How to treat diabetes in Arabs: A rational approach based upon the pathogenesis of the disease

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Background and Aims:
Type 2 diabetes mellitus (T2DM) is a complex disease with multiple metabolic defects including insulin resistance and beta cell dysfunction. Although both insulin resistance and beta cell dysfunction are present in type 2 diabetic individuals in all ethnic groups, we previously have shown that the contribution of each abnormality to the deterioration of glucose homeostasis is ethnic dependent with the greatest role of beta cell dysfunction being in Arab individuals. In the present study, we compare the efficacy and safety of a novel therapeutic approach of initiating subjects with new onset T2DM on triple therapy with agents that correct the metabolic defects in T2DM (metformin/pioglitazone/exenatide) versus the American Diabetes Association guidelines (starting metformin and sequential addition of sulfonylurea and basal insulin) which are based upon the concept of lowering the plasma glucose concentration.

Research Design and Methods:
133 new onset T2DM patients (age = 45±1 y; BMI=36±0.5; HbA1c = 8.8±0.1%; diabetes duration = 5.6±0.5 mo) were randomized to receive metformin (2000 mg/d), plus pioglitazone (45 mg/d), plus exenatide (10 micrograms BID) (triple therapy, n=64) or escalating doses of metformin (2000 mg/d), followed by sequential addition of sulfonylurea (glipizide, 20 mg/d) and basal insulin to maintain HbA1c <6.5 (conventional therapy, n = 69).

Results:
Subjects who received triple therapy, HbA1c decreased from 8.6 to 6.1% at 6 mo and to 6.0% at 24 mo, while in the conventional therapy, HbA1c declined to 6.2% at 6 mo and subsequently increased to 6.5% at 24 mo. Despite lower HbA1c, subjects in triple therapy arm experienced a 13.6-fold lower rate of hypoglycemia compared to subjects in conventional therapy arm. 14 of 66 (21%) of T2DM patients in the conventional therapy arm have required insulin therapy to maintain the target A1c value. Subjects in the triple therapy arm experienced mean weight loss of 1.2 kg compared to mean weight gain of 3.6 kg (p=0.02) in subjects in the conventional therapy arm.

Conclusion:
The present results demonstrate that antidiabetic therapy targeting the metabolic abnormalities responsible for hyperglycemia is more effective and safe than therapy simply aimed at lowering the plasma glucose concentration in T2DM.