Vegetarian diet as prevention and treatment of hypercholesterolemia and atherosclerosis

Introduction

Hypercholesterolemia and atherosclerosis are the subject of intensive research the world over. Epidemiological studies investigating different diets, laboratory studies aimed at elucidating the different etiologic factors and their pathogenic mechanisms, as well as a number of clinical and interventional studies, are all active fields of investigation.

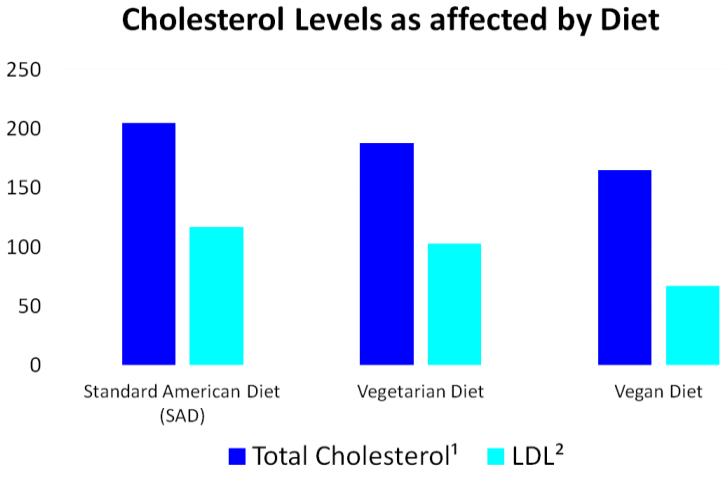
As is well known, hypercholesterolemia raises the risk and is a prime etiologic factor of atherosclerosis, which in turn is an etiologic factor in a number of diseases such as essential hypertension, coronary artery disease, and ischemic stroke, just to name a few. Other factors such as insulin resistance and inflammation may be pathogenic, and levels of C-Reactive protein, E-selectin, myeloperoxidase, and metalloproteinases, are biomarkers for hypercholesterolemia and atherosclerosis and may be pathogenic as well.

Vegetarians, and most especially vegans, have a much lower risk of hypercholesterolemia (for both total cholesterol and LDL) and a less atherogenic profile. A plant-based diet has been shown to be a safe and efficacious prophylaxis and therapy.

Here we report on a selection of studies of particular interest to those wishing to use vegetarian nutritional medicine either as a monotherapy or as an adjunct to other therapies.

Epidemiology

Vegetarians and vegans have lower total and LDL cholesterol levels on average. The following chart shows the average cholesterol levels on among three dietary groups. (1, 2) Vegans, or total vegetarians, have the lowest levels.



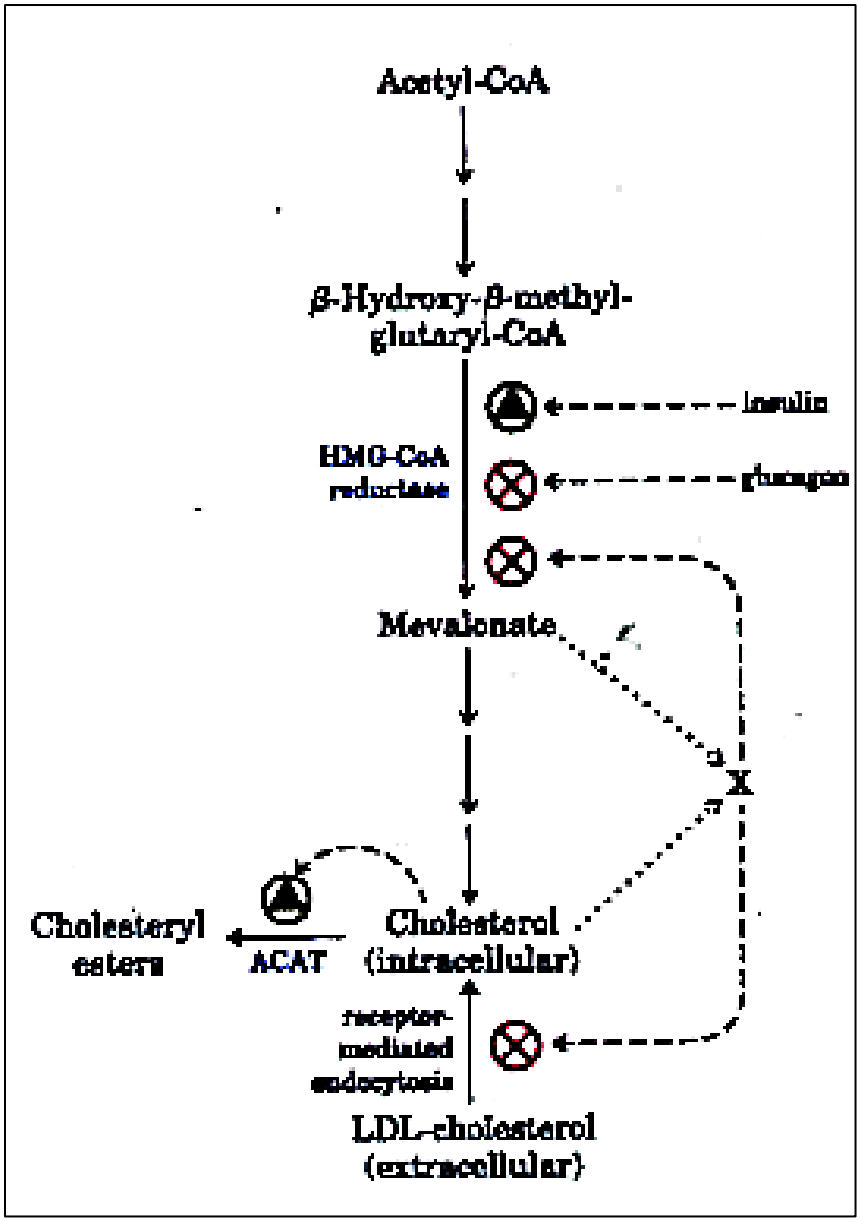
Vegetarians have also been shown to have better cholesterol ratios. (3)

