the ultimate treatment for Graves' disease. He developed hypothyroidism post RAI ablation and commenced on levothyroxine. Improvement of the metabolic acidosis was noticed in line with improvement of thyroid function. Na bicarb and spironolactone tablets were stopped eventually as the patient was euthyroid clinically and biochemically.
Overt hyperthyroidism is associated with accelerated bone remodelling, leading to hypercalciuria, which can predispose to nephrocalcinosis and renal tubular damage, and therefore causes type 1 renal tubular acidosis. Once the patient becomes euthyroid, bone remodelling and urine calcium return to normal levels and that would correct the renal acidosis.
This case report serves to highlight the effect of Graves' disease on renal tubules which may result in type 1 renal tubular acidosis. This effect could be reversible with normalization of thyroid function.

Diabetes Mellitus and Glucose Metabolism

METABOLIC INTERACTIONS IN DIABETES

Bypassing Skeletal Muscle Lipid Handling Deficiencies as a Therapy for Metabolic Disease

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SUN-653

Metabolic diseases and their serious sequelae such as non-alcoholic fatty liver disease (NAFLD) pose a substantial clinical burden. It is now well recognized that skeletal muscle is a major site for the metabolism of all major macronutrients, and derangements in these muscle processes significantly contribute to metabolic disease. Studies over the last 15 years have identified the transcription factor Krüppel-like factor 15 (KLF15) as an important regulator and effector of metabolic processes across various tissues, and furthermore, genome-wide studies have identified human KLF15 variants with increased body mass index and diabetes. Given the importance of skeletal muscle in maintaining metabolic homeostasis, we generated a skeletal muscle specific KLF15 knockout (K15-SKO) mouse to study the role of skeletal muscle KLF15 in regulating systemic metabolism. We found that this animal is prone to developing obesity and insulin resistance at baseline, a phenotype that is greatly exacerbated in response to high fat diet (HFD). Strikingly, K15-SKO mice show a propensity toward developing NAFLD, as demonstrated by increased micro- and macrovesicular steatosis, hepatocellular ballooning, increased hepatic fatty acid and triglyceride deposition, and elevated *Cd36* expression. A potential cause of NAFLD is the accumulation of excess lipids and lipid intermediates due to defects in the lipid flux pathway in extrahepatic tissues. Indeed, we see defects in the expression of genes involved in the carnitine shuttle and a paucity of long-chain acylcarnitines in K15-SKO skeletal muscle. Furthermore, RNA sequencing of skeletal muscle from K15-SKO mice shows downregulation in a number of pathways involved in lipid handling. This indicates that KLF15 serves as a novel extrahepatic molecular regulator of hepatic health. It has been previously shown that a diet rich in short-chain fatty acids (SCFA) can bypass defects in lipid handling and ultimately improve metabolic health. To explore this therapeutic avenue, we gave K15-SKO mice either normal chow (NC) or a SCFA-rich diet for 7 weeks. We observed decreased weight gain and improved glucose homeostasis in SCFA-rich diet fed mice. In addition to being a preventative strategy, SCFA-rich diets may also serve as a potential therapy to rescue from metabolic disease. To this end, we gave K15-SKO mice HFD for 5 weeks followed by 7 weeks of either NC or SCFA-rich diet. We observed that providing SCFAs can improve metabolic health and ameliorate the phenotype seen due to defects in skeletal muscle lipid handling: mice given SCFA-rich diet following HFD had significantly decreased weight gain and improved insulin sensitivity. These studies demonstrate that skeletal muscle KLF15 serves as an important regulator of lipid flux and hepatic health, and that SCFA-rich diets are a promising candidate for metabolic disease resultant of impaired lipid handling.

Diabetes Mellitus and Glucose Metabolism

DIABETES TECHNOLOGY

Self-Reported Psychological Stress and Glucose Variability in Type 1 Diabetes on Sensor Augmented Pump over 5 Weeks

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SAT-641

Self-reported psychological stress and glucose variability in Type 1 Diabetes on sensor augmented pump over 5 weeks
Introduction: Patients and their families and medical providers have assumed that psychologic stress impacts glucose control in T1D (Type 1 Diabetes) though studies providing confirmatory evidence in real world settings are, to our knowledge, lacking. We hypothesized that self-reported psychologic stress worsens glucose control in T1D.
Method: We studied 20 adults with T1D on continuous glucose monitor (CGM), sensor augmented insulin pump (SAP) prospectively at 2 clinical research centers. Patients reported psychological stress through stress diaries for 5 weeks on a severity scale of 1-7 using hard copy logs including time of onset and offset of stress and severity. For analytic purpose, grades 1-4 are classified as mild and grades 5-7 as severe.
Results: Baseline characteristics were age 44.9±15.0 years, F/M 12/8, HbA1c 6.8 ± 0.7%, and diabetes duration of 22.9±15.9 years. We analyzed glucose variability during days of stress versus days without stress. During a 24 hour period, patients experienced less hypoglycemia during days with stress versus days without stress (p value 0.03). During the 5 week period, patients reported 23 ± 19.5 events. We analyzed the

