cushingoid features, acne and ecchymosis. BP - 166/110 mm Hg. Proximal myopathy, Pedal edema, clubbing & cervical lymphadenopathy was present (largest node - 2.5cm). Fasting & postprandial blood sugars were 190 & 285 mg/dl respectively. Serum K^+ was 3.0 meq/L (3-5-5.0meq/L), 11pm serum cortisol was 51.6 mcg/dl (cutoff < 7,5mcg/dl), 8 am cortisol after overnight 1mg dexamethasone was 60.7 mcg/dl (cutoff<1.8mcg/dl). Serum ACTH(8am) - 178 pg/ml.(>20 pg/ml-ACTH dependent Cushing's) Biopsy of neck node revealed poorly differentiated adenocarcinoma. PET scan showed left lung upper & lower lobe masses. A diagnosis of ectopic ACTH syndrome was made, the source of which was adenocarcinoma of lung, which has been very rarely reported to be associated with it. Oral ketoconazole was started followed by Chemotherapy with paclitaxel & carboplatin. Within the next 7 days patient developed pleural effusion, neutropenia & worsened rapidly. BAL revealed Nocardia species, known to be associated with hypercortisolism. He was treated with appropriate antibiotics & supportive treatment but succumbed to septic shock. **CONCLUSION** If a patient presents with rapidly evolving symptoms of Cushing's syndrome, ectopic ACTH syndrome should be considered. The presence of wasting and weight loss, hypokalemic alkalosis, pedal edema & marked hyperpigmentation should also alert towards the diagnosis. Histopathological confirmation of malignancy is important, as in our case with ectopic ACTH where the source was an adenocarcinoma of the lung, of which only 5 cases have been reported till now (Ectopic ACTH more commonly associated with SCLC). Finally, in cases of severe hypercortisolemia, there should be a high index of suspicion for opportunistic infections including invasive fungal infections, Nocardiosis etc, so that specific antibiotic therapy can be initiated. Typical features like fever, leukocytosis can be absent. Treatment of underlying hypercortisolism with surgical/medical management prior to initiation of chemotherapy has been shown to reduce the frequency of infections.

Diabetes Mellitus and Glucose Metabolism

METABOLIC INTERACTIONS IN DIABETES

Praliciguat, a Clinical-Stage Soluble Guanylate Cyclase Stimulator, Improves Lipid Handling and Insulin Sensitivity in Diet-Induced Obese Mice

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SUN-662

Praliciguat (PRL) is a soluble guanylate cyclase (sGC) stimulator which in animal models distributes broadly to tissues and elicits hemodynamic, anti-inflammatory, antifibrotic, and metabolic effects. Here, we assessed metabolic effects of PRL in a mouse diet-induced obesity model.

Six-week-old male C57BL/6N mice were maintained on a low-fat diet (LFD, lean mice) or placed on a 60% high-fat diet (HFD, obese mice). At age 14 weeks, one group of obese mice was maintained on HFD (obese controls) and one group of obese mice was switched to HFD formulated with PRL to achieve a C_{max} similar to a 6-mg/kg oral dose (PRL-treated mice). After 38 days of treatment, an oral lipid tolerance test (LTT) was conducted. In a 2nd study under the same dosing paradigm, overnight fasted blood and organs were collected on day 28.

As reported previously (1), compared to obese controls, PRL-treated mice had lower fasting insulin (-28%), HOMA-IR (-26%) and triglycerides (-16%) as well as lower plasma triglycerides AUC after LTT (-34%). Gene expression and phosphorylated proteins associated with insulin pathways were measured in liver, skeletal muscle and white adipose tissue. PRL treatment normalized expression of genes involved in lipid handling (liver *Pnpla3*, *Slc27a1*, *Lpl*; muscle *Lipe*; white adipose tissue *Fdft1*, *Ppara*). Expression of proinflammatory genes (liver *Tnf*; muscle *Ccl2*; white adipose tissue *Akt1, Icam1*) was lower in PRL-treated mice than in obese controls. Liver insulin signaling was assessed by determining pAKT (T308) and pAKT (S473), markers of PI3K pathway activity and pERK, a marker of MAPK pathway activity. Compared to lean mice, pAKT (T308) and pERK were lower in obese controls, whereas pAKT (S473) was similar; PRL-treated mice had higher pAKT (T308) and pAKT (S473) compared to obese controls while pERK was unchanged. In skeletal muscle and white adipose tissue, levels of pVASP, a key mediator of the sGC pathway, were higher in PRL-treated mice than in obese controls.

In summary, PRL improved insulin sensitivity and lipids in diet-induced obese mice by affecting mechanisms of lipid handling, inflammation, and insulin signaling in key tissues associated with metabolism.

1. Author information excluded, 1924-P: Praliciguat, a Clinical-Stage sGC Stimulator, Improves Insulin Sensitivity, Lipid Tolerance, and Energy Utilization in a Mouse Diet-Induced Obesity Model Housed at Thermoneutrality. Diabetes, 2019. **68**(Supplement 1): p. 1924-P.

