T2DM Subgroups and Response to Glucose-lowering Therapy: Results from EDICT and Qatar Study

Abdelgani S, Abdul-Ghani T, Puckett C, Migahid O, Migahed A, Adams J, Triplitt C, DeFronzo RA, Jayyousi A, Abdul-Ghani M

Division of Diabetes, University of Texas Health Science Center and Texas Diabetes Institute, San Antonio, TX.

Hamad General Hospital, Doha, Qatar.

Aim

To examine the efficacy of glucose lowering medications in subgroups of T2DM patients

Design and methods

Cluster analysis was performed in EDICT and Qatar Study participants using age, BMI, HbA1c, HOMA-IR and HOMA-B. The metabolic characteristics were measured with plasma glucose, insulin and C-peptide concentrations during the OGTT and the response to glucose therapies was measured in each cluster for 3 years.

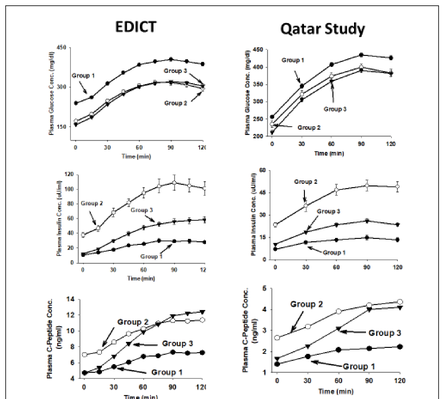

Figure 1: Plasma glucose, insulin, and C-peptide concentrations during the OGTT in the 3 subgroups in EDICT and Qatar study

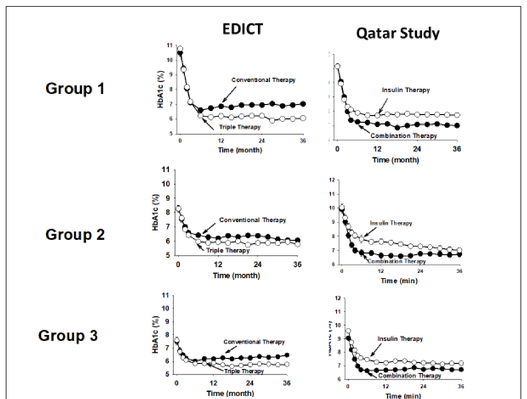

Figure 2: Change over time in the HbA1c in the 3 subgroups in subjects receiving Conventional Therapy and Triple Therapy in EDICT and in subjects receiving Insulin Therapy and Combination Therapy in Qatar Study

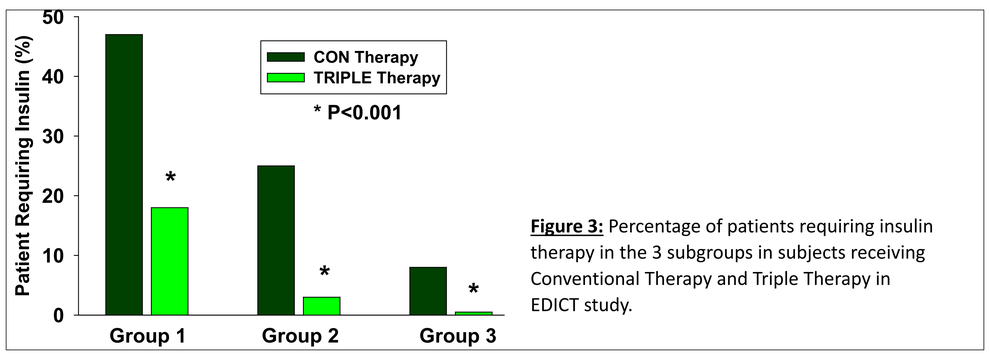

Figure 3: Percentage of patients requiring insulin therapy in the 3 subgroups in subjects receiving Conventional Therapy and Triple Therapy in EDICT study.

Results

3 distinct clusters of T2DM patients were identified in EDICT and Qatar Study. Prevalence of 3 clusters was similar in both studies. Patients in Group 1 had the highest HbA1c and manifested severe insulin deficiency. Patients in Group 3 had comparable insulin sensitivity to Group 1 but better beta cell function and better glucose control. Patients in Group 2 had the highest BMI with severe insulin resistance accompanied with marked hyperinsulinemia which was primarily due to decreased insulin clearance. Unexpectedly, subjects in Group 1 had better response to combination therapy with pioglitazone plus exenatide than with insulin therapy or metformin sequentially followed by glipizide and basal insulin, while subjects in group 2 responded equally well to all 3 therapies despite very severe insulin resistance.

Conclusion

Distinct metabolic phenotypes characterize different T2DM clusters and differential response to glucose-lowering therapies characterize each cluster. Patients with severe insulin deficiency respond better to agents that preserve beta cell function, while patients with severe insulin resistance did not favorably respond to insulin sensitizers.

References

1)Abdul-Ghani M, Puckett C, Adams J, Baskoy G, Cersosimo E, Triplitt C, DeFronzo RA. Durability of triple combination therapy versus stepwise addition therapy in new onset T2DM subjects: 3-year follow-up of EDICT. Diabetes Care 2020.

2) Abdul-Ghani M, Migahid O, Megahed A, DeFronzo RA, Al-Ozairi E, Jayyousi A. Combination therapy with pioglitazone/exenatide improves beta-cell function and produces superior glycaemic control compared with basal/bolus insulin in poorly controlled type 2 diabetes: A 3-year follow-up of the Qatar study. Diabetes Obes Metab. 22:2287-2294, 2020.