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Effects of Walnuts on Serum Cholesterol Levels in People with Normo- or Hyperlipidemia

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Introduction

Heart disease is the leading cause of death in the United States (1) and is predicted to be the main cause of death worldwide by 2020 (2). Hypercholesterolemia is a major risk factor for coronary artery disease and thus for myocardial infarction and stroke (3). High serum low-density lipoprotein (LDL) levels particularly pose a significantly increased risk for heart disease (3,8). Numerous studies have shown that a diet low in saturated fatty acids (SFAs) and cholesterol tends to decrease one's risk of heart disease (8,13). Foods, such as nuts, that are rich in monounsaturated or polyunsaturated fats (MUFAs or PUFAs) have been recommended as substitutes for foods high in SFAs to reduce risk of coronary heart disease by favorably altering cholesterol levels in the body (6,7,8).

Walnuts are unique from other nut family members as walnuts contain high amounts of PUFAs such as linoleic acid and α -linolenic acid (5). PUFAs are thought to decrease serum low-density lipoprotein (LDL) levels and thus exhibit cardioprotective effects by decreasing risk of atherosclerosis (6,7). Recent studies have assessed effects of walnut consumption on serum lipid levels in normocholesterolemic and in hypercholesterolemic people.

Walnuts and cholesterol levels in normolipidemic people

A crossover study conducted by Sabate et al. was among the first to examine the effects of walnut consumption on serum lipid levels in humans (11). Eighteen men, ages 21-43, with normal cholesterol levels were randomized to one of two 4-week diets and then were crossed-over to the other diet. Eight subjects followed the reference diet first, while 10 subjects were initially placed on the walnut diet. The reference diet contained foods from major food groups but excluded nuts and nut products. The walnut diet was identical to the control except that the former included 84g/day walnuts and fewer foods high in SFAs.

The researchers found that the mean serum total cholesterol level in subjects following the walnut diet irrespective of diet order was 12.4% (22.4 mg/dL) lower than that during the reference diet. The total cholesterol of *all* subjects on the walnut diet decreased, with the reduction ranging from 2mg to 41mg. Possible reasons for this variety in reduction were not discussed. Mean LDL level of subjects on the walnut diet was 16.3% (18.2 mg/dL) lower than that of people on the control diet. Mean HDL level of subjects on the walnut diet was reduced by 2.3 mg/dL relative to that of people on the reference diet, but mean ratio of LDL to HDL was lower during the walnut diet. The authors concluded that replacing foods high in SFAs with 84g of walnuts daily for 1 month can lower LDL and total cholesterol by 10% in normocholesterolemic men (11).

In 1994, Abbey et al. reported similar results from their study conducted on 16 normocholesterolemic men (ages 32-60) initially placed on a reference diet and later placed on a 3-week diet with a 68g/day-walnuts supplement replacing some SFAs (10). A 5% decrease in serum total cholesterol and 9% decrease in LDL levels were seen following the walnut diet relative to values during the reference diet. However, when the subjects continued the walnut diet for 3 more weeks, no significant changes in plasma lipids were observed. HDL levels remained fairly constant throughout the trial.

Are walnuts really beneficial for normocholesterolemic people?

The studies by Sabate et al. and Abbey et al. indicate that eating 70-80g of walnuts per day may further help reduce one's risk of heart disease by lowering LDL and total serum cholesterol levels in normocholesterolemic people (10,11). However, these studies do not address the effects of walnuts on serum cholesterol levels in normocholesterolemic women. Additionally, confounding factors such as ethnicity may not have been accounted for and may be especially

important in light of the small sample sizes. Furthermore, neither of the studies mentioned how long one must eat walnuts to continue reaping benefits of healthier total cholesterol and LDL levels. The finding by Abbey et al. that plasma lipid levels did not change after 3 additional weeks of the walnut diet seems significant and should be further explored to assess ideal time frames for and long-term consequences of walnut consumption.

Perhaps the most significant disadvantage of these studies is that they do not provide direct evidence that the walnuts, rather than decreased intake of SFAs, were indeed the cause of reduced cholesterol levels. Sabate et al. pointed out that walnuts in the experimental diet were replacing all types of fats (MUFAs, PUFAs, and SFAs), but the majority of replaced foods listed in the study appear to be particularly high in SFAs (11,12). Abbey et al. specifically states that the walnut supplement was used to replace a portion of saturated fats in the diet (10). Decreased intake of SFAs, relative to other fatty acid types, tends to have the greatest effect on serum lipid levels (3). Therefore, more studies need to be conducted to determine the extent of cholesterol-reducing properties attributed to either walnuts or to other present dietary changes (e.g. decreased SFA intake) so that more accurate dietary strategies can be available for normocholesterolemic people.

More recent studies have focused on people with hyperlipidemia, as they are generally at higher risk for heart disease than people with normocholesterolemia are.