Adipose Tissue, Appetite, and Obesity

CNS, INFLAMMATORY, AND THERMOGENIC INFLUENCES OF BODY WEIGHT

MYOD1 Is Associated with Eosinophil-Mediated Browning of Subcutaneous Adipose Tissue

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OR04-05

A novel role for adipose tissue (AT)-resident eosinophils (EOS) in metabolism has been suggested. These data were obtained using genetic animal models with either whole-body overexpression of Interleukin-5 (IL-5Tg) leading to eosinophilia or gene ablation resulting in complete lack of EOS. These models limit the specificity of the findings. We hypothesized that AT-resident EOS play a specific role in whole-body metabolism. To this end, we generated a transgenic mouse model overexpressing human eotaxin-2 (hE2) under the control of a fat-specific aP2 promoter, which would exclusively recruit circulating EOS into AT (hEo2Tg), without any changes in the overall EOS numbers. Compared

with wild type (WT) mice, AT-EOS numbers were markedly increased in multiple fat depots from hEo2Tg mice, including subcutaneous white adipose tissue (sWAT). After 12 weeks of high-fat diet (HFD), hEo2Tg mice showed significantly less body weight gain and fat mass compared with WT littermates. These changes were associated with an improvement in glucose tolerance. We also found increased oxygen consumption and heat production in hEo2Tg mice under room temperature conditions. The increased thermogenesis was accompanied with an increased expression of browning genes such as Ucp1, Prdm16, Dio2 in sWAT from hEo2Tg HFD mice. So far, our data suggest that AT-resident EOS promote browning of sWAT. This, in turn, protects our animals against development of HFD-induced obesity and insulin resistance. Next, whole transcriptome mRNA sequencing and bioinformatic analyses were performed and showed a significant increase of myogenic differentiation 1 (Myod1) gene expression in hEo2Tg sWAT mice. This was confirmed by qRT-PCR. Myod1 is a key regulator of skeletal muscle differentiation. Given the shared features between brown fat and skeletal muscle, we speculate that by increasing Myod1 gene expression, (AT)-resident EOS mediate sWAT browning. Additional studies are needed to determine the molecular mechanism(s) underling the regulation of Myod1 gene expression by AT-resident EOS and its effect on sWAT browning.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH THROUGHOUT THE LIFESPAN

Effect of Testosterone Replacement Therapy Added to Intensive Lifestyle Intervention on Cognitive Functions in Frail, Older Veterans with Hypogonadism and Obesity: A Randomized Clinical Trial

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OR02-05

Background: Both hypogonadism and obesity are common in older men which might additively exacerbate their age-related decline in cognitive functions. We tested the hypothesis that the addition of testosterone replacement therapy to intensive lifestyle intervention would enhance the benefits of intensive lifestyle intervention on cognition in older men with hypogonadism and obesity.

Methods: Eighty-three older (age≥65 years) male veterans with obesity (BMI≥30 kg/m^2) and evidence of persistently low AM testosterone (<300 ng/dl) associated with frailty (modified Physical Performance Test score <31) were randomized to six months of: 1) lifestyle therapy (diet-induced weight loss and supervised aerobic and resistance exercise training) + testosterone replacement therapy (LT+Test) or 2) lifestyle therapy + placebo (LT+Pbo). In this secondary analyses, outcomes were changes in cognition as assessed through comprehensive cognitive test battery (Modified Mini-Mental State Exam, Word Fluency Test, Trail Making Test Parts A and B Rey Auditory Verbal Learning Test, Stroop Color and Word Test, and Symbol Digit Modalities Test). We used z scores of changes in the cognitive tests to assess changes in attention, memory, executive function, language, global, and composite cognitive functions in response to the lifestyle and hormonal interventions.

Results: After 6 months, body weight decreased similarly in the LT+Test group and LT+Pbo group (decrease of 9.7 kg vs. 10.3 kg, respectively; P=0.91) whereas testosterone levels increased more in the LT+Test than in the LT+Pbo group (increase of 324 ng/dl vs 88 ng/dl, respectively; P<0.001). Memory z-score increased more in the LT+Test group than in the LT+Pbo group (0.73 vs. 0.39, respectively; P=0.03). Moreover, attention z-score increased more in the LT+Test group than in the LT+Pbo group (0.89 vs. 0.38, respectively; P=0.01). On the other hand, changes in executive function z-score, language z-score, and global z-score did not significantly differ between the LT+Test group and LT+Pbo group (0.45 vs 0.37, 0.34 vs 0.07, and 0.55 vs 0.29, respectively; P=0.13 to 0.56). More importantly, the composite cognitive z-score obtained by averaging all z-scores from each domain increased more in the LT+Test group than in the LT+Pbo group (0.56 vs 0.27; P=0.003).

Conclusion: These findings suggest that in the specific population of older men with hypogonadism and obesity associated with frailty, testosterone replacement therapy can augment the positive effects on cognition from intensive lifestyle intervention by diet-induced weight loss and combined aerobic and resistance exercise.

Thyroid

BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID II

Utilizing Patient Online Forums to Capture Experiences and Perceptions Associated with the Use of Desiccated Thyroid Extract

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SUN-432

Background: It is estimated that 10-25% of patients with hypothyroidism use desiccated thyroid extract (DTE) as their primary thyroid hormone replacement medication, despite concerns about the risk of thyrotoxicosis associated with DTE use. It is unclear why many patients prefer the use of DTE as a thyroid hormone replacement formulation