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AACE
ANNUAL MEETING
May 12-14, 2022

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGY

ANNUAL MEETING 2022

DAILY COVERAGE

TOP 7 SESSIONS: DAY-2

TOPIC OF CONTENT

SESSION-1: DIABETES TECHNOLOGIES IN 2022

PREDICTORS OF TYPE 2 DIABETES (T2D) REMISSION USING DIGITAL TWIN TECHNOLOGY BASED ON ARTIFICIAL INTELLIGENCE (AI) AND INTERNET OF THINGS (IOT) TECHNOLOGIES

Friday, 13th May 2022

This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Drs. Shashank Joshi, DM, Paramesh Shamanna, MD, Lisa Shah, MD, Jahangir Mohammed, MD from Lilavati and Twin Health.

To identify pre-intervention anthropometric and biochemical parameters that predict diabetes remission after applying AI-based IoT technology and post-intervention parameters that are improved in patients achieving remission.

Twin Precision Treatment (TPT) is a mobile application and intervention based on the patented Whole-Body Digital Twin (WBDT) enabled precision treatment. An independent ethics committee approved this RCT. 167 patients with T2D completed 180 days of TPT. Remission was defined as an A1C level < 6.5% for ≥180 days without diabetes medication use for at least 90 days. 141 of the 167 patients (84.4%) had remission of diabetes using this definition (group R).

At baseline, patients in R group, compared with patients in the Non-remission Group (group NR) had shorter duration of diabetes (yrs) (R: 3.3±2.7, 95% CI 2.9 to 3.7) vs. (NR: 4.7±2.4, 95% CI 2.9 to 3.7), p=0.015; lower pre-TPT A1C (R: 8.8±1.8, 95% CI 8.5 to 9.1) vs. (NR: 9.7±1.8, 95% CI 9 to 10.5), p=0.021; lower estimated A1C (eA1C) (R: 8±2.2, 95% CI 7.7 to 8.4) vs. (NR: 9.5±2.5, 95% CI 8.5 to 10.5), p=0.002; lower glucose management indicator (GMI) (R: 7.5±1.9, 95% CI 7.2 to 7.8) vs. (NR: 8.6±1.7, 95% CI 7.9 to 9.3), p=0.006; lower Time Above Range level 2 (TAR2; target >250 mg/dl < 5% time) (R: 17.4±23.8, 95% CI 13.5 to 21.4) vs. (NR: 33.6±31.5, 95% CI 20.9 to 46.3), p=0.003; higher Time In Range (TIR; target 70–180 mg/dl >70% time) (R: 52.5±32, 95% CI 47.2 to 57.9) vs. (NR: 36.6±34.8, 95% CI 22.5 to 50.6), p=0.023; and lower fasting plasma glucose (R: 168.8±54, 95% CI 157.8 to 175.8) vs. (NR: 197.8±82.8, 95% CI 164.4 to 231.3), p=0.015. At 180 days, the difference in the change, in R was better than NR for Time Below Range1 - TBR1 (< 70–54 mg/dl) < 4% (12.7±16.9, 95% CI 9.9 to 15.5) Vs (5.7±6.6, 95% CI 3.2 to 8.3), p=0.04; HOMA2IR (%) (1±0.43, 95% CI 0.9 to 1.1) Vs (1.22±0.47, 95% CI 1 to 1.4), p=0.019; HOMA2B (%) (92.5±32.3, 95% CI 87.1 to 97.9) Vs (72.8±23.8, 95% CI 63.2 to 82.4), p=0.004; WBC (thousand/mm3) (6453.9±1486.4, 95% CI 6206.4 to 6701.4) Vs (7410.4±1480.1, 95% CI 6812.6 to 8008.2), p=0.003. The baseline and change in body weight, LDL-C, HDL-C, TGs, sdLDL were comparable. The final mean A1C in NR was 6.3% Vs 5.5% in R. The mean baseline antidiabetic drug count was lower in R (1.73) Vs NR (2.23).

A shorter duration of diabetes, lower A1C, eA1C, GMI, and TAR2 at baseline are reliable predictors for diabetes remission with the TPT intervention. The TBR1, HOMA2B, and HOMA2IR by 180 days improved in patients

who achieve remission. TPT is a promising lifestyle intervention for diabetes remission.

DURABILITY OF HIGH-FREQUENCY 10-KHZ SPINAL CORD STIMULATION FOR PAINFUL DIABETIC NEUROPATHY: 18-MONTH MULTICENTER RANDOMIZED CONTROLLED TRIAL RESULTS

Friday, 13th May 2022

This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Drs. Erika Petersen, MD Thomas Stauss, MD James Scowcroft, MD from University of Arkansas for Medical Sciences.

Approximately 6 million US adults are living with painful diabetic neuropathy (PDN) and many find conventional treatments ineffective.1-3 The published 6- and 12-month SENZA-PDN data demonstrate that high-frequency 10-kHz spinal cord stimulation (SCS) substantially relieves pain and may improve sensation in patients with refractory symptoms.

Prospective, multicenter, randomized controlled trial (SENZA-PDN, NCT03228420) to document the impact of 10-kHz SCS on PDN. Participants had PDN symptoms ≥12 months, refractory to medications including gabapentinoids and at least one other class of analgesic, lower limb pain intensity ≥5cm (0-10cm visual analog scale [VAS]), and hemoglobin A1c ≤10%. Patients (n=216) were allocated 1:1 to 10-kHz SCS (Nevro Corp.) plus conventional medical management (CMM) or CMM alone and followed for 18 months with an option to crossover at 6 months if they had insufficient pain relief (< 50%), were dissatisfied with treatment, and the physician approved it was medically appropriate.

Patients assigned 10-kHz SCS experienced substantial, sustained pain relief with 78% improvement over 18 months (baseline VAS=7.6 cm, 18-month VAS=1.7 cm). Additionally, this group reported average 65% reduction in sleep disturbance due to pain and 65% improvement in pain interference with mood and daily activities. No 10-kHz SCS participants elected to crossover.

At 6-month follow-up, 93% of eligible CMM patients elected to crossover and results were similar to those seen in the original SCS group: 70% pain relief over 18 months (baseline VAS=7.3 cm, 18-month VAS=2.2 cm). Crossover patients reported average 55% reduction in sleep disturbance due to pain and 61% improvement in pain interference. There were no significant differences between the crossover results and those observed in patients originally assigned 10-kHz SCS.

There were no stimulation-related neurological deficits and no explants due to ineffectiveness. There were 6 total explants (3.9%), 5 due to procedure-related infections and 1 as a precaution for endocarditis. All-cause hospitalization rate was 1.5 times higher for patients treated with CMM alone compared with 10 kHz SCS, with per-patient, per-month rates of 0.025 and 0.016, respectively. Additionally, there was a trend for longer average length of stay per hospitalization for the CMM alone group.

SENZA-PDN, the largest RCT to-date of SCS management of PDN, will inform the treatment continuum. Observed short-term results are durable over 18 months for patients with symptoms refractory to conservative care.

