

statistical significance using paired t test analysis. Part1: For patients in prediabetic, controlled & uncontrolled DM subgroups, the mean difference between A1cNow+ & standardized venous HbA1c testing was 0.68% (p= 0.004), 1.15% (p= <0.0001) and 1.36% (p= 0.0003) respectively. Part2: After standardization of test strip storage, the mean difference between A1cNow+ & venous HbA1c testing for prediabetic, controlled & uncontrolled DM patients was 0.33% (p= 0.002), 0.41% (p= 0.011) and 1.26% (p= <0.0001) respectively.

POCT HbA1c provides a unique opportunity to immediately address glycemic control. Its advantages are especially apparent in a patient population with limited resources & poor follow up, as in our clinic. Although standardizing test storage improved overall concordance between A1cNow+ HbA1c testing & venous HbA1c, there was still a statistically significant larger mean difference in uncontrolled DM patients. In prediabetic & controlled DM patients, however, POCT HbA1c was accurate within previously published reports of a 0.5% range when compared to venous HbA1c. An algorithm has since been developed to guide our clinical decision making with these findings.

Diabetes Mellitus and Glucose Metabolism

TYPE 2 DIABETES

Alpha and Beta Cell Dysfunction Improves With Effective Insulin Therapy in Treatment Naive Type 2 Diabetes - a Prospective Observational Study.

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Abstract: Type 2 diabetes mellitus is characterized by insulin resistance and progressive beta cell decline. Elevated glucagon levels and impaired incretin axis also contribute to the poor glycemic status. Early intensive glycemic control, reduces long-term vascular complications and may preserve β -cell function. Clinical studies of effect of early insulin therapy on combined alpha and beta cell function are lacking. **Objective:** To determine the effect of early insulin therapy on combined alpha and beta cell dysfunction (islet cell dysfunction) in newly diagnosed type 2 diabetes. **Methods:** 56 newly diagnosed type 2 diabetes patients, attending the endocrinology OPD at a tertiary teaching hospital were enrolled in this treatment related follow up study after institutional ethical committee clearance, conducted between May 2017 to December 2018. Patients with HbA1C > 8.5% to <12.5% (n=56) were included in the study. Metabolic (FPG, PPG, HbA1c), and Hormonal parameters (plasma glucagon levels, fasting and 2 hour mixed meal stimulated C peptide and levels) were assessed both at baseline and after 6 months of insulin treatment. Initiating dose of insulin was 0.5 U/kg/day and the dose

was titrated according to FPG and 2 hr PPG in order to maintain glycemic goals as per ADA standards. **Results:** The study included 56 subjects with mean age of 41.24 \pm 5.64 years and a mean BMI of 25.5 kg/m². At the end of 6 months of the study, a significant reduction in the mean FPG, PPG, HbA1C were observed, [FPG (139 \pm 14.47 mg/dl), PPG (179.89 \pm 19.42mg/dl), HbA1c (7.54 \pm 0.63%)] as compared to baseline mean FPG, (216.30 \pm 42.35 mg/dl), 2 hour PPG (338.44 \pm 62.89 mg/dl), HbA1C (10.39 \pm 1.56 %) (p <0.001). Baseline glucagon levels were high (197.68 \pm 49.09 pg/ml), and were significantly reduced at 6 months of insulin therapy (107.06 \pm 49.09 pg/ml). (p <0.001). In comparison to the baseline a significant increase in both fasting (0.73 \pm 0.27 ng/ml) and stimulated c-peptide (1.54 \pm 1.02 ng/ml) (p<0.001) levels was observed at end of the study. **Conclusion:** Combined alpha and beta cell (Islet) dysfunction prevails in newly diagnosed T2DM. And early insulin therapy significantly improves both these defects. The documentation of this novel beneficial effect on islet cell dysfunction in our study strengthens the concept of early insulin therapy in newly diagnosed Type 2 diabetes patients.

Diabetes Mellitus and Glucose Metabolism

TYPE 2 DIABETES

Association of NOS3 Genetic Polymorphism With the Predisposition to Diabetes and Pre-Diabetes, Retrospective Study

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Background: Endothelial nitric oxide synthetase (eNOS) encoded by NOS3 gene has an important role in modulating vascular endothelial function. Many studies reported a possible role of NOS3 in the pathogenesis of diabetes mellitus (DM). This study investigated the association of NOS3 (G>T) rs1799983 genetic polymorphism with DM, pre-diabetes (pre-DM), and insulin resistance (IR).

Methods: A random sample of 220 subjects (DM & pre-DM) compared with 220 healthy subjects. Sample obtained from Palestinian adults who consented to genetic and biochemical testing. All subjects genotyped for NOS3 (G > T) rs1799983 SNP using ARMS PCR. Fasting blood sugar (FBS) and triglyceride (TGA) levels were obtained for all subjects. Triglyceride glucose index (TyG) was used as a surrogate marker for IR. Regression analysis adjusted for age and body mass index (BMI) was performed to investigate the association between DM & Pre-DM status, FBS, and TyG with NOS3 genetic polymorphism.

Results: NOS3 minor allele frequency positively correlated with FBS levels after controlling for age and BMI (P-value 0.006). DM & pre-DM were more frequent in homozygous NOS3 subjects with an odds ratio of 2.04 (P = 0.05). NOS3 minor allele frequency positively correlated with TyG but not statistically significant association (P = 0.061).

