of cardiovascular disease (CVD). Typical advice is to limit saturated fatty acids to <10% of dietary energy and to aim for a PUFA intake (mainly linoleic acid) of between 5 and 10% of energy[2,3]. Despite commonly held views to the contrary, the impact on CHD or CVD mortality of replacing saturated fat with linoleic acid without changes in other fatty acids, such as trans or omega-3, has rarely been investigated. Authorities have instead used the biomarker blood cholesterol as the basis for advice and recommendations. In 2013 Ramsden et al. published newly recovered results from the Sydney Diet Heart Study, a randomised controlled trial conducted from 1966 to 1973, reporting total, CHD and CVD mortality data in middle-aged men with a recent coronary event randomised to a diet rich in linoleic acid or to continuation of their habitual diet rich in saturated fatty acids[4]. Curiously, the CHD and CVD mortality data from the Sydney Diet Heart Study had never been published. Despite significant cholesterol lowering in the linoleic acid group (13%), all cause mortality and risk of mortality from CHD or CVD were all higher in the linoleic acid group[4]. The study called into question the traditional diet-heart hypothesis and the widely accepted advice on healthy eating[5]. Ramsden et al. have now conducted a second remarkable piece of detective work, uncovering and analysing a set of data of possibly even greater importance than that from the Sydney Diet Heart Study[6].

The Minnesota Coronary Experiment (MCE) was a double blind randomised controlled trial conducted from 1968 to 1973 in over 9,500 men and women aged 20-97 years and living in a nursing home or in one of six mental hospitals in Minnesota, USA. Thus, unlike the Sydney Diet Heart Study, the MCE included women and older participants, although the average age of participants was 52 years. Participants in the MCE were of normal body weight and had normal blood pressure and serum cholesterol concentrations. They were randomised to a diet rich in linoleic acid or a control diet. All meals were provided to participants throughout the trial, were highly controlled with regard to nutrient content, and were eaten under supervision. The linoleic acid group had meals in which corn oil was used for cooking and was added into many food items and used a corn oil based margarine. This resulted in a 50% reduction in dietary saturated fatty acid intake compared with the participant's habitual diet and an increase in linoleic acid intake from an average of 3.4 to 13.2% of energy. Linoleic acid intake in the control group was about 4% of dietary energy.

Follow-up time was 41 to 56 months, depending upon the location. Data were recovered from 9-track magnetic tapes and paper documents. Longitudinal data on serum cholesterol were available for 2355 participants who were in the study for at least one year.

Some data from the MCE were published in 1989[7], but for reasons that are not clear the data on all cause and CHD mortality in the participants with known serum cholesterol concentrations at study entry and after at least one year of intervention were never published. Likewise, findings from autopsy investigation on participants who died were never published. In those participants who were followed for at least one year, total serum cholesterol was lowered by an average of 13.8% in the linoleic acid group. This is very close to the value predicted from Ancel Keys' equation. Lowering of serum cholesterol was associated with increased, not decreased, mortality but there was no difference between groups for mortality outcomes. However, the mortality rates were low, perhaps because many participants were young and had a healthy risk factor profile. The authors then used the new data generated from the MCE to update their earlier meta-analysis[4]. A total of five linoleic acid intervention trials that reported CHD and CVD mortality were included, including the Sydney Diet Heart Study and the MCE; the five trials involved 10,808 participants. This updated meta-analysis found no benefit from linoleic acid rich diets on all cause or CHD mortality.

These data from the MCE confirm the well established observation that replacing saturated fat with linoleic acid lowers blood cholesterol concentration. However, this was not associated with reduced mortality from CHD. Why? It is possible that enrichment of LDL particles with linoleic acid makes them more susceptible to oxidation, so counteracting the effect of lowering the concentration of LDL-cholesterol. Another possibility is that high linoleic acid intakes may have deleterious consequences, such as increasing inflammation, that negate the cholesterol-lowering effect. Whatever the mechanisms involved, these new findings uncovered from the MCE argue against the diet-heart hypothesis, the "saturated fat bad, omega-6 PUFA good" dogma and much current dietary advice, just as the data uncovered from Sydney Diet Heart Study did. However, the findings of these studies cannot be used to argue that lowering of total and LDL-cholesterol concentrations by means other than replacing saturated fat by omega-6 PUFAs (e.g. through other dietary strategies or by using statins) may not be effective in lowering CHD and CVD risk and mortality. Furthermore, there are limitations of this study, for example data on intake of trans fatty acids are not available although the authors argue that this is likely to be low, and its generalisability to populations beyond those institutionalised is not clear. It is also important to note that the intake of linoleic acid achieved in the treatment group in the MCE is beyond

the upper limit of intake recommended by some authorities[2], and is beyond what most individuals in most countries are habitually consuming. While these data add to the current debate about healthfulness of different dietary fatty acids[8,9,10], it seems premature to consider altering current recommendations for dietary intake of fat and fatty acids.

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