SESSION-2: MANAGING T2DM IN CKD

MANAGING TYPE 2 DIABETES MELLITUS IN CHRONIC KIDNEY DISEASE

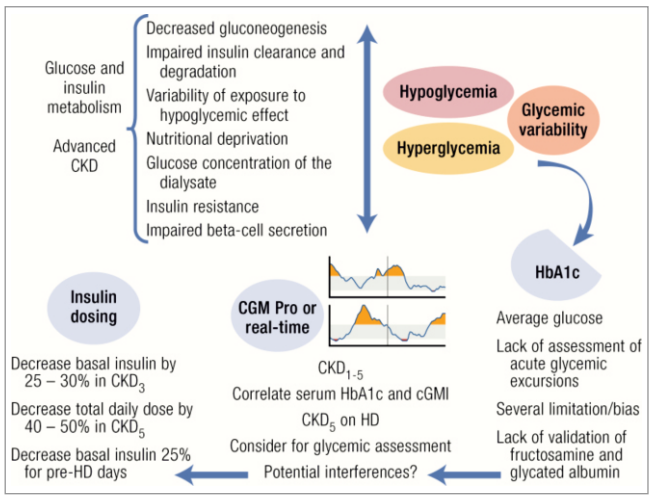
Friday, 13th May 2022

This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Dr. Rodolfo J. Galindo, MD, FACE Emory University, Atlanta, Georgia, United States.

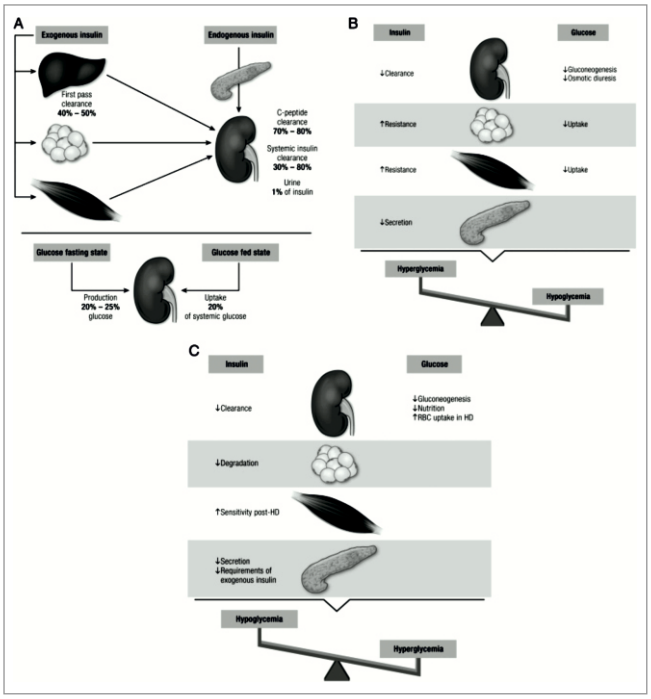
Dr. Rodalfo presented his talk on Glycemic Monitoring and Management in Advanced Chronic Kidney Disease. The key learning objectives of the sessions were to -

- Review challenges in the management of dysglycemia in patients with advanced CKD/Dialysis
- Discuss the newer glycemic monitoring options in dialysis
- Review medications adjustments needed to avoid hypoglycemia in advanced CKD

Graphical Abstract of the Study –



Challenges in the management of dysglycemia in CKD patients



A, Insulin and glucose metabolism by the liver, fat and muscle tissues, and kidney with normal renal function. B, Insulin and glucose metabolism by the kidney, fat and muscle tissues, and pancreas in early chronic kidney disease (CKD) resulting in higher risk of hyperglycemia. C, Insulin and glucose metabolism by the kidney, fat and muscle tissues, and pancreas in advanced CKD and hemodialysis (HD) resulting in higher risk of hypoglycemia. RBC, red blood cells.

Clinical Implications of Hypoglycemia in Patients with Advanced Chronic Kidney Disease

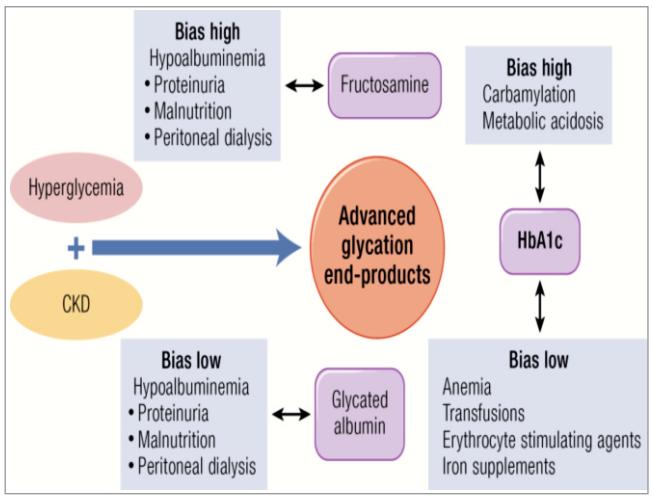
Hypoglycemic episodes are associated with a higher risk of recurrent hypoglycemia and mortality after initiation of dialysis. Recently, Rhee and colleagues analyzed the Veteran Affairs database to study 20 156 veterans with diabetes and predialysis CKD transitioning to dialysis over 1 to 2 years. One or more hypoglycemia-related hospitalizations occurred before initiating dialysis in 5.9%. Independent risk factors for hypoglycemia-related hospitalization were Hispanic ethnicity,

heart failure, cerebrovascular disease, high HbA1c, and use of insulin. Furthermore, hypoglycemia-related hospitalizations before transition to hemodialysis were strongly associated with higher mortality after transition to dialysis.

Given the large comorbidity burden of patients with ESKD, it is unclear whether hypoglycemia-related morbidity and mortality is causal or a marker of overall disease severity and burden. In addition, hypoglycemia is associated with increased risk of cardiac arrhythmias, stroke, seizures, and sudden cardiac death. In a descriptive study of admissions by Haviv et al among 1545 patients with ESKD and with and without diabetes, 3.6% were admitted for hypoglycemia. The most commonly identified causes were drug-induced hypoglycemia (46%), followed by sepsis (39%) and severe malnutrition (7%). Importantly, high GV commonly occurs in tandem with hypoglycemia among patients with type 2 diabetes. Frequent hypoglycemic events are associated with high GV values, and reducing hypoglycemia strongly correlates with decreased GV. In addition, high GV is linked to increased risk of cardiovascular events and death and all-cause mortality.

Glycemic Treatment Goals

Overall, the available evidence suggests that among patients with diabetes and advanced CKD, the target HbA1c levels may be different from those recommended by current guidelines for other patients. Although targeting HbA1c levels of less than 7% is associated with greater survival in patients with lower comorbidity burden and adequate nutritional status, lower HbA1c levels are associated with an increased risk of death in those with comorbidities and malnutrition.



The National Kidney Foundation–Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) guidelines recommend an HbA1c target of approximately 7% for most patients with CKD. However, a personalized approach with less strict glycemic targets (HbA1c 7%-8%) is endorsed by NKF-KDOQI and other diabetes guidelines for patients with advanced CKD because of shorter-life expectancy, high comorbidity burden, or high risk of hypoglycemia. These recommendations were largely driven by the high risk of iatrogenic hypoglycemia from treatment with antihyperglycemic agents. However, newer agents (eg, incretin therapies) with a lower risk of hypoglycemia have not been extensively studied in this group. In addition, HbA1c has less reliability in the setting of advanced CKD (Fig), as discussed further later. The goal for glycemic targets to optimize clinical outcomes in these patients is unknown and an important topic for research.