Discussion: Many studies reported a potential role of NOS3 genetic polymorphism in DM and IR pathogenesis. In this study, NOS3 minor allele frequency positivity

correlated with FBS levels. Homozygous NOS3 was associated with a 2-fold increase in the prevalence of DM & pre-DM. NOS3 genetic polymorphism didn't show a statistically significant correlation with TyG ($P = 0.061$). With the increasing availability of genetic testing, NOS3 may serve as an early screening tool to identify subjects with a high risk for elevated FBS. Further studies are required to understand the exact role of NOS3 genetic polymorphism in the pathogenesis of DM, and to evaluate the clinical efficacy and cost-effectiveness of genetic testing.

Conclusion: NOS3 genetic polymorphism has a statistically significant relationship with the FBS level. Further studies are required to confirm the association between NOS3 and DM.

Diabetes Mellitus and Glucose Metabolism

TYPE 2 DIABETES

Clinical And Biochemical Outcomes Of Sodium-Glucose Co-Transporter-2 (SGLT2) Inhibitors In Type 2 Diabetes Mellitus Patients

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Background: SGLT-2 inhibitors are a group of oral medications that work independently of insulin working as anti-diabetics by enhancing the excretion of glucose. The purpose of our study was to assess the improvement in terms of HbA1c, weight, blood pressure and BMI and the hepatics and renal effect in terms of SGPT and Creatinine in patients already on three oral glucose lowering agents when SGLT-2 inhibitor was added to their medications.

Methods: This retrospective, real world, single center study included 99 patients (mean age [Standard Deviation]: 53.8 [9.63] years) with poorly control type 2 diabetes. Data was recorded at three times, before the addition of SGLT-2 inhibitor and then at 3 and 6 month follow up after the drug had been added in patient's medications. Physical parameters namely weight, BMI and blood pressure were recorded in the clinic while HbA1c, SGPT and Creatinine were checked by laboratory. **Results:** Improvement was seen in all parameters at both 3 and 6 month follow up interval. The reduction in HbA1c was statistically significant (P -value < 0.001) with (Mean Reduction [Standard Deviation]) 0.81[1.02] % at 3 months and 1.07[1.11] % at 6 months. Weight was also significantly reduced (P -value < 0.001) with (MR [SD]) 1.83[2.32] kg at 3 and 4.02[6.04] kg at 6 months. Statistically significant reduction (P -value < 0.001) in BMI was also seen with 0.69[0.95] kgm^{-2} at 3 months and 2.13[3.41] kgm^{-2} at 6 months of follow up. The systolic blood pressure showed significant reduction (P -value < 0.05) of 5.9[15.76] mmHg at 3 months and 6.37[18.33] mmHg at 6 months. The creatinine and SGPT values of the patient showed minimal variation over the course of these 6 months of follow up. **Conclusion:** Our study showed that SGLT-2 can be reliably used in patients

in which diabetes is not being controlled by other glucose lowering agents and is safe for use in patients in which hepatic and renal function needs to be preserved. **Keywords:** SGLT-2 inhibitors, Type 2 Diabetes Mellitus, Pakistan

Diabetes Mellitus and Glucose Metabolism

TYPE 2 DIABETES

Combination Therapy With Premixed & Basal Insulin Analogues in Asian Indians With Type 2 Diabetes

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Many individuals with type 2 diabetes (T2DM) eventually need insulin for better glycaemic control. Different insulin regimens like basal, premixed, basal plus, split mixed and basal bolus are used in T2DM management. There is not much literature on a combination of premixed insulin in the morning along with basal insulin at night. Such a regimen is preferred by people with T2DM, who do not want to take an afternoon insulin dose due to inconvenience. To study the effect of a premixed insulin given in the morning and long acting basal insulin analogue given at night in T2DM subjects, we looked into this combination. We performed a retrospective study to look into the effects of premixed and basal insulin analogue combination in patients with T2DM (in addition to oral antidiabetic agents). From the diabetes electronic medical records of a tertiary care hospital for diabetes at Chennai in South India, 648 patients on premixed and basal insulin analogue combination, who came for a follow-up visit were included in the final analysis. Baseline characteristics included body weight, BMI, blood pressure, fasting lipid profile, fasting and post prandial plasma glucose and HbA1c were analysed at baseline, and a change in the parameters was studied at the first follow up visit between 5 to 7 months. Mean age of the study population was 60.7 ± 13.1 years with mean diabetes duration of 20.5 ± 8.0 years. Out of 648 patients included, three fifths were male. Statistically significant improvement was observed in body weight, BMI, HbA1c, systolic blood pressure, lipid profile, fasting blood sugars ($P < 0.001$) and post prandial blood sugars ($P = 0.005$) in comparison to baseline values. Significant reduction in HbA1c (1.7 %, $p < 0.0001$) was observed in those with in the highest tertile of HbA1c (11.3 ± 1.0 %) in comparison to the baseline values. At follow up, nearly a third of study subjects achieved a HbA1c target of $< 8\%$ (30.1 % vs 18.4 0%, $p = 0.0005$) in comparison to the baseline values. 28.7 % patients on combination therapy achieved a fasting blood sugar value of < 130 mg/dl at follow up compared to 18.2 % patients at baseline ($p < .0001$). Similarly, 22 % of the patients on combination therapy also achieved post prandial blood sugars of < 180 mg/dl at follow up, compared to 12.2 % ($P < .0001$) at baseline. This study shows that in T2DM subjects, a simple regimen of premixed and basal insulin analogue combination helps in improving the glycaemic control.