Walnuts and serum lipids in people with hyperlipidemia

A randomized crossover study was conducted in 1998 by Chisholm et al. to examine the effects of walnut consumption on serum lipids in people with polygenic hyperlipidemia (9). Twenty-one men with a mean LDL level of 4.63mmol/L and mean total cholesterol of 6.58mmol/L were placed on a weeklong baseline diet. They were then randomly placed on

either a low-fat reference diet or a walnut diet for 4 weeks and switched diets for another 4 weeks. Walnut consumption was not initially monitored by the researchers, who found that most subjects ate walnuts in addition to, rather than in place of, other fatty foods. LDL and total cholesterol levels were lower after the two experimental diets as compared to baseline. HDL levels were higher during the experimental diets. Only a slight reduction in LDL levels was observed during the walnut diet as compared to during the low-fat diet. This finding is inconsistent with those of other studies (6,7). The authors explain that equal plasma levels of myristic acid, which tends to raise cholesterol, present in both experimental groups may have masked the effects of walnuts on plasma cholesterol levels.

The authors report the major contributions of walnuts were significant increases in linoleic and α -linolenic acid in plasma fatty acids after subjects consumed the walnuts. Linoleic acid tends to protect against coronary heart disease (6), and cardioprotective benefits of α -linolenic acid from foods such as walnuts have recently been discovered even in groups with existing coronary artery disease (4). Chisholm et al. reasoned that walnuts may have significant cardioprotective effects if consumed in place of other high-fat foods rather than in addition to them (9).

In 2000, Zambon et al. conducted a randomized crossover trial with hypercholesterolemic people to examine effects of consuming walnuts in place of some MUFAs (7). In contrast to the studies previously mentioned, this study includes both males and females. Forty-nine subjects completed the trial. Patients were randomly assigned to one of two 6-week diets first and then crossed-over to the other diet. The control diet was Mediterranean, excluding nuts. The walnut diet was identical except that 41-56g of walnuts partially replaced foods high in MUFAs. The

article did not appear to take into account differences in subjects' preparation of the walnuts (e.g. salted, oiled, etc.), which could have affected the study outcome.

During the walnut diet, mean total serum cholesterol decreased by 9%, while the control diet yielded a 5% decrease. LDL levels were reduced by 11.2% and 5.6% during the walnut and control diets, respectively. HDL levels remained constant. The authors found that despite the presence of PUFAs in LDL particles, the particles retained resistance to oxidation, supporting the idea that walnuts have antiatherogenic properties (7).

In contrast to other studies, this study does *not* include reduction of saturated fat intake, thus strengthening the argument that the walnuts themselves, and not just cutting SFA intake, accounts for decreased cholesterol levels observed.

This argument is further supported by a 2001 Almario et al. study in which 13 women and 5 men with hyperlipidemia were placed on 4 sequential diets: a 4-week habitual diet, a 6-week habitual diet plus 48g/day walnuts, a 6-week low-fat diet, and a 6-week low-fat diet plus 48g/day walnuts (6). During the latter diet, significant reductions in total cholesterol and LDL levels as compared to the low-fat diet without walnuts (in which there was no decrease in LDL or total cholesterol) were observed. This adds support to the hypothesis that the walnuts, rather than just reduced fat intake, were helping to lower cholesterol levels. This study is quite convincing, but similar studies should be done with randomization to eliminate confounders.

Mechanisms by which walnuts lower serum LDL levels are also currently of great interest. A randomized crossover trial by Munoz et al. in 2001 examined ten men with polygenic hypercholesterolemia. The subjects were placed on either a 6-week Mediterranean diet or a diet in which walnuts replaced 35% of MUFAs. Results were consistent with previous studies showing that a diet rich in walnuts lowers serum LDL and total cholesterol while HDL levels

remain the same. The authors also found that during the walnut diet, there was a major increase in LDL binding to HepG2 receptors. The correlation of this phenomenon to α -linolenic acid incorporation from walnuts into LDL suggested that LDL compositional changes due to walnut consumption increase LDL uptake from the circulation into cells, thereby decreasing serum LDL levels.

These studies of favorable effects of walnuts on serum lipid levels in hypercholesterolemic people illustrate the ability of walnuts to reduce one's risk of heart disease. However, these studies do not mention whether or not the initial degree of hypercholesterolemia affects results of walnut consumption. Caution should also be used when assessing the credibility of the last 3 studies discussed, as they were funded by the California Walnut Commission. Further studies should be done using larger samples sizes.

Conclusion

Studies conducted to examine effects of walnut consumption on serum lipid profiles vastly agree that walnuts tend to lower LDL and total cholesterol while minimally affecting HDL levels in both normo- and hyperlipidemic groups. These studies demonstrate the promising role of walnuts in lowering coronary heart disease risk. More randomized studies should be conducted using larger sample sizes and groups inclusive of both men and women to better represent the general population. Clearer standards for comparison of walnut diets to control diets should be established so outcomes can be more accurately attributed to the appropriate factors. Through these methods, properties of walnuts can hopefully be better understood and maximally utilized to help prevent coronary heart disease.

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