Limitations of glycemic biomarkers (hemoglobin A1c [HbA1c], fructosamine, and glycated albumin) in patients with advanced chronic kidney disease (CKD)

Role of continuous glucose monitoring in advanced chronic kidney disease—moving beyond hemoglobin A1c

CGM use has the advantage of providing better assessment of glycemic patterns and insulin needs among diabetic patients with advanced CKD. CGM has the potential to become a new standard of care for assessment of glycemic control in diabetic patients treated by maintenance hemodialysis given the well-known limitations of HbA1c and other glycemic

biomarkers. However, there are limited studies in the CKD population, particularly using novel factory-calibrated sensors. With the expansion of CGM studies and growing clinical use, there has been an evolution of "new/nontraditional glucose metrics," such as 1) time in target range; 2) time in hyperglycemia range; 3) time in hypoglycemia range; and 4) GV. In the clinical realm, HbA1c targets remains commonly used because of strong predictive capacity for diabetic complications. Additionally, there is headway to "move beyond HbA1c", and a recent international consensus conference provided guidance on clinical targets for CGM-derived glucose metrics. Although there is consensus on the adoption of such novel CGM-derived glucose metrics, no studies have yet been conducted among patients on maintenance dialysis. Of note, a recent study by Beck et al showed a strong association of time in target range with retinopathy and microalbuminuria among patients with type 1 diabetes in the Diabetes Control and Complications Trial cohort.

The 24-hour glucose profile provided by CGM allows patients and health care providers to recognize glucose patterns, including responses to meals, medications, acute illness, or other stressors. Factory-calibrated CGM devices reduce the burden of diabetes care by reducing use of finger sticks for blood glucose monitoring. Moreover, CGM systems provide a benefit of recognizing declining glucose levels before occurrence of hypoglycemia and enable closed-loop insulin programs ("artificial pancreas") by adjusting the insulin infusion rate to prevent hypoglycemia (eg, Tandem Basal and Control IQ, Medtronic G670.

CGM data can be used to generate a CGM index (glucose management indicator or GMI), which is a proxy for long-term glycemia in conjunction with the HbA1c measurement in individual patients, allowing adjustment of glycemic goals accordingly. CGM-estimated HbA1c (eA1c) was a term previously reported on CGM reports and derived from the CGM measured mean glucose. However, it was well recognized that CGM-eA1c and laboratory-measured HbA1c did not correlate in clinical practice and in research studies. A formula (GMI [%] = 3.31 + 0.02392 × [mean glucose in mg/dL]) to calculate GMI was developed and validated by Beck and colleagues using modern CGM technology. After that, a multidisciplinary team of diabetologists, patients, and laboratory experts recommended the use of GMI in CGM reports, instead of eA1c. An online calculator is provided by the Jaeb Center at http://www.agpreport.org/agp/links. GMI may be useful for patients with advanced CKD, including those treated with dialysis, for whom reliability of HbA1c is low. It should be noted that the assay bias of HbA1c relative to GMI could potentially change over time within patients, particularly when there are changes in clinical characteristics that affect red blood cell turnover or protein glycation.

Essential points of his talks are summarized below -

- Glucose and insulin metabolism are profoundly altered by advanced chronic kidney disease
- Risk of hypoglycemia is increased by several factors, including failure of kidney gluconeogenesis, impaired insulin clearance by the kidney, defective insulin degradation due to uremia, increased erythrocyte glucose uptake during hemodialysis, impaired counterregulatory hormone responses, nutritional deprivation, and variability of exposure to antihyperglycemic agents and exogenous insulin effect
- Patients with end-stage kidney disease frequently experience wide glycemic exposures, with common occurrences of both hypoglycemia and hyperglycemia
- Assessment of glycemia by hemoglobin A1c is hampered by a variety of chronic kidney disease–associated conditions that can bias the measure either to the low or high range

- Except for documented interferences from icodextrin metabolites and nonglucose sugars in peritoneal dialysis solutions with the use of glucose dehydrogenase-based–pyrroloquinoline-quinone/glucose oxidase–based glucose meters, the evidence is very limited in the end-stage kidney disease population
- Emerging data on the use continuous glucose monitoring in this population suggest the potential for more precise monitoring and treatment adjustments in patients with diabetes and advanced chronic kidney disease

SESSION-3: DISCOVER A GLP-1 RA FOR YOUR ADULT PATIENTS WITH T2D AND ASCVD SPONSORED BY NOVO NORDISK

GLUCAGON-LIKE PEPTIDE 1-RECEPTOR AGONISTS AND A1C: GOOD FOR THE HEART BUT LESS SO FOR THE EYES?

Friday, 13th May 2022

This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Drs. Stewart Albert, MD Emily Wood, DO from Saint Louis University School of Medicine.

Glucagon-like peptide 1- receptor agonists (GLP1-RA) are preferred treatments for people with DM type 2 and risk for cardiovascular disease. The FDA has recommended caution in the use of semaglutide and dulaglutide because of the risk of exacerbating diabetic retinopathy (DR). Others have suggested that the worsening of DR, is independent of the class of drug, but related to the rate of fall of A1C. We have performed meta-analyses of the major trials of GLP1-RA regarding alterations in major adverse cardiovascular events (MACE) and DR and the association of these differences with changes in A1C.

Meta-analyses and meta-regressions were performed on the 7 major RCTs (n=56004 patients) of GLP1-RA which have been the basis for determining the effectiveness of GLP1-RA regarding prevention of MACE.

Six of the studies evaluated DR, and 4 defined changes as new onset photocoagulation, intravitreal injection, or hemorrhages. There was a significant increase in DR only for parenteral semaglutide (relative rate (rr)=1.73, 95% CI; 1.10:2.71, p= 0.02, rate difference (rd)= 0.013; 0.002:0.023, p=0.02). For all GLP1-RA there was no increase in DR (rr=1.05; 0.94:1.17, p=0.36). There were significant benefits for GLP1-RA in decreasing MACE (rr=0.89; 0.85:0.94, p< 0.001, rd= -0.013; -0.018: -0.007, p < 0.001). Meta-regression analysis showed that the rate of improvement of MACE directly correlated with decrease in A1c (log rr=0.364 *(change in A1c), p=0.014). There was a trend for worsening of DR with decrease in A1c (log rr= (-0.67 *(change in A1c), p=0.076). Taking all studies of the class of GLP1-RA, for DR rd =0.001 (number needed to harm [NNH], 1000) compared with that for MACE rd= -0.013 (number needed to treat [NNT], 77) whereas the comparable computation for semaglutide as a single agent are NNH=77 and NNT= 43.

GLP1-RA are associated with improvements in A1c, which correlates with improvement in the rates of MACE. There is a trend showing decreases in A1c may be associated with worsening of DR. In individuals with diabetes who are high risk for cardiovascular disease, GLP1-RA should be recommended with close monitoring by ophthalmology for worsening DR. Further prospective studies of GLP1-RA on DR need to evaluate whether changes are unique to semaglutide, and whether a grading system for DR will assist in assigning patients safely to GLP1-RA therapy.

SESSION-4: DIABETES DIETS: A ROUNDTABLE DISCUSSION

SCOPING REVIEW OF TWO DECADES OF PUBLICATIONS FOR OUTCOMES OF GLUTEN FREE DIET ON DOUBLE DISEASE OF TYPE 1 DIABETES AND COELIAC DISEASE

Friday, 13th May 2022

This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Dr. Meena Chhabra from the Dr. Meena Chhabra's Diabetic Care Centre Delhi.

The aim of this study was to examine the outcomes and metabolic effects of Gluten Free Diet (GFD) in T1DM with Coeliac Disease (CD).

