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outcome. “Understanding the condition/complications” and “attending medical appointments” were seen as having relatively higher priority for endocrine TC. Barriers related to lack of financial support and low institutional priority. Involving key stakeholders facilitated implementation. Having a dedicated nurse was noted as an opportunity for improving TC. **CONCLUSIONS:** Implementation of structured TC has been piecemeal and most practices do not fully utilize recommended best practices (‘Got Transition’). Few practices formally collect outcome data. The major perceived barrier to implementing TC is financial. Practices incorporating nurses value discipline-specific contributions. These pilot data point to a role for nursing in providing comprehensive, high quality, comprehensive care for AYAs with chronic endocrine conditions.

Diabetes Mellitus and Glucose Metabolism

IMPACTS OF METABOLISM ON CLINICAL CHALLENGES

Lower Serum Myostatin Levels Are Associated with Higher Insulin Sensitivity in Adults with Overweight/Obesity

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In preclinical models, inhibition of the myokine myostatin prevents or improves insulin resistance (IR). However, studies investigating the association between serum myostatin levels and IR in humans are discrepant, perhaps in part because myostatin immunoassays lack specificity and sensitivity. New sensitive and specific myostatin LC-MS/MS assays make it possible to determine if higher serum myostatin levels are independently associated with greater IR in adults with overweight/obesity. If true, therapeutic manipulation of myostatin pathways may be a potential therapeutic target to prevent or treat type 2 diabetes (T2DM) in this high-risk population, in which current strategies, e.g. weight loss, are difficult to implement and maintain.

We studied 75 adults (53% women), 20–65 yo, BMI ≥ 25 kg/m² and generally healthy without T2DM. Serum myostatin levels (1^o independent variable) were measured by LC-MS/MS (Brigham Research Assay Core, Boston, MA), with no cross-reactivity with growth differentiation factor 11 (GDF11), activins or transforming growth factor beta (TGF- β), sensitivity of 0.5 ng/mL and intra- and inter-assay coefficient of variation of 10 and 12%. Insulin sensitivity (IS) (1^o dependent variable) was estimated by QUICKI, appendicular lean mass (ALM) by DXA, visceral adipose tissue (VAT) by CT and intrahepatic (IHL) and intramyocellular lipids (IMCL) by MR spectroscopy. Models were run sex- combined and stratified given sex differences in muscle mass.

Mean age was 47.9 \pm 12.2 years and BMI was 33.2 \pm 5.7 kg/m² (mean \pm SD). Compared to men, women had lower mean ALM (20.9 \pm 3.3 vs 29.2 \pm 3.3 kg, $p < 0.0001$) and serum myostatin levels (7.28 \pm 1.87 vs 8.28 \pm 1.89 ng/mL, $p = 0.02$) and similar mean IS (0.16 \pm 0.02 vs 0.15 \pm 0.02, $p = 0.13$). Lower serum myostatin levels were associated with higher IS in the whole group ($R = -0.32$, $p = 0.008$) and in women ($R = -0.41$, $p = 0.02$)—both remained significant after controlling for ALM—but not in men ($R = -0.16$, $p = 0.36$). In a multivariate model including VAT, IHL, IMCL and ALM, lower serum myostatin levels were associated with higher IS in the whole group ($B_1 = -0.37$, $p = 0.003$), in women ($B_1 = -0.43$, $p = 0.02$) and in men ($B_1 = -0.37$, $p = 0.05$). In a stepwise regression model including VAT, IHL, IMCL and ALM, VAT explained 18%, IHL explained 10% and myostatin explained 8% of the variability in IS in the whole group; in women, myostatin explained 18% and IHL explained 12% of the variability; in men, VAT explained 26% of the variability and myostatin was not a significant determinant.

In conclusion, lower serum myostatin levels were associated with greater IS in adults with overweight/obesity, independent of muscle and adipose depots known to be associated with T2DM risk. Future studies should investigate potential sex differences in the association between myostatin and IS. Therapeutic manipulation of myostatin pathways may be a potential therapeutic target to prevent or treat T2DM.

Bone and Mineral Metabolism

PARATHYROID HORMONE TRANSLATIONAL AND CLINICAL ASPECTS

Bioactivity of Long Acting PTH Fusion Molecules Tested in a Novel Non-Surgical Animal Model of Hypoparathyroidism

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SAT-408

Introduction: There is an unmet need for the development of long-acting PTH molecules to treat patients with hypoparathyroidism. We have established a novel non-surgical rodent model of hypoparathyroidism using oral Cinacalcet-HCl to test long acting analogues of PTH. Here we have tested the pharmacodynamics properties of two long acting PTH fusion molecules.

