Annexures
Post Prandial Hypertriglyceridaemia leads to the development of type 2 diabetes mellitus

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Post prandial hypertriglyceridaemia (PPTg) has been consistently reported in diabetic patients and insulin resistance is an important determinant of PPTg. Whether PPTg in turn causes diabetes and insulin resistance is not known. We hypothesize that PPTg plays a central role in the development of type 2 diabetes (T2DM).

To investigate the role of PPTg in the development of glucose intolerance and T2DM, fat challenge at 2, 10, 18 & 26 wks and OGTT at 4, 16, 20, 26 & 30 wks were done in four groups (24 each) of male wistar rats. Group A was given control diet, group B high sucrose diet, group C high sucrose diet + pioglitazone (10 mg/kg) and group D high sucrose diet + atorvastatin (20 mg/kg). At 26 wks, low dose streptozotocin (STZ, 15mg/kg, i.p.) was given to half the rats in each group. Significantly higher PPTg area under curve was seen in groups B (1392.67±252.35; p=0.001), C (1239.54±174.93; p=0.002) and D (1414.25±228.20; p=0.001) as early as 2 wks after high sucrose diet as compared to Group A(1017.17±210.50). Groups C (1416.79±303.79; p=0.001) and D (1258.21±402.52; p=0.001) showed significant blunting of the PPTg responses as compared to Group B(1839.0±396.21) at 10th wk. Glucose area under curves after OGTT(AUC-Gl) were not significantly higher in any of the 3 experimental Groups(B, C or D) as compared to controls(A) till 16 wks. At 20 wks, there was a significant increase in AUC -GI in Group B (279.72±29.16) compared to Group A (253.26±34.38; p=0.006) and Group D (256.14±27.90; p=0.006). Similarly, at 30 wks AUC-Gl remained significantly higher in group B compared to groups A(p=0.005) and D (p=0.008) but not group C(p=0.93). Also, AUC -GI was not significantly different in Groups C and D compared to Group A either at 20 or 30 wks. Frank diabetes developed at 30 wks in 2/11 (18.18%) in Group A, 9/11 in Group B (81.81%), 4/12 in group C (33.33%) and 2/12 in Group D(16.67%). This was significantly higher in group B as compared with Groups A(p=0.008) and D(p=0.003).

This study clearly demonstrates that Post prandial hypertriglyceridaemia is an early phenomenon in high sucrose diet induced type 2 diabetes model in rats and is followed much later by glucose intolerance and diabetes. When PPTg response to fat challenge is blunted by drugs, particularly atorvastatin there is blunting of subsequent glucose intolerance as well as significant reduction in development of Type 2 diabetes.

The results of this study provide unequivocal evidence for the first time in rat model that post prandial hypertriglyceridaemia leads to the development of glucose intolerance and type 2 diabetes mellitus and could play a key role in its pathogenesis.
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Dear Dr. Mohd Aslam,

On behalf of the planning Committee of the 1st American Diabetes Association Middle East Congress, December 4-6, 2012, Dubai, UAE, it is our pleasure to inform you that your abstract has been accepted for Poster Presentation.

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Atorvastatin prevents type 2 diabetes – an experimental study

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Abstract

Background: Atorvastatin, a well known drug for treatment of dyslipidemia in patients with increased cardiovascular risk has recently been reported to be associated with incident diabetes. However, evidence in this regard is conflicting with some studies in literature reporting no such increase and few even reporting protection against diabetes. The present study aims to clarify whether atorvastatin can prevent diabetes development in a rat model of diet induced diabetes.

Objective: To investigate the effect of atorvastatin treatment on development of diabetes in rats fed on high sucrose diet.

Methodology: Eight week old male wistar rats were randomly divided into three groups (n = 12 in each group). Group A was given standard chow diet (control diet), group B and group C were offered high sucrose diet. In addition to their respective diets, group C was given atorvastatin (20 mg/kg/day) from beginning of study whereas group A and B were given only vehicle (0.5% carboxymethyl cellulose) till 26th week. After 26 weeks of follow up, mild dose of streptozotocin (15 mg/kg, i.p.) was given to all the 3 groups who were further followed for 4 weeks. Fasting blood samples were collected for insulin and lipid profile and oral glucose tolerance tests (OGTTs) were done at week 4 and week 26. OGTT was repeated after 4 weeks of streptozotocin dose i.e., at week 30.

Results: At the end of 30 weeks 2/11 (18.18%) rats in group A, 9/11 (81.81%) in group B and 2/12 (16.66%) in atorvastatin treated group C developed overt diabetes. Development of diabetes was significantly lower in control group A (p=0.003) and atorvastatin treated group C (p=0.002) as compared with high sucrose group B. Insulin levels decreased significantly after development of diabetes in group B (0.492±0.279 vs 0.898±0.822, p=0.001) but remained same in group A and group C as compared with insulin levels of week 26.

Conclusion: This study clearly demonstrates and provides unequivocal evidence that in rat model atorvastatin prevents development of type 2 diabetes.