A comprehensive literature search was done to extract publications from Medline-PubMed and Cochrane library, since inception till October 27, 2021, then screened and reviewed by two independent reviewers. Data including, study title, year of publication, name of the journal, study design, and the evaluated outcomes were charted for evidence synthesis. Scoping review was performed according to PRISMA-SR checklist.

We analysed 18 publications, including two case reports. 57.7% (n=208) patients across 10 studies were from seven countries in Europe. Three publications each were from Australia and Europe, one each from India and Tunisia. The mean number of patients and duration of evaluation across 16 studies were 22 (± 9.6, 95% CI 17 to 27), 14 months (± 8, 95% CI 9.7 to 18), respectively. In the first study (in 1999) GFD had no effect on the metabolic control of T1DM. Recent studies (2021) demonstrate the improvement in HRQoL and self-perceived wellness. Renoprotection is demonstrated by three studies, improvement in height-weight across five studies and two studies showed remission. Other benefits include improvement in glycemic status, GI symptoms, slower c-peptide decline, and prevention of osteopenic status.

Globally, during the last two decades, the research for the effects of GFD in T1DM with CD has expanded, with Europe having the highest contribution to evidence-based medicine. The majority of evidence (16/18 publications) favor GFD for metabolic benefits in T1DM with CD, with improvement in anthropometric parameters.

SESSION-5: DISEASE STATE NETWORK YEAR-IN-REVIEW: LIPIDS AND CV HEALTH

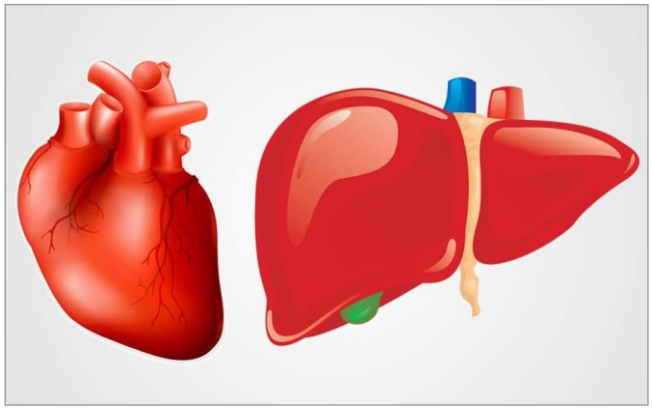
LIVER FAT AND CARDIOVASCULAR EVENTS: BYSTANDER OR CAUSATIVE RELATIONSHIP?

Friday, 13th May 2022

This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Drs. Minhda Le, MD, Jarret Berry from the UT Southwestern Dallas, Texas, United States.

Non-alcoholic fatty liver disease (NAFLD) and cardiovascular disease (CVD) share common metabolic risk factors, and there is a high prevalence of CVD in patients with NAFLD. We aimed to determine if liver fat is an independent risk factor for CVD events.

Methods: We analyzed data from participants in the Dallas Heart Study (a multi-ethnic sample of the Dallas County adult population)



without baseline CVD who underwent liver fat quantification by proton magnetic resonance spectroscopy (N=1932). The primary outcome was the composite of any incident CVD event (CV death, non-fatal myocardial infarction, non-fatal stroke, coronary or peripheral artery revascularization, hospitalization for heart failure, and hospitalization for atrial fibrillation). Secondary outcomes were all atherosclerotic events, all non-atherosclerotic events, and all-cause mortality. Data was analyzed by (1) groups defined by tertile of baseline liver fat content (median for each tertile: 1.6, 3.6, 9.2%), and (2) grouped by BMI (< or ≥30 kg/m2) and liver fat (< or ≥5.5%). Unadjusted and multivariable adjusted (for age, gender, race, BMI, diabetes, HTN, smoking, family history of CVD, statin use, physical activity, alcohol use) Cox regression for liver fat tertiles or BMI/liver fat groups were performed for all outcomes, and further validated by comparisons of restricted mean survival times (RMST), which were restricted to 13.5 years for the primary outcome (the length of the study period).

Mean age was 43 years, 62% were women, and 48% were African-American. A total of 168 participants (8.7%) experienced a primary outcome event. For the primary outcome, the RMSTs were similar at 13.1, 13.0, and 13.1 years for the lowest to highest tertile (p=0.512). In the multivariable analysis, liver fat tertiles were not associated with cardiovascular events for either the middle tertile (HR= 1.06; 95% CI 0.7-1.61) nor for the highest tertile (HR=0.78; 95% CI 0.5-1.22) compared with lowest tertile. Compared with non-obese participants with normal liver fat, obese participants with elevated liver fat had a HR 0.77 (95% CI 0.42-1.43), obese participants with normal liver fat had a HR 0.78 (95% CI 0.42-1.43), and non-obese participants with increased liver fat had a HR 0.69 (95% CI 0.39-1.23) for the primary outcome. None of the secondary outcomes were associated with liver fat content, and no differences were found in the RMSTs for any of the secondary outcomes between groups defined by tertiles of liver fat or BMI/liver fat.

NAFLD was not independently associated with cardiovascular events in the multi-ethnic DHS population. Our findings should be validated in other cohorts, especially in those with documented advanced NAFLD (NASH or cirrhosis).

THE IMPACT OF DIABETES KETOACIDOSIS ON HEART FAILURE: AN ANALYSIS OF NATIONAL INPATIENT SAMPLE STUDY 2016-2018

Friday, 13th May 2022

This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Dr Pyi Phyo Aung, MBBS PGY-2 Internal Medicine Resident Memorial Healthcare System Pembroke Pines, Florida, United States.

Heart failure (HF) is one of the common complications of diabetes mellitus. Patients with history of diabetes are associated with higher risk of mortality and hospitalization in patients with cardiovascular diseases. It is hypothesized that presence of DKA can be associated with poor outcomes in HF population. We conducted this study to evaluate the impact of DKA on HF.

We conducted a retrospective analysis of 3 years of the National Inpatient Sample (NIS) database, 2016 to 2018, and 2 years of Nationwide Readmission Database (NRD), 2018 to 2019. Study population were selected using ICD-10 diagnosis codes. Discharge-level weight analysis was used to produce a national estimate. We conducted multivariate regression analysis to calculate odds ratio with STATA 17.

106,709,435 of HF patients and 314,840 of DKA patients were discharged during the study period. DKA was more prevalent in HF patients when it was compared to non-HF patients (0.32% v 0.29%). According to the further study within HF group, patients with DKA were younger (mean age 64.52 vs 71.53), higher risk of in-hospital mortality (6.52% v 4.74%), major cardiovascular events (14.77% v 9.53%), acute kidney injury (60.29% v 31.06%), deep vein thrombosis (2.52% v 2.25%) and longer length of stay (7.51 SD 0.088 vs 6.18 SD 0.004) than non-DKA patients. However, atrial fibrillation was less prevalent with DKA (16.14% v 27.87%). After adjusting for age, sex, race, chronic kidney disease (CKD) and comorbid burden, DKA is associated with higher in-hospital mortality (OR 1.61, 1.48 – 1.74, $p < 0.0001$) and higher incidence of MACE (OR 1.56, 1.48-1.65, $p < 0.0001$) in HF population. DKA was associated with premature readmission in HF patients. Within HF patients, 16.69% (n=10,217) of DKA patients readmitted within 30 days compared to 14.72% (n=1,600,298) of patients without DKA. After adjusting for age, sex and CKD, DKA was associated with higher 30-days readmission in HF (OR 1.12, 1.08 – 1.15, $p < 0.0001$).

