with diabetes [3]. Consequently, in order to ensure an adequate insulin supply method for patients, after a sentinel weather event, we developed a UAV delivery solution using a vertical take-off and landing (VTOL) Wingcopter 178 drone which we operated under beyond visual line of sight (BVLOS) conditions. After a lengthy planning process, we ensured compliance with all Irish (European) Aviation Aerospace regulations. In addition we complied with regulations surrounding the dispensing of prescribed fridge medications. We had our maiden flight on September 13, 2019 from Galway, Ireland to the Aran Islands (20Km each way) delivering insulin from the pharmacist to the patient's clinician. This represents the first documented autonomous delivery of insulin for a patient with diabetes.

References 1. Ackerman E, Strickland E. Medical delivery drones take flight in east africa. IEEE Spectrum. 2018 Jan 1;55(1):34-5. 2. Rabta B, Wankmüller C, Reiner G. A drone fleet model for last-mile distribution in disaster relief operations. International Journal of Disaster Risk Reduction. 2018 Jun 1;28:107-12. 3. da Rocha Fernandes J, Ogurtsova K, Linnenkamp U, Guariguata L, Seuring T, Zhang P, Cavan D, Makaroff LE. IDF Diabetes Atlas estimates of 2014 global health expenditures on diabetes. Diabetes research and clinical practice. 2016 Jul 1;117:48-54.

Cardiovascular Endocrinology

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

Ketone Bodies in Critical Illness Alter Cholesterol Synthesis in Skeletal Muscle, Interlinked with Protection Against Weakness

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SUN-548

Background: Critically ill patients often develop muscle weakness, which hampers recovery. In septic mice, supplementing parenteral nutrition (PN) with ketone body 3-hydroxybutyrate (3HB) attenuated muscle weakness, but also normalized sepsis-induced low cholesterol[1]. As 3HB can be metabolized into cholesterol, we hypothesized that improved muscle function with 3HB was related to altered cholesterol metabolism. **Methods**: In a catheterized, fluid-resuscitated, antibiotics-treated mouse model of prolonged sepsis (cecal ligation and puncture), septic mice received PN supplemented with either D,L-3HB sodium salt (PN+3HB; 150 mg/day) or isocaloric glucose (PN+gluc) and healthy pair-fed mice served as controls (n=15-17 mice/group). After 5 days, *ex vivo* muscle force and markers of cholesterol metabolism were assessed. In 600 weak and non-weak human critically ill patients (weakness assessed on day 8±1 in ICU by MRC sum score), serum total cholesterol concentration was measured on ICU day 3 or last day for shorter stayers. **Results**: In mice, PN+3HB counteracted the sepsis-induced lowering of plasma cholesterol (p=0.04), which correlated positively with absolute muscle force (R^2=0.19, p=0.002). Plasma mevalonate concentration, a surrogate marker of cholesterol synthesis, was reduced by sepsis (p=0.03 vs. controls), but normalized by PN+3HB (p=0.001 vs. PN+gluc). Skeletal muscle expression of cholesterol synthesis genes *Srebf2, Hmgcr* and *Hmgcs1* was higher in PN+3HB than in PN+gluc septic mice (p≤0.01). Expression of cholesterol uptake receptor *Ldlr* was also increased in PN+3HB septic mice (p=0.02 vs. PN+gluc), whereas PN+3HB did not affect cholesterol efflux transporters. In contrast, PN+3HB did not alter sepsis-induced alterations in markers of hepatic cholesterol metabolism. Plasma concentration of ubiquinone, a central co-factor of the mitochondrial respiratory chain derived from mevalonate, was increased by sepsis, irrespective of PN+3HB (p<0.0001 vs. controls) and PN+3HB could not counteract sepsis-induced muscular mitochondrial dysfunction (p≤0.0009 vs. controls). This excludes the involvement of ubiquinone in muscle weakness attenuation by 3HB supplementation. However, higher muscular *Nceh1* expression was observed with PN+3HB (p≤0.04 vs. controls and PN+gluc), suggesting enhanced shuttling of newly formed free cholesterol to the membranes. In human ICU patients, lower serum cholesterol concentration was observed in weak vs. non-weak patients (p=0.0002). In a multivariate model adjusted for baseline risk factors, low serum cholesterol concentrations were independently associated with muscle weakness (p=0.05). **Conclusion**: 3HB supplementation of PN enhanced muscle cholesterol synthesis and increased plasma cholesterol, which appeared to independently protect against sepsis-induced muscle weakness. 1 Goossens et al. (2019). Crit Care. 23: 236.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS II

Association of Sleep Quality and Painless Diabetic Peripheral Neuropathy in Type 2 Diabetes

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MON-698

Abstract

Aims

Diabetic peripheral neuropathy (DPN) is one of the most common and early manifested complication in T2D. Previous reports have shown that painful sensation of diabetic peripheral neuropathy (DPN) results in sleep problems in type 2 diabetes (T2D)[1, 2]. However, it is not known that subtype of DPN, the painless DPN also is associated with poor sleep quality in T2D. The purpose of the current study was to investigate the association between painless DPN and poor sleep quality in T2D.

Methods

A total of 146 patients of T2D who did not previously diagnose with symptomatic DPN were recruited into the study. Among the patients, painless DPN was diagnosed by using the current perception threshold (CPT) test. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI) questionnaire.

