Role of Post Prandial Lipaemia in the Development of Type 2 Diabetes Mellitus (T2DM) and Related Macrovascular Disease

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Abstract

Title: Role of Post Prandial Lipaemia in the Development of Type 2 Diabetes Mellitus (T2DM) and Related Macrovascular Disease

Objective: The present study aimed to investigate the role of post prandial lipaemia in modulating the development of glucose intolerance, diabetes and its atherosclerotic complication in the setting of a high sucrose rat model of diet induced diabetes.

Methodology: 96 male wistar rats of same age were randomized into four groups (24 rats each group). Control Group 1 was given standard chow diet, Group 2 high sucrose diet, Group 3 high sucrose diet + Pioglitazone (10 mg/kg, oral) and Group 4 high sucrose diet + Atorvastatin (20 mg/kg, oral). All the rats were followed up till 72 weeks. Fat challenge and glucose tolerance tests were done alternatively at fortnightly intervals in all the four groups besides estimation of insulin, leptin, adiponectin and inflammatory biomarkers. After 26 weeks of follow up, low dose streptozotocin (STZ, 15mg/kg, i.p.) was given to half of the rats in each group to induce partial destruction of β cells. Visceral fat content, hepatic fat content and histopathology of aorta and pancreas were also done in sacrificed rats.

Results: Rats fed high sucrose diet had the highest post prandial triglyceride burden (PPHTg) compared to control chow diet group. Atorvastatin pretreatment in the high sucrose diet fed rats abolished the post prandial hypertriglyceridemia which became comparable to the control group, while pioglitazone pretreatment partially blunted the post prandial hypertriglyceridemic response resulting in an intermediate post prandial triglyceride (PPTg) burden. High sucrose diet fed rats with the highest post prandial triglyceride (PPTg) burden displayed highest glucose intolerance, highest number of rats developing diabetes, highest insulin resistance, highest hyperleptinemia and endothelial dysfunction and highest risk of atherosclerosis compared to controls. Atorvastatin pretreated rats who had post prandial triglyceride (PPTg) levels similar to controls, also displayed lowest glucose intolerance, lowest number of rats developing diabetes, lowest insulin resistance, lowest hyperleptinemia and endothelial dysfunction and lowest risk of
atherosclerosis compared to other two groups receiving high sucrose diet. Pioglitazone pretreated rats showed intermediate values of all the above parameters.

**Conclusion:** Present study provides for the first time, unequivocal evidence that post prandial hypertriglyceridemia leads to the development of insulin resistance, glucose intolerance and type 2 diabetes mellitus in a rat model of type 2 diabetes mellitus. In addition, post prandial hypertriglyceridemia associated with high sucrose feeding, also leads to greater endothelial dysfunction and atherosclerosis risk.