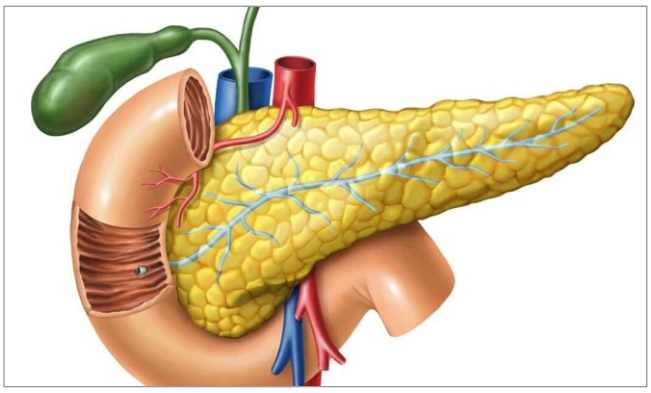
Our study concludes that the presence of DKA is associated with poor outcomes and increases the risk of complications. The higher rate of readmission in HF population emphasizes the importance of proper post-hospitalization management. Further studies are needed to untangle the risk factors and develop a standard management of DKA in HF population.

HYPERTRIGLYCERIDEMIC PANCREATITIS IN A RARE CASE OF TYPE A PYRUVATE CARBOXYLASE DEFICIENCY

Friday, 13th May 2022

This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Dr. Brian Wojeck, MD from the Yale University Plymouth, Connecticut, United States.

Pyruvate carboxylase (PC) deficiency is a spectrum of rare autosomal recessive disorders that can have significant metabolic consequences. Decreases of PC activity limits utilization of lactate and alanine for anaplerotic and synthetic fluxes. PC deficiency can lead to hypoglycemia, lactic acidosis, and hyperammonemia. Patients can develop central nervous system disease (via glial damage and demyelination leading to hydrocephalus), hepatotoxicity and insulinopenia. The latter can result in hypertriglyceridemia, though not a hallmark of PC deficiency. Metabolic supplements help overcome defects by providing key moieties for PC function (e.g., biotin), promoting ammonia clearance (via carglumic acid), or providing substrates that are utilized independently of PC (e.g., aspartate, citrate, glutamine, and arginine). We present a case of mosaic type A PC deficiency to bring awareness to this disorder.



The patient was evaluated at age 21 with many complications related to PC deficiency, including recurrent VP shunt infections, leading to emergent abdominal surgery for peritonitis, shunt erosion of his sigmoid colon leading to sigmoidectomy and G/J tube placement. He was born at 38-weeks gestation with hydrocephalus, excessive sleepiness and hypotonia. He developed seizures and underwent placement of a VP shunt at age 2 to treat hydrocephalus, reducing his seizure frequency. By age 8 he had developmental delay, hepatotoxicity, bouts of lactic acidosis, and hypoglycemia. Genetics evaluated him and suspected PC deficiency. A skin fibroblast biopsy revealed 10% of expected PC function leading to a diagnosis of mosaic type A PC deficiency. He began treatment with carglumic acid, citrate, aspartic acid, biotin, arginine, and glutamine. At this admission, he presented with abdominal pain due to pancreatitis with hypertriglyceridemia of 2,529 mg/dL and chronic hyperammonemia. Due to abnormal bowel anatomy and significant illness, TPN was started. He was treated with hyperinsulinemic-euglycemic clamp which reduced triglycerides to 1,345 mg/dL. Endocrinology was consulted late in his course and recommended reduction of TPN, D5W and insulin via euglycemic clamp. His triglycerides decreased to 701 mg/dL and he was discharged. 2 weeks later he presented to the hospital with abdominal pain, and vomiting. Rifaximin was started for known pancreatitis. He developed sepsis, and worsening acidosis which led to PEA arrest. Pressors were initiated, enteral access was lost, and he was intubated. He was made comfort measures only and passed away.

PC deficiency is a rare disorder that can have devastating metabolic consequences. Diagnosis includes identifying clinical features, analysis of pyruvate, lactate, amino acids, and genetic testing via skin fibroblast or DNA testing. Treatments include improving activity of the urea and TCA cycles while bypassing abnormalities caused by PC deficiency. Liver transplantation may treat metabolic abnormalities with no effect on neurologic disease. In the future gene therapy may be an option. Life expectancy varies with disease severity, though few type A patients survive into adulthood.

ASSOCIATION OF TRIGLYCERIDE AND GLUCOSE (TYG) INDEX WITH CAROTID INTIMAL MEDICAL THICKNESS (IMT) IN APPARENTLY HEALTH SUBJECTS: THE CHENNAI URBAN RURAL EPIDEMIOLOGY STUDY (CURES)

Friday, 13th May 2022

This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Dr Brijendra K. Srivastava, MBBS, FRCP (Edin & Glasg), FACE from the Madras Diabetes Research Foundation, Chennai.

Insulin resistance has been associated with metabolic syndrome, diabetes and cardiovascular disorders. The triglyceride and glucose (TyG) index can be obtained easily by measuring blood glucose and serum triglyceride levels. It has also shown to be a useful surrogate to identify insulin resistance in healthy subjects. Carotid intimal medial thickness (IMT) is a marker, which is strongly associated with cardiovascular disease. This paper deals with the relationship between TyG index and carotid IMT in apparently healthy subjects.

1719 apparently healthy nondiabetic subjects and 365 diabetic subjects were recruited from the Chennai Urban Rural Epidemiology Study, an ongoing epidemiological study in South India. The TyG index was calculated as the natural logarithm (Ln) of the product of plasma glucose and TG using the formula: Ln (TG [mg/dL] × glucose [mg/dL]/2). Carotid IMT was measured as per standard protocol. Statistical analysis was done using SPSS software version 20.0.

The mean TyG index was 4.5 in nondiabetic subjects. Statistically significant association was observed with age, waist and hip measurement, lipid parameters, HbA1c and carotid IMT ($P < 0.001$) in insulin resistant group. The homeostasis model assessment of insulin resistance (HOMA IR) index was well correlated with TyG index and was significantly higher in high TyG index group as compared to normal TyG index group (2.2 ± 1.3 vs 1.7 ± 1.2, $p < 0.001$). The mean carotid IMT was strongly associated with the tertiles of TyG index; 0.65 mm in first tertile, 0.69 mm in the second tertile and 0.72 mm in the third tertile, with a p value for trend of < 0.001. Mean TyG index and mean carotid IMT value was significantly higher in diabetic subjects compared to non-diabetic study subjects (5.0 vs 4.5- and 0.81-mm vs 0.69 mm with p value of < 0.001 for both).

This study shows that TyG index, a simple analytical tool of insulin resistance measurement can help to find out early atherosclerotic changes, even in a healthy individual, so that preventive strategies can be planned for a better cardiovascular outcome.

PREVALENCE, PATHOPHYSIOLOGY, AND MANAGEMENT OF LEAN NONALCOHOLIC FATTY LIVER DISEASE

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This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Drs. Hassan Heshmati, MD from Endocrinology Metabolism Consulting LLC.