	TC:HDL-C Ratio	LDL-C:HDL-C Ratio
Vegetarians	2.9	1.7
Boston Marathon Runners	3.5	2.0
Average female w/o CHD	4.4	2.9
Average male w/o CHD	5.1	3.3
Average female with CHD	5.3	3.5
Average male with CHD	5.8	3.8

Pathophysiology

Cholesterol Synthesis

One reason why low-fat vegetarian and vegan diets result in lower serum cholesterol levels is that they improve insulin sensitivity, which in turn can reduce cholesterol synthesis. This may account for a portion of the lower prevalence of hypercholesterolemia among vegetarians and vegans and for the results obtained in interventional studies. (4, 5)



The fact that vegetarians and especially vegans have lower cholesterol levels, and better cholesterol ratios, leads to much lower levels of atherosclerosis. One of the important mechanisms whereby LDL cholesterol results in atherosclerotic lesions involves the oxidation of LDL cholesterol. (6, 7) There is evidence that the LDL cholesterol in vegetarians is much less oxidizable. (8)

Vegans have also been found to have better regulation of the metabolism of triglyceride-rich lipoproteins than omnivores, because they are more efficient in removing remnants that are potentially atherogenic. In addition, the diminished cholesteryl ester transfer shown in the study, and the diminished LDL cholesterol levels that have been previously documented in

other published studies, clearly suggest that a vegan diet offers some protection against atherogenesis. (9)

Inflammatory Marker

The role of C-reactive protein in atherosclerosis is still being actively investigated, both as a pathogenic factor and as a marker for cardiovascular disease risk, with positive results in some studies but called into question in others. A vegetarian diet results in lower levels of C-reactive protein. (10, 11)

Histopathology

Myeloperoxidase (MPO) is a leukocyte-derived pro-oxidant enzyme that is released from granules of neutrophils and monocytes. (12) MPO and its oxidant products, nitrotyrosine and chlorotyrosine, have been identified in atherosclerotic plaque and at the site of plaque rupture, and play important role in the genesis of atherosclerosis. (12) MPO promotes a number of pathological events involved in plaque formation and rupture, including uptake of oxidized lipid by macrophages and impaired nitric oxide bioavailability. MPO levels independently predict outcomes in patients presenting with acute coronary syndromes or for evaluation of chest pain of suspected cardiac etiology and endothelial dysfunction. (12)

Matrix metalloproteinases (MMPs) are extracellular enzymes that are important in many physiologic and pathologic processes. Their activity is regulated mainly by tissue inhibitors of metalloproteinases (TIMPs). Their expression is associated with classical cardiovascular risk factors as well as with inflammation. They play a central role in atherosclerosis, plaque formation, platelet aggregation, acute coronary syndrome, restenosis, aortic aneurysms and peripheral vascular disease. Many studies have shown that commonly prescribed antihypertensive medications, glitazones and statins, may influence MMPs activity. (13)

It is known that the arterial wall consists of collagen types I and III, macrophages and smooth muscle cells. The evolution of the atherosclerotic plaque from the fatty streak to advanced plaque is associated with an increase in its content of collagen, (14) in the number of smooth muscle cells, (15) and in MMP-9 levels. (15) Increased levels of MMP-9 are found more often in patients with unstable angina compared with those with stable angina. (16) Human coronary plaques that are less likely to rupture demonstrate lower MMP-9 expression. (15) In patients with coronary artery disease, higher MMP-9 levels are an independent risk factor of cardiovascular mortality. (17) Increased TIMP-1 levels have been reported consistently in human atherosclerotic plaques, mainly in relation to areas of calcification. (18) Increased circulating TIMP-1 levels have also been related to stable coronary, (19) carotid, (20) and peripheral artery atherosclerosis. (20)

One study of circulating cardiovascular biomarker profiles compared the plasma concentrations of myeloperoxidase (MPO), matrix metalloproteinases MMP-9 and MMP-2**,** and tissue inhibitors of MMP TIMP-1 and TIMP-2, between healthy vegetarians and healthy omnivores.

