Post-Prandial Hyperlipidemia and Hypertriglyceridemia

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Hyperlipidemia i.e. the elevation of blood lipids is believed to be an important risk factor for coronary heart disease.[1] During the last three decades, evidence has accumulated for a possible role of dietary fat in the aetiology of cardiovascular disease.[2,3] Research has suggested that as well as LDL cholesterol, the triglycerides rich lipoproteins may be involved in the pathogenesis of atherosclerosis[4,5] but whether hypertriglyceridemia itself is a risk factor for heart disease is controversial. Some of this controversy obviously stands from the fact that fasting triglyceride levels did not correlate with CAD in some studies. More recently there is accumulating evidence to suggest that the link between plasma triglyceride concentration and risk of coronary heart disease (CHD) may be related to aspects of postprandial fat metabolism.[6]

Most of the available literature relating to triglyceride levels and CHD risk have been however with regard to triglyceride levels in fasting plasma. Classically, this has been the condition under which samples for triglyceride assays are drawn. This is because the assay is easier to standardize and requires less effort from the patient than asking him or her to consume a standard fat load and subsequently have blood samples taken over several hours. However, as human beings we spend most of our day in the postprandial state. Hence, it stands to reason that if triglyceride - rich lipoproteins are important in atherosclerosis, they should be measured in the postprandial blood.

The hypothesis that chylomicrons are atherogenic lipoproteins was formulated almost twenty years ago[7]. Since then, a number of cross-sectional studies have shown that postprandial concentrations of triglyceride are increased in individuals with CHD and in those with carotid disease.[8,9] One study had found that the progress of angiographically evaluated CHD in young male survivors of myocardial infarction is positively related to the postprandial levels of apoB-48 containing triglyceride rich lipoproteins.[10]

Postprandial hyperlipidemia in type 2 diabetes mellitus:

It is becoming increasingly recognised that postprandial hyperlipidemia co-segregates with the dyslipidemia of insulin resistance / type 2 diabetes mellitus.[11,12] The most florid abnormality of postprandial hyperlipidemia is an increase in plasma triglyceride which is contained in both chylomicrons and VLDL, collectively known as triglyceride-rich lipoproteins (TRL). There is some inconsistency regarding the time course of the postprandial state. Karpe et al[13] have reported that the triglyceride concentrations at 6-8 hours correlate best with vascular disease whereas Chen et al[14] have shown that the maximum differences between type 2 diabetes mellitus and non-diabetic subjects is at 4 hours.

Patsh et al[15] found that postprandial triglyceride levels had a very high sensitivity and predictive power with respect to CHD. They concluded that postprandial triglyceride levels are good predictors for CHD, but that fasting triglyceride levels are only weak predictors. Not only triglycerides, but low-density lipoproteins of the postprandial state have also been implicated as a risk factor for CHD. Lechleituer et al[16] found that cholestryl ester formation was greater when postprandial serum was incubated in vitro with macrophages compared to serum in the postabsorptive state.

Pathophysiology

Increased post-prandial levels of triglycerides may result from excess production or reduced clearance.[17] VLDL secretion is elevated in type 2 diabetes mellitus in the post-absorptive state. Insulin resistance in either the liver or adipose tissue fails to curtail VLDL output in the postprandial period. There is also evidence of clearance defects contributing to postprandial hyperlipidemia.[18] Defective postprandial lipoprotein lipase action could account for both fasting and postprandial hypertriglyceridemia.

Clinical significance of postprandial hyperlipidemia

Epidemiological studies point to postprandial hyperlipidemia as a powerful risk factor for atherosclerosis. Two studies have suggested an association between elevated postprandial levels of chylomicron remnants and the presence of CHD.[19,20] Two recent studies have suggested that VLDL remnants are also linked to progression of CHD.[21] A study by Jastizebcka et al[22] found that levels of factor VII, fibrinogen and plasminogen activator inhibitor were increased in ischaemic heart patients with postprandial hypertriglyceridemia in comparison to raised fasting triglyceride levels. Longer periods of postprandial lipemia might constitute an additional factor promoting thrombus formation in patients with dysfunction of the vascular endothelium.

Alimentary lipemia does not lead to thrombus formation by itself and it is therefore difficult to evaluate the potential pathophysiological significance of these findings. It could be hypothesized that increased generation of factor VII activity in the postprandial state through the intrinsic coagulation pathway augments the potential for thrombin production in the event of plaque rupture with exposure of tissue factors.[23]

Therapeutic strategy

A surprisingly wide range of therapeutic interventions improve postprandial hyperlipidemia in type 2 diabetes. Postprandial hyperlipidemia can be reduced by life style changes in patients with type 2 diabetes and in non-diabetic subjects. Weight loss, increasing exercise and dietary changes can reduce postprandial hypertriglyceridemia. Isocaloric low carbohydrate low fat have been shown to reduce postprandial lipid levels.[24]

Acarbose has its main mechanism of action during the postprandial period and improves postprandial hyperlipidemia as well as glucose intolerance.[25] Addition of metformin to sulphonylurea treated patients with type 2 diabetes with less than - optimal glycemic control, lowers postprandial triglyceride concentrations with a decrease in postprandial concentration of triglyceride rich lipoproteins of intestinal origin.[26] Insulin therapy improves fasting triglycerides and fasting VLDL concentrations as well as postprandial hyperlipidemia in type 2 diabetes mellitus. Fibrate group of drugs also improve postprandial hyperlipidemia as well as fasting lipids in NIDDM.

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