Nonalcoholic fatty liver disease (NAFLD) is a pandemic with a prevalence of approximately 25% among adult population worldwide. The highest prevalence is observed in the Middle East (32%) and the lowest prevalence in Africa (13%). NAFLD is a spectrum of liver disorders ranging from simple steatosis to nonalcoholic steatohepatitis (NASH). NASH is the aggressive form of NAFLD that can progress to cirrhosis and hepatocellular cancer. Although NAFLD is commonly associated with overweight and obesity, some NAFLD subjects are lean. The purpose of this review is to present an update on the prevalence, pathophysiology, and management of lean NAFLD subjects.

A systematic search of literature was conducted using the search terms nonalcoholic fatty liver disease, lean, overweight, obesity, prevalence, pathophysiology, and management.

A meta-analysis of 84 studies including 10,530,308 subjects showed that in the general population, 5.1% of the subjects have lean NAFLD and within the NAFLD population, 19.2% of the subjects are lean. The prevalence of lean NAFLD is higher in the middle-aged individuals of Asian countries. The underlying pathophysiology of lean NAFLD is not fully understood. Genetic and environmental factors may predispose to lean NAFLD. Several studies have reported that lean NAFLD subjects have a greater proportion of the variant PNPLA3 allele. Lean NAFLD subjects have the same comorbidities in comparison to non-lean NAFLD subjects (e.g., hypertension, type 2 diabetes, and dyslipidemia) and remain at risk for development of severe complications and high mortality. There are no specific treatments for lean NAFLD. While the first-line therapy of non-lean NAFLD is based on lifestyle intervention (diet and exercise) with a targeted weight loss of at least 7%, the relevance of diet and exercise in lean NAFLD is questionable. However, some lean NAFLD subjects may have visceral obesity not detected by body mass index (BMI) and can benefit from lifestyle intervention and weight loss. Also, exercise, independently of weight loss, may have a favorable impact.

Lean NAFLD is a distinct entity with several metabolic abnormalities. It represents a signifi-

cant portion of subjects with NAFLD even after using an ethnicity-specific BMI criterion (cut-offs of 25 in Caucasian and 23 in Asian subjects, respectively). The pathogenesis of lean NAFLD may be very different than non-lean NAFLD. In the absence of overweight or obesity (as defined by BMI), lean NAFLD may remain underrecognized. The treatment of lean NAFLD is a medical challenge. Lifestyle intervention and weight loss can be beneficial in some subjects.

SESSION-6: DISEASE STATE NETWORK YEAR-IN-REVIEW: DIABETES

HYPERTENSION (HTN) AND DIABETES (DM) IMPROVEMENT DURING OSILODROSTAT THERAPY IN PATIENTS WITH CUSHING'S DISEASE (CD): ANALYSES FROM THE PHASE III LINC 3 STUDY

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This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Dr Alberto M. Pedroncelli, MD, PhD Head of Clinical Development and Medical Affairs – Endocrinology Recordati AG Basel, Switzerland.

CD is a deleterious hypercortisolism disorder. Alleviating the burden of CD-associated comorbidities, including HTN and DM, is a key treatment goal. Osilodrostat, a potent oral 11 -hydroxylase inhibitor, normalized urinary free cortisol (UFC) and improved clinical signs and symptoms in CD patients (pts) in the Phase III LINC 3 study (NCT02180217). We describe blood pressure (BP) and glucose homeostasis changes in pts with baseline (BL) HTN and DM.

Adults with CD and mean UFC >1.5 times the upper limit of normal received osilodrostat during the 48-week (W) core study, including an 8W randomized-withdrawal phase (W26–34) for eligible pts (Pivonello et al. Lancet Diabetes Endocrinol 2020). BL HTN defined as prior diagnosis, taking antihypertensive medication, and/or systolic/diastolic blood pressure (SBP/DBP) >130/ >90 mmHg. BL DM defined as prior diagnosis, taking antidiabetic medication, HbA1c ≥6.5%, and/or fasting plasma glucose (FPG) ≥126 mg/dL. Exploratory data presented for all pts with data at BL and given visit, unless otherwise stated.

At BL, 87% (119/137) of pts were classed as hypertensive; mean SBP and DBP decreased in these pts during osilodrostat therapy. Of pts with BL SBP >130 mmHg (n=79), 58%, 51% and 49% had SBP ≤130 mmHg at W12, W24 and W48. Of pts with BL DBP >90 mmHg (n=50), 72%, 62% and 66% had DBP ≤90 mmHg at W12, W24 and W48. SBP/DBP remained stable in pts without BL HTN. Higher BL SBP and DBP correlated with greater reductions in these parameters at W24 (SBP, r=−0.57; DBP, r=−0.57 [both P < 0.0001]) and W48 (SBP, r=−0.58; DBP, r=−0.57 [both P < 0.0001]). 40% (34/85) of pts taking antihypertensive medication at BL stopped or reduced the dose by W48; 40% (34/85) increased dose or number of medications. Mean 11-deoxycorticosterone (DOC) increased during the study. Mean potassium levels remained largely unchanged and did not

correlate with DOC increases. 45% (61/137) of pts were classed as diabetic at BL. Of pts with BL FPG ≥100 mg/dL (n=36), 58%, 64% and 44% had FPG < 100 mg/dL by W12, W24 and W48. 49% (21/43) of pts taking antidiabetic medication at BL stopped or reduced the dose by W48; 23% (10/43) increased dose or number of medications. BP or glycemic status change did not correlate with mUFC change from BL.

Many CD pts with comorbid HTN or DM had improvements in these parameters during osilodrostat therapy. Close follow-up is needed as concomitant medication adjustments are required in some pts, including those with improvements in HTN or DM. Osilodrostat is effective at improving clinical signs and may alleviate hypercortisolism-associated treatment burden, which could benefit some CD pts.

DIABETIC MYONECROSIS: AN UNDERREPORTED AND FREQUENTLY MISDIAGNOSED COMPLICATION OF DIABETES MELLITUS

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This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Dr. SM Swayamsidha Mangaraj, MD, DM IMS and SUM Medical College and Hospital, Bhubaneswar.

Diabetic muscle infarction (DMI), also referred as diabetic myonecrosis, is a rare and underdiagnosed complication of longstanding and poorly controlled diabetes mellitus. The usual presentation is sudden onset of pain at the involved muscles associated with swelling and tenderness. The diagnosis may be easily missed if clinical vigil is not high.

A 40-year-old male patient, known case of type 2 diabetes mellitus (T2DM) for 8 years presented with swelling and tenderness of the right thigh for past two weeks. Prior medical history was significant for hypertension and chronic kidney disease. The pain was sharp aching in nature and worsened with weight bearing or movement of affected limb. There was no prior history of trauma or fall. On examination, the right thigh was grossly swollen and tender to palpation. Complete blood count revealed presence of anemia (Hemoglobin 8.9 gm%) and neutrophilic leukocytosis (total leucocyte count 18,000/cu.mm). His current fasting plasma glucose(224mg/dl), post prandial plasma glucose(356mg/dl) and glycosylated hemoglobin (HbA1c) levels (11.9%, normal < 6.5%) were significantly elevated. Renal function tests were as follows: serum creatinine (2.4mgdl, normal: 0.8-1.5), serum urea (71 mg/dl, normal:20-40), serum sodium (135 meq/l) and serum potassium (5.1 meq/l). Inflammatory markers like serum C-reactive protein (CRP) (28.9 mg/dL, normal:1-5) and erythrocyte sedimentation rate (80 mm/hr, normal:0-20 mm/hr) were significantly elevated. Serum creatinine phosphokinase (CPK) level (215IU/L, normal: 46-171) was raised. Blood culture revealed no growth. Chronic diabetic complications assessment revealed presence of moderate non-proliferative diabetic retinopathy, distal symmetrical polyneuropathy and chronic kidney disease. Doppler ultrasonography of bilateral lower limbs revealed presence of diffuse subcutaneous oedema of affected right thigh without evidence of deep vein thrombosis or significant occlusive atherosclerotic disease. Magnetic resonance imaging (MRI) of the right leg revealed presence of diffuse subcutaneous edema, intramuscular fascial edema and increased T2 signal intensity in affected muscle groups. A diagnosis of DMI affecting the right thigh was made. The patient was managed with insulin therapy for glycemic control, limb rest, judicious analgesic use and physical therapy resulting in improvement of his overall clinical status.