The study found significantly lower concentrations of MPO, MMP-9, MMP-2 and MMP-9/TIMP-1 ratio in vegetarians compared to omnivores. Moreover, MMP-9 concentrations were correlated positively with leukocyte and neutrophil counts in both groups. Therefore, a vegetarian diet is associated with a healthier profile of cardiovascular biomarkers compared to omnivores. (21)

E-selectin (cE-Selectin) is a cell adhesion molecule expressed only on endothelial cells activated by cytokines. Like other selectins, it plays an important role in inflammation. (22)

The intercellular adhesion molecule-1 (cICAM-1) is an Ig-like cell adhesion molecule expressed by several cell types, including leukocytes and endothelial cells. It can be induced in a cell-specific manner by several cytokines, for example, tumor necrosis factor alpha, interleukin 1, and interferon gamma, and inhibited by glucocorticoids. (23)

Upregulation of leukocyte adhesion molecules under atherogenic conditions is accompanied by the release of soluble forms of adhesion molecules into the bloodstream. (24) One study assessed the levels of circulating E-selectin (cE-selectin) and circulating intercellular adhesion molecule-1 (cICAM-1), in both vegetarians and subjects from the general population. (24)

In this study vegetarians were characterized by a significantly lower cE-selectin levels. Vegetarians also showed a tendency towards lower cICAM-1 levels in comparison with control subjects. (24) Low cE-selectin levels of vegetarians may reflect the favorable cardiovascular risk profile of this group.

The lower levels of myeloperoxidase, matrix metalloproteinases and cE-selectin combine to give vegetarians a less atherogenic profile and helps explain their lower levels of atherosclerotic plaque.

Microbiome

Another new area of research has focused in on the role of the gut microbiota in the pathogenesis of atherosclerosis. It has been found that vegetarians and vegans have bacterial flora that produce less TMAO, thought to be atherogenic, than the flora of meat eaters. (25)

The most recent evidence that a vegan diet promotes a gut microbiota that directly reduces metabolic disease risk is the research linking diet to l-carnitine metabolism and atherosclerosis risk. One study found that microbial metabolism of dietary l-carnitine, a trimethylamine found in red meat, produces trimethylamine-*N*-oxide (TMAO), which has been shown to promote atherosclerosis. (26, 27) Through a separate mechanism, the choline found in egg yolks promotes the production of TMAO in a dose-response manner. (28)

Treatment

Vegetarian and vegan diets can be very efficacious in reducing serum cholesterol. One study showed that a low fat vegetarian diet was as effective as the Standard Heart Association diet plus Lovostatin. (29) This study is notable because it contains nuts in the treatment regimen. The research has been accumulating on the value of nuts in the prevention and treatment of a variety of diseases, including cardiovascular, indicating that the low-fat regimen now more commonly employed may be enhanced by moderate amounts of tree nuts.

Another study examining children and their adult parents found that a plant-based, or vegan, diet reduced total cholesterol, LDL cholesterol and C-reactive protein more than the American Heart Association diet. This study is especially important given the recent increase in the incidence of hypercholesterolemia in children and the fact that atherosclerosis seems to start early in life. (30)

Discussion

Hypercholesterolemia and atherosclerosis are perhaps the most important diseases for the physician to address given the human and the financial impact of cardiovascular disease.

Epidemiological research points to the lower risk vegetarians and vegans have of both hypercholesterolemia and atherosclerosis. Since studies correct for other lifestyle factors, one is left with their diet as the determinative prophylactic factor. Research-based evidence indicates, therefore, for the efficacy and the safety of the plant-based diet for the prevention of hypercholesterolemia and atherosclerosis.

Investigations into the pathophysiology of hypercholesterolemia and atherosclerosis have demonstrated that vegetarians have a profile that is less atherogenic, and sheds light on the mechanism by which this is achieved.

Interventional studies point to the safety and efficacy and, indeed, the superiority of plant-based diets over pharmacotherapy for the treatment of hypercholesterolemia and atherosclerosis in many cases.

The prevention and treatment of hypercholesterolemia with a plant based diet would seem to be both safe and efficacious. It has no contraindications, adverse effects and reduces the risk of common comorbidities.

Finally, research is increasingly elucidating the prophylactic factors for the lower risk of these diseases experienced by vegetarians and vegans, as well as the pathogenic factors and mechanisms for the higher risk experienced by omnivores.

Another, much more detailed, post covers coronary heart disease, and forthcoming posts will address ischemic stroke and essential hypertension, all of which have hypercholesterolemia and atherosclerosis as etiologic factors.

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