Methods: PTH fusion molecules tested: Fusion-1 is PTH (1–34) linked to GHBP (residues 1–238), and Fusion-2 is a Hybrid PTH-PTHrP (1) linked to GHBP (residues 1–238). For in vivo studies, normal male wistar rats were gavaged with 30 mg/kg Cinacalcet-HCl, immediately followed by a subcutaneous dose of PTH Fusion at 20 nmol/kg. Control animals received PTH (1–34) and vehicle only. Serum samples were taken and analysed for ionised calcium (iCa). **Results:** Oral administration of Cinacalcet-HCl caused a reduction in iCa that was significantly different from vehicle controls at 2 to 24hrs post dose (ANOVA $P < 0.0001$). PTH

1–34 maintained iCa levels for 2 hours after administration above that of Cinacalcet-HCl (AUC±SD (mmol/L).hr from baseline, 0.076 ±0.047 and 0.168±0.0874, t-test $P=0.0289$) but then levels fell and recovered as for Cinacalcet-HCl alone. Subcutaneous doses of both fusions were able to abrogate the effects of Cinacalcet-HCl from 4hrs post dose onwards giving a prolonged response, with iCa levels quicker to return to baseline levels at 48hrs compared to Cinacalcet-HCl. The AUC±SD (mmol/L).hr from baseline for iCa over 72 hours was 3.93±1.4 for Fusion-1, 5.0±2.7 for Fusion-2 & 10±2.8 for Cinacalcet-HCl and were significantly reduced for both fusions compared to Cinacalcet-HCl alone (t-test $P = 0.0028$ & $P = 0.019$, respectively) and not significantly different from vehicle only.

Conclusions: Cinacalcet-HCl behaved as expected in terms of iCa lowering (2). PTH maintained iCa but only for 2 hours. Both PTH fusion molecules showed a delayed and prolonged response and reduced the impact of Cinacalcet-HCl induced low iCa levels from 4hrs to 24hrs. These data provide proof of concept for long acting biological activity of these novel PTH fusion proteins.

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Pediatric Endocrinology

UNDERSTANDING AND TREATING PEDIATRIC GROWTH DISORDERS

Diagnosis of Severe GH Deficiency in Newborns: New Reference Range for the Preterm and Confirmation of the GH Cut-Off

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OR10-02

Introduction

Inborn severe GHD is caused by rare disorders of pituitary morphogenesis or function and frequently associated with additional pituitary hormone deficiencies. Affected newborns commonly present with recurrent hypoglycemia; therefore early diagnosis and therapy is warranted. The GH content of the newborn screening card is a reliable indicator of severe neonatal GHD. Here, we studied the GH content in screening cards and the history of 25 newborns with severe GHD. In addition, we determined the reference range of the GH content in screening cards from 282 healthy preterm newborns.

Patients and Methods

Since 2010, a total of 110 screening cards from hospitalized ill newborns were sent to our laboratory for measuring GH content. Using a questionnaire we obtained relevant clinical information from senders in 61 cases. Severe GHD was

defined by the presence of recurrent neonatal hypoglycemia with either a significant cerebral MRI morphology or two additional pituitary hormone deficiencies. In addition, the GH content of screening cards from 282 healthy newborns born preterm with a gestational age at birth from 34.0 to 37.9 weeks was prospectively analyzed. The GH concentration of the eluate from the screening card was measured by a highly sensitive ELISA (Mediagnost, Germany); the GH serum concentration was calculated.

Results

In 25 patients, the definition of severe GHD of the newborn was fulfilled; based on recurrent hypoglycemia in combination with ectopia of the neurohypophysis in 17, septum pellucidum agenesis plus opticus hypoplasia in two, severely hypoplastic pituitary gland in two, and combined TSH and ACTH deficiency with no cMRI findings in four newborns. Five newborns with severe GHD were preterm. The median GH concentration of the term newborns with severe GHD (n=20) was 3.9 µg/l (range; 1.1 to 11.8). This was significantly below the previously reported reference data from healthy term newborns (n=269) (median 16.4 µg/l; 95% reference range 7.0 to 39.4) ($p<0.001$). Using ROC plot analysis a GH serum concentration of 7.0 µg/l was identified as cut-off with the highest accuracy (90.0% sensitivity and 98.7% specificity). The median GH concentration of the 5 preterm newborns with severe GHD was 7.7 µg/l (range; 2.1 to 9.9). The newly determined 95% reference range for healthy newborns born preterm with a gestational age from 34.0 to 37.9 weeks (n=282) spanned from 7.9 to 41.1 µg/l with a median of 20.3 µg/l.

Conclusions

A GH content below 7.0 ng/ml in the newborn screening card identified severe GHD with 90% sensitivity and 98.7% specificity. In preterm newborns, the lower limit of the 95% reference interval was by 0.9 µg/l higher than in term newborns. The newborn screening card is a valuable source for the diagnosis of GH deficiency in newborns and young infants.

Neuroendocrinology and Pituitary HYPOTHALAMIC-PITUITARY DEVELOPMENT AND FUNCTION

Osteocalcin and Exercise Improve Mood and Cognition in Female Mice with High-Fat Diet Induced Type 2 Diabetes.

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SAT-293

The skeleton has been characterized as an endocrine organ, demonstrating a capacity to modulate cognition, mood and energy homeostasis (1,2). These endocrine actions of the skeleton have been attributed to the osteoblast-derived peptide osteocalcin. In mice, uncarboxylated osteocalcin (ucOCN) decreased the acquisition of type 2 diabetes mellitus (T2DM) and ameliorated depressive- and anxiety-like behaviours (1,2). Clinically, T2DM patients present with reduced serum osteocalcin levels and approximately 1 in 4 also suffer from co-morbid depression (3,4). The cognitive and metabolic benefits of ucOCN are similar to the