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Editorial Open Access

Editorial on Treatment of Dyslipidemia in Patients with Diabetes Mellitus

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Lifestyle measures are important in the treatment of diabetics with dyslipidemia. The diabetic should achieve and maintain a desirable weight. The diet should be low in cholesterol (less than 200 mg daily). Less than 30% of total caloric intake should be fatty acids. Saturated fatty acids should comprise less than 7% of total calories, polyunsaturated acids up to 10% of total calories, and monounsaturated fatty acids 10% to 15% of total calories. The diet should also be high in fiber and high in fruits and vegetables. There is no strong evidence to support any dietary supplements. A more liberalized diet is warranted in elderly persons prone to malnutrition. Moderate intensity exercise is recommended for 30 to 60 minutes daily. Smoking should be stopped, hypertension treated, and the hemoglobin A1C level controlled.

Numerous studies have documented that statins reduce cardiovascular events including stroke and mortality in patients with diabetes mellitus [1-4]. In the Collaborative Atorvastatin Diabetes Study, 2,838 patients (62% older than 60 years) with diabetes mellitus, no cardiovascular disease, and a serum low-density lipoprotein cholesterol level less than 160 mg/dL were randomized to atorvastatin 10 mg daily or to placebo [1]. At 3.9-year median follow-up, compared with placebo, atorvastatin significantly reduced time to first occurrence of acute coronary events, coronary revascularization, or stroke by 37%, acute coronary events by 36%, and stroke by 48% [1].

In the Heart Protection Study, 5,963 United Kingdom adults aged 40 to 80 years with diabetes mellitus were randomized to simvastatin 40 mg daily or to double-blind placebo [2]. First major vascular event (major coronary event, stroke, or revascularization) was reduced by simvastatin 22% by simvastatin in diabetics ($p<0.001$), 33% in diabetics without occlusive arterial disease ($p = 0.0003$), and 27% in diabetics with a serum low-density lipoprotein cholesterol level below 116 mg/dL [2]. Statin treatment for 5 years prevented 45 diabetics per 1,000 treated from having at least one major vascular event and among these 45 persons, to prevent 70 first or subsequent events. This study showed that statin therapy reduced major vascular events in diabetics, regardless of age, gender, and serum lipid levels.

In an observational prospective study of 171 men and 358 women, mean age 79 years, with prior myocardial infarction, diabetes mellitus, and a serum low-density lipoprotein cholesterol level of 125 mg/dL or higher, 53% of persons were treated with statins [3]. At 29-month follow-up, compared with no treatment with statins, use of statins significantly decreased in diabetics coronary death or nonfatal myocardial infarction by 37% and stroke by 47% [3].

A meta-analysis was performed of 14 randomized trials of statins used to treat 18, 686 diabetics (1,466 with type 1 diabetes and 17,220 with type 2 diabetes) [4]. Mean follow-up was 4.3 years. All-cause mortality was decreased 9% per mmol/L reduction in serum low-density lipoprotein cholesterol, $p=0.02$. Major cardiovascular events were reduced 21% per mmol/L reduction in serum LDL cholesterol, $p<0.0001$. Statins caused in diabetics a 22% reduction in myocardial infarction or coronary death ($p<0.0001$), a 25% reduction in coronary revascularization ($p<0.0001$), and a 21% reduction in stroke ($p = 0.0002$). After 5 years, 42 fewer diabetics per 1,000 diabetics treated with statins had major cardiovascular events [4].

In the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study, 9,795 type 2 diabetics (2,131 with cardiovascular disease) were randomized to fenofibrate or placebo [5]. Mean follow-up was 5.0 years. The primary outcome of coronary events was not significantly reduced by fenofibrate. Fenofibrate insignificantly increased coronary artery disease mortality 19% [5].

In the ACCORD trial, 5,518 type 2 diabetics at high risk for cardiovascular disease were randomized to simvastatin plus fenofibrate or to simvastatin plus placebo [6]. Mean follow-up was 4.7 years. Compared with simvastatin plus placebo, simvastatin plus fenofibrate did not lower the rate of fatal cardiovascular events, nonfatal myocardial infarction, or nonfatal stroke. Among 3,414 patients with atherosclerotic cardiovascular disease and low serum high-density lipoprotein cholesterol levels treated with simvastatin plus ezetimibe if needed to maintain the serum low-density lipoprotein cholesterol level less than 70 mg/dl, at 36-month follow-up, patients randomized to niacin had improvements in serum high-density lipoprotein cholesterol and triglyceride levels but no clinical improvement compared to patients randomized to placebo [7]. In this study, patients treated with niacin had a 67% increase in ischemic stroke or stroke of uncertain origin ($p=0.09$) [7].

Professor Jane Armitage presented on March 9, 2013 at the Annual Scientific Meeting of the American College of Cardiology in San Francisco, California the results of HPS_2-THRIVE (Heart Protection Study 2-Treatment of HDL to Reduce the Incidence of Vascular Events). In this study of 25,673 patients at high risk of cardiovascular events, adding extended-release niacin plus the anti-flushing agent laropriprant to treatment with simvastatin or simvastatin/ezetimibe did not decrease at 3.9-year follow-up cardiovascular events. However, there were 31 serious adverse events among every 1000 niacin-treated patients including 3.7% excess diabetic complications ($p<0.0001$), 1.8% excess new onset diabetes ($p<0.0001$), 1.4% excess infections ($p<0.0001$), 1% excess gastrointestinal complications ($p<0.0001$), and 0.7% excess bleeding (gastrointestinal and intracranial) ($p<0.0002$).

Diabetics at high risk for cardiovascular events should have their serum low-density lipoprotein cholesterol level cholesterol decreased to less than 70 mg/dL with statins [8]. Lower-risk diabetics should have their serum low-density lipoprotein cholesterol level lowered to less than 100 mg/dL Combination therapy of a statin with either a fibrate or niacin has not been found to provide additional cardiovascular benefit above statin therapy alone and is not recommended [8].

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Hypertriglyceridemia should be treated with dietary and lifestyle changes [8]. Severe hypertriglyceridemia should be treated with drug therapy to reduce the risk of acute pancreatitis [8].

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