impact of self-reported stress on CGM data streams after excluding stress events associated with missing CGM data, nocturnal events (from 12 MN to 6 AM, too few events) and events for which subjects did not provide duration of stress. Thus, we analyzed 19.5 ± 17 events per patient from 6AM to 12MN. From 6 AM to 12 MN, the episodes lasted 179 ± 255 minutes with 83 % episodes being mild/moderate and 17% moderate/ severe. Number of CGM readings during daytime stress episodes were 717± 1120 compared to 8768± 1238 during non-stress periods. Impact of stress from 6 AM to 12 MN (Mid-Night) on CGM glucose was analyzed using matched paired t test. Mean glucose (160.6±41.9 vs 148.3± 28.6) and SD (53.2 ±17.7 vs 56.1±14.6) did not show a difference; however % of time spent below 70 mg/dl was less (4 ± 5) in patients during stressful periods compared to times without stress (6.3± 5.5, P value 0.02).

Conclusions: To our knowledge, this is the first study attempting to analyze the impact of self-reported stress using daily stress diaries on CGM data streams in T1D patients on SAP. The study revealed significant challenges experienced by patients in reporting adequate data. Self-reported stress was not associated with hyperglycemia. However, days of self-reported stress and periods during patients reported stress were characterized by less hypoglycemia on CGM data streams.

Pediatric Endocrinology

ADVANCES IN PEDIATRIC OBESITY AND CANCER

Novel Variants in Protein Kinase a Signaling-Related Genes Identified in Obese Children with and Without NAFLD

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OR22-07

Context: Nonalcoholic fatty liver disease (NAFLD) is estimated to affect nearly 10% of Americans age 2-19 and about 38% of those affected are obese[i]. NAFLD is characterized by triglyceride accumulation in hepatocytes and can progress to nonalcoholic steatohepatitis, end stage liver disease and hepatocellular carcinoma. The underlying causes of NAFLD in youth are unclear although obesity, insulin resistance, type 2 diabetes mellitus and metabolic syndrome are risk factors. Genome-wide association studies and candidate gene studies have found several single nucleotide polymorphisms that affect susceptibility to and progression of NAFLD, but clinical translation for some of these genetics is lacking[ii].

Study design: Because mouse models of dysregulated PKA signaling demonstrate the centrality of this pathway in hepatic lipid metabolism and glucose homeostasis, we hypothesized that defects in hepatic PKA signaling genes could affect susceptibility to or severity of NAFLD in children. We asked whether identified variants might be associated with differences in clinical markers in a cohort of obese pediatric patients (non-NAFLD, n=295; NAFLD, n=165) followed at Yale Medical School, where clinical data and genomic DNA were collected. Exon sequencing of 54 PKA-related candidate genes included those coding for PKA subunits, PDEs and other proteins integral to the hepatic PKA system. Variants were ranked by allele frequency and potential pathogenicity. Ongoing analyses aim to identify associations between single variants and potential additive effects with clinical parameters (anthropometric, liver function, glucose metabolism, plasma lipids).

Results: Gene variants were identified in ABCA1, ADCY4, ADCY5, AKAP7, CREB3L1, CREB3L4, CREM, CYP27A1, DHCR7, ERN1, GYS2, IL6, IL10RB, MC2R, PDE1B, PDE2A, PDE3B, PDE4A, PDE7B, PDE10A, PDE11A, PPARGC1B, PRKAR2A, and PRKAR1B. Reported variants met criteria of high to moderate impact based on 9 in silico scores that predict pathogenicity. Allele frequency ranged from 2.5 to over 50 times higher in our cohort than the general population. One or more variant was identified in 34.9% of non-NAFLD and 19.4% of NAFLD patients (p=.0004).

Conclusion: We report PKA-related gene variants among a cohort of pediatric obese patients that might serve as useful predictors of risk of NAFLD or obesity. Further analyses will help determine whether any of these variants may play a functional role in NAFLD.

Endnotes

[i] Schwimmer JB, Deutsch R, Kahen T, Lavine JE, Stanley C, Behling C. Pediatrics. 2006;118(4):1388.

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Cardiovascular Endocrinology

HYPERTRIGLYCERIDEMIA; INFLAMMATION AND MUSCLE METABOLISM IN OBESITY AND WEIGHT LOSS II

18-Day Lifestyle Program Improves Metabolic Equivalent Measures, BMI, and Exercise Capacity Among Overweight and Obese Adults

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SUN-546

Introduction Various kinds of diets, workout programs, exist to lower one's Body Mass Index (BMI), increase strength, and endurance. Metabolic Equivalent Measures (METS) is often used to measure exercise intensity[1]. A simple 18-day lifestyle program may be effective in raising METS, lowering BMI, and building endurance among overweight and obese adults. Methods Participants took part in an 18-day residential lifestyle program that encouraged daily outdoor exercise. Those with a BMI greater than 24.9kg/m^2 were selected for this study. BMI, METS, and miles walked per day were measured at baseline and 14 days into the program. METS was measured using the Bruce Protocol while participants reported miles walked per