Diabetic muscle infarction is a rare and serious complication seen in long-standing poorly controlled diabetes whose exact

aetiopathogenesis remains poorly understood. It usually presents with the abrupt onset of pain, tenderness, and swelling of affected limb. The most common affected regions include thigh and calf muscles though other muscle groups may also be affected. The important differentials include muscle abscess, hematoma, deep vein thrombosis and myositis. MRI plays an invaluable role in arriving at correct diagnosis and muscle biopsy (though diagnostic) is very rarely needed. Knowledge of this relatively rare entity will be helpful for early identification and appropriate management.

PREVALENCE OF HYPOGONADISM AND ITS RELATION WITH GLYCEMIC CONTROL IN YOUNG ADULTS WITH CHRONIC TYPE 2 DIABETES MELLITUS

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This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Drs Banshi Saboo, Bharat Saboo from Diacare Diabetes Centre.

There is an increased prevalence of hypogonadism in type 2 diabetes mellitus our study was aimed at to study the prevalence of hypogonadism in young adults with chronic type 2 diabetes mellitus.

Sectional study 260 patients from 3 different cities of India were included between age group 30-39 with history of type 2 diabetes mellitus. Patients were divided into 2 groups, group A (130 patients) with history of type 2 diabetes mellitus more than 6 years and group B (130 patients) with history of type 2 diabetes less than 6 years.

Levels of hypogonadism and erectile dysfunction was compared between 2 groups on the basis parameters of Total Testosterone values and ADAMS questionnaire, glycemic parameters were measured on the basis of HbA1c. One-way ANOVA followed by post hoc Tukey's test and Pearson's coefficient of correlation tests were used for analysis. Hypogonadism was measured with levels of total testosterone less than 250.

Mean HbA1c levels of group A was 8.12% and group B was 8.09%. 9 patients opted out of the study due to non-consent, 5patients from group A and 4 patients from group B. Hypogonadism TT < 250 was observed in 25.6% of males (32/125) in group A as compared to 10% of males (13/126) in group B. Prevalence of erectile dysfunction was observed in 54.4% of males (68/125) in group A as compared to 31.74 % in males (40/126) in group B. Higher degree of low testosterone was observed in group A with chronic history of type 2 diabetes as compared to group B, prevalence of erectile dysfunction in group A was non significantly higher as compared to group B. An overall positive correlation was found between levels of hypogonadism and chronic history of type 2 diabetes.

We observed hypogonadism as indicated in significant proportion of males with chronic history of type 2 diabetes mellitus.

SAFETY OF SGLT2-INHIBITORS IN PATIENTS WITH MULTIPLE MYELOMA AND DIABETES

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This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Dr. Tracey Rosa, MD Icahn School of Medicine at Mount Sinai Hospital, New York.

An estimated 10-20% of patients with multiple myeloma (MM) have type 2 diabetes (T2DM). About half of patients with MM will experience renal insufficiency, the risk of which increases

in the setting of T2DM. While sodium-glucose cotransporter 2 inhibitors (SGLT2i) are beneficial in patients with chronic kidney disease (CKD) due to diabetic or hypertensive nephropathy, the role of SGLT2i in MM-related CKD is unknown. MM therapies target the immune system and may increase the risk of infections associated with SGLT2i. The current work is the first to examine the potential benefit and safety of SGLT2i in patients with MM and T2DM.

A retrospective cohort study was performed on patients aged 18 years or older with MM who received SGLT2i therapy between March 2013 and December 2020 at a quaternary academic medical center. Electronic medical records were reviewed for the following data: demographics, comorbidities, MM parameters, medication and medical history, SGLT2i usage and duration, and hemoglobin A1c (HbA1c) and serum creatinine pre- and post-SGLT2i initiation. Data are presented as mean ± standard deviation, or counts and percentages. This study was approved by the Institutional Review Board.

In total, 50 patients were identified. Patients who were diagnosed with MM after initiation of SGLT2i (n= 12), did not have any MM data available (n=1), or for whom SGLT2i usage could not be verified (n= 4) were excluded. Thirty-three patients were included in the final analysis. The mean age was 63 (±7.8) years, 63.6% were male, and 87.9% had active MM or MM in remission. Most had received stem-cell transplantation (55.0%) and multiple lines of chemotherapy (63.6%) prior to SGLT2i initiation. The average HbA1c was 7.4% (±1.2%) and 20% of patients had CKD prior to SGLT2i initiation. The overall SGLT2i discontinuation rate was 42.4%, and the mean duration of therapy was 2.2 (±1.5) years. Notably, 21.4% of discontinuation events were due to an increase in creatinine; however, there were no statistically significant changes in serum creatinine, total body weight, HbA1c, or 24-hour urine protein at 15 months follow-up. Other reasons for SLGT2i discontinuation included loss to follow-up, change of health insurance coverage for SGLT2i, and unrelated hospital admission. Genitourinary infection was not cited as a reason for SGLT2i discontinuation.

SGLT2i therapy may be safe in patients with MM and T2DM, but no benefit was found with respect to serum creatinine, HbA1c, or 24-hour urine protein. Prospective research is required to further evaluate the potential benefit and safety of SGLT2i therapy in this population.

SESSION-7: CARDIOVASCULAR DISEASE AND DIABETES: ASSESSING RISKS AND PRIORITIZING THERAPIES

EXENATIDE IMPROVES CARDIOVASCULAR RISK FACTORS IN ABSENCE OF CLINICALLY SIGNIFICANT WEIGHT LOSS IN OVERWEIGHT AND OBESE WOMEN WITHOUT DIABETES

Friday, 13th May 2022

This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Drs. Antea DeMarsilis, MD Alexandra Migdal, MD Jody Dushay, MD, MMSc from the Beth Israel Deaconess Medical Center.

Glucagon-like peptide-1 (GLP-1) receptor agonists, initially used as powerful agents for glycemic control and cardiovascular benefit in individuals with diabetes, have emerged as weight loss therapies for those with obesity and without diabetes. Benefits beyond weight loss for this new population are not fully known. Prior studies suggest that the GLP-1 receptor agonist exenatide improves cardiovascular risk

factors, including blood pressure and lipid profile, in overweight and obese women without diabetes who achieve clinically significant weight loss. In this study, we investigate whether these benefits are seen even in the absence of clinically significant weight loss.