Results

The percentage of painless DPN was significantly higher in the poor sleep quality group than the good sleep quality

group (70.0% vs. 35.5%, *P*<0.001). In the subscale results, stimulus values in 2000 Hz, hypoesthesia and hyperesthesia were significantly higher in the poor sleep quality group, than in the good sleep quality group (45.7% vs. 25.0%, *P*=0.009; 34.3% vs. 18.4%, *P*=0.029; 40.0% vs. 19.7%, P=0.007, respectively). The association of painless DPN and poor sleep quality remained significant after adjustment for significant variants (odds ratio, 3.825; 95% confidence interval, 1.674-8.742; *P*<0.001).

Conclusions

The current study showed that painless DPN was associated with poor sleep quality. Future studies are required to clarify the pathophysiologic causal relationship between painless DPN and sleep quality.

References

1. Gore M, Brandenburg NA, Dukes E, Hoffman DL, Tai K-S, Stacey B. Pain severity in diabetic peripheral neuropathy is associated with patient functioning, symptom levels of anxiety and depression, and sleep. Journal of pain and symptom management. 2005;30(4): 374-385.

2. Zelman DC, Brandenburg NA, Gore M. Sleep impairment in patients with painful diabetic peripheral neuropathy. Clin J Pain. 2006;22(8): 681-685.

Pediatric Endocrinology

PEDIATRIC PUBERTY, TRANSGENDER HEALTH, AND GENERAL ENDOCRINE

Urine Steroid Profile of Girls with Premature Adrenarche

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SUN-073

Background: Adrenarche describes the development of the human adrenal cortex when the zona reticularis increases the synthesis of C19 steroids (DHEA/-S). Girls with premature adrenarche have a higher risk to develop adverse outcomes including polycystic ovary syndrome and metabolic syndrome later in life. The role of novel biosynthetic pathways of androgen production in health and disease remains largely unsolved.

Objective: This study aimed to compare the urinary steroid metabolome between girls with premature adrenarche and healthy girls with focus on metabolites originating of novel, alternate androgen pathways.

Methods: In 23 girls with premature adrenarche (median age 7 years) and 22 healthy, age-matched girls, we measured 39 steroid metabolites comprising progesterones, corticosterones, aldosterone, androgens, estrogens and glucocorticoids in the urine collected over 24 h by gas chromatography mass spectrometry. We compared metabolites and metabolite ratios between both groups of girls using Mann-Whitney tests with Bonferroni correction to account for multiple testing.

Results: Girls with premature adrenarche were heavier than healthy girls (median weight 26.2 kg vs. 21.5 kg, p=0.003) and had a higher BMI SDS (0.8 vs -0.3, p=0.013). Gestational age and birth weight was similar between groups. Overall androgen excretion was different between groups, in particular amounts of androsterone, etiocholanolone, androstanediol, dehydroepiandrosterone, androstenediol, androstenetriol and pregnenetriol were higher in girls with premature adrenarche than in healthy girls (p<0.05). Some of these metabolites originate from alternate androgen pathways, e.g. androsterone. We found no differences in progesterones, corticosterones, aldosterone, estrogens and glucocorticoids, except for 20β-dihydrocortisone, which was higher in girls with premature adrenarche. Activities of 17βHSD and of 17,20-lyase via the Δ4pathway were higher in girls with premature adrenarche than in healthy girls.

Conclusions: Girls with premature adrenarche produce more androgens than healthy girls of similar age. The urinary steroid signature of adrenarche includes metabolites of alternate pathways. Androstanediol seems a marker of adrenarche. Future studies should assess whether the steroid signature of adrenarche is just appearing earlier in girls with premature adrenarche or earlier and different compared to adrenarche at normal timing.

Adipose Tissue, Appetite, and Obesity

ADIPOSE TISSUE BIOLOGY AND OBESITY

Cold-Acclimation Prevents the Onset of Glucocorticoid-Induced Adipose Dysfunction in Male Mice

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SAT-586

Glucocorticoid (GC) excess, either endogenously or exogenously, has been causally linked to the development of chronic diseases such as obesity and type-2 diabetes mellitus. Continuously elevated GC levels result in an expansion of white adipose tissue (WAT) depots and a dramatic decrease in the thermogenic capacity in brown and beige adipose tissue (BAT and BeAT, respectively). Herein we aimed to examine the interaction between GCs and the sympathetic nervous system (SNS) in the regulation of WAT, BAT, and BeAT. To this end, we utilized an altered environmental temperature as a non-invasive method for the modulation of sympathetic activity - cold is an activator of SNS-mediated non-shivering thermogenesis. Thus, during a 4-week treatment with either corticosterone or placebo, 10-week-old male C57BL/6NRj mice were maintained at two different temperature levels: 29°C (thermoneutrality) or 13°C (cold temperature). Body weight, as well as energy and water intake, were monitored throughout the study. At sacrifice, serum and adipose tissues were collected for analysis. GC-exposed mice showed a marked increase in circulating corticosterone concentrations compared to placebo controls with no appreciable difference between temperature levels. At thermoneutrality, GC-treated mice gained more weight and consumed more food than their placebo-treated littermates. This GC-induced body weight gain was accompanied by increased (visceral & subcutaneous) WAT