As part of a larger study of overweight and obese women without diabetes, 69 women (age 43.0±11.9 years, BMI 36.4±5.4 kg/m2) were treated with exenatide 10 mcg twice daily. Participants were classified by weight loss response by 12 weeks: those without clinically significant weight loss (<5% body weight) were low responders (LR, n=38, average weight change -2.3%; range +2.6% to -4.9%); high responders lost ≥ 5% body weight (HR, n=31, -7.1%; -5.1% to -15.1%). We measured high-sensitivity C-reactive protein (hs-CRP), systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL), and triglycerides (TG) at randomization and 12 weeks of treatment. Our primary outcome was change in hs-CRP. Secondary outcomes were change in SBP, DBP, and lipid parameters. Data were analyzed with Student's T-test; p-values < 0.05 were considered significant.

At 12 weeks, hs-CRP levels did not change in either weight loss HR (4.6±4.1 to 4.2±3.8 mg/L; p=0.51) or LR (4.2±3.5 to 4.9±4.2 mg/L; p=0.06). In HR, exenatide significantly reduced SBP (-6.3 mmHg; p< 0.02), TC (-20.3 mg/dL; p< 0.0001), LDL (-9.9 mg/dL; p< .02), and TG (-19.3 mg/dL; p< 0.05). In LR, exenatide also significantly reduced SBP (-4.7 mmHg; p< 0.05), TC (-11.3 mg/dL; p< 0.001), and LDL (-4.9 mg/dL; p< 0.02), but not TG (+0.04 mg/dL; p=0.83).

After 12 weeks of treatment with exenatide, the subset of overweight and obese women without diabetes who demonstrated early clinically significant weight loss achieved significant reductions in blood pressure and improved lipid profile. Notably, the subset of participants who did not achieve at least 5% weight loss also had significantly reduced SBP, TC, and LDL levels. This suggests that some cardioprotective benefits of GLP-1 receptor agonists emerge regardless of weight loss; these agents could be more widely considered for cardiovascular benefit among those without diabetes.

HYPOGLYCEMIA ASSOCIATED WITH WORSE OUTCOME IN TAKOTSUBO CARDIOMYOPATHY: PERSPECTIVE FROM THE NATIONAL INPATIENT SAMPLE AND NATIONAL READMISSION DATABASE

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This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Drs Navya Konindala, MD, KP Kyeeun Park, MD Memorial Healthcare System Weston, Florida, United States.

Stress induced cardiomyopathy, Takotsubo cardiomyopathy (TC) is characterized by transient left ventricular (LV) wall motion abnormality beyond the territories perfused by a single coronary artery. LV dysfunction is reversible, but the complications and mortality of TC is severe enough to compete with acute coronary artery syndrome. Especially, the role of blood glucose level in prognosis of TC has

been controversial. Here, we sought to national in-hospital outcome and readmission rate of TC associated with glycemic control.

We conducted a retrospective analysis of 3 years of the National Inpatient Sample (NIS) database, 2016 to 2018, and 2 years of Nationwide Readmission Database (NRD), 2018 to 2019. Study populations were selected using ICD-10 diagnosis code. Discharge-level weight analysis was used to produce a national estimate. We conducted multivariate regression analysis to calculate odds ratio with STATA 17.

During the study period, 116,735 of TC patients were discharged and 23.01% (n = 26,865) of them had diabetes mellitus (DM). Within TC population, 900 of patients (0.07%) experienced the hypoglycemia and only 2.22 % of them had DM. Hypoglycemia patients tended to be more male (20.00 % v 16.31 %), younger (mean age 59.25 ± 1.28 v 67.14 ± 0.09), less diabetic (2.22% v 23.18%) and have more CKD (1.67% v 1.38%). Hypoglycemia patients had more complications and worse outcomes associated with TC; higher in cardiogenic shock (12.22% v 6.13%), in-hospital mortality (13.89% v 5.83%) and longer length of stay (10.91± 0.73 v 6.78 ± 0.06). After adjusting for age, sex, race, DM and comorbid burden, hypoglycemia is associated with higher in-hospital mortality with TC (OR 2.60, 1.69 – 4.02, p < 0.0001). According to readmission database, hypoglycemia is not related with 30-days premature readmission (p = 0.996), but DM is associated with premature readmission after adjusting for age, sex and comorbidities (OR 1.18, 1.10 – 1.26, p < 0.0001).

As catecholamine plays a pivotal role in pathophysiology of TC, the sympathoadrenal system activation and a catecholamine release in response to hypoglycemia could reproduce a similar pathogenesis. Hypoglycemia is associated with worse outcome of TC, higher rate of complications, but not readmission rate. Perhaps improved risk stratification and optimal glycemic control may improve the outcome of TC.

EFFECT OF EXENATIDE VERSUS HYPOCALORIC DIET ON HIGH-SENSITIVITY C-REACTIVE PROTEIN AND OTHER CARDIOVASCULAR RISK FACTORS IN OVERWEIGHT AND OBESE WOMEN WITHOUT DIABETES

Friday, 13th May 2022

This paper was presented on Friday May 13th at the 30th Annual meeting of the American Association of Clinical Endocrinologists (AACE) at San Diego, by Dr. Antea DeMarsilis, MD Beth Israel Deaconess Medical Center.

Obesity is associated with poor cardiovascular outcomes independent of comorbid diabetes; inflammation is a proposed link. In overweight and obese individuals with diabetes, glucagon-like peptide 1 (GLP-1) receptor agonists improve markers of inflammation and cardiovascular risk. Whether this effect persists in individuals without diabetes is not known. We evaluated the effect of exenatide, a GLP-1 receptor agonist, on inflammation and cardiovascular risk factors compared to hypocaloric diet and placebo injections in overweight and obese women without diabetes who demonstrated early clinically significant weight loss.

108 women were randomized to treatment with either exenatide (E, 10 mcg twice daily) or hypocaloric diet plus placebo injections (D/PBO). High responders (age 44.1±12.2 years, BMI 36.2±5.7 kg/m2) lost ≥ 5% body weight by 12 weeks. In a subset of high responders (E: n=31, D/PBO: n=17), high-sensitivity C-reactive protein (hs-CRP), systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL), and triglycerides (TG) were measured at baseline and after 12 weeks of treatment. Our primary outcome was change in hs-CRP.

Secondary outcomes were change in SBP, DBP, and lipid parameters. Data were analyzed with Student's T-test; p-values < 0.05 were considered significant.

There was no significant change in hs-CRP by 12 weeks in either E (4.6±4.1 to 4.2±3.8 mg/L, p=0.51) or D/PBO (4.7±3.9 to 4.4±5.0 mg/L, p=0.67) high responders. However, at 12 weeks, E showed significantly reduced SBP (-6.3 mmHg; p< 0.02), TC (-20.3 mg/dL; p< 0.0001), LDL (-9.9 mg/dL; p< .02), and TG (-19.3 mg/dL; p< 0.05). D/PBO had significantly reduced SBP (-10.0 mmHg; p< 0.02), DBP (-6.1 mmHg; p< 0.01), TC (-18.9 mg/dL; p< 0.03) and TG (-26.9 mg/dL; p< 0.006) but did not significantly change LDL (-6.8 mg/dL; p=0.59).

Many studies report that weight loss is associated with decreased hs-CRP, though time course and degree of weight loss varies. Our study population of overweight and obese women without diabetes had well-controlled blood pressure and lipid profiles at baseline, yet still benefited from weight loss ≥ 5%, with significant improvement in cardiovascular risk factors including SBP, TC, TG, and LDL. In contrast, this clinically significant weight loss did not lower serum hs-CRP. To detect an anti-inflammatory benefit of GLP-1 agonists in this population, future studies might require increased time to measurement of hs-CRP or higher degree of weight loss.

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