HORMONE
RESEARCH IN
PÆDIATRICS

58th Annual Meeting of the European Society for Paediatric Endocrinology (ESPE)

Vienna, Austria, September 19–21, 2019

Abstracts

KARGER
Basel · Freiburg · Paris · London · New York · Chennai · New Delhi · Bangkok · Beijing · Shanghai · Tokyo · Kuala Lumpur · Singapore · Sydney

Erratum
December 20, 2019. DOI: 10.1159/000505087

Abstracts

HORMONE RESEARCH IN PÆDIATRICS

Horm Res Paediatr 2019;91(suppl 1):1–682
DOI: 10.1159/000501868

Published online: September 6, 2019

Presenting authors are underlined

Plenary Lectures

PL1

"RANKL and RANK: Bone and beyond"

Josef Penninger

University of British Columbia, Vancouver, Canada

RANKL was identified as an osteoclast differentiation factor as well as a T cell-derived stimulator of dendritic cells. The essential role of RANKL in osteoclastogenesis has been genetically proven in both mice and humans. In addition, RANKL was shown to play a critical role in various tissues including the thymus, gut, and mammary gland. The fully human monoclonal antibody against RANKL, denosumab, has been successfully utilized and approved for the treatment of bone metastasis and osteoporosis. We also studied the mechanism of bone destruction in rheumatoid arthritis and proposed that RANKL is a key therapeutic target for arthritis-associated bone destruction. Recently, denosumab has been indeed approved for rheumatoid arthritis in Japan. I will discuss the function of RANKL in multiple tissues and introduce recent findings providign an evolutionary perspective of RANKL/RANK signaling.

PL2

Abstract not available

PL3

Glucocorticoid rhythms, stress response and the brain from neonates to adults

Stafford Lightman

University of Bristol, Bristol, UK

Biological systems are invariably dynamic, with both stochastic interactions and deterministic processes across multiple timescales ensuring the maintenance of homeostatic regulation and allowing us to adapt to changes in both internal and external environments. It is no surprise therefore that the stress responsive hypothalamic-pituitary-adrenal (HPA) axis shows multiple levels of regulation which come together to regulate oscillating levels of glucocorticoid secretion with both diurnal and ultradian rhythmicity.

I shall describe the mechanisms underlying the HPA pulsatility and how these interact with higher level circadian control by the hypothalamic suprachiasmatic nucleus. I will show how the adrenal adapts to pulsatile ACTH and how tissues respond to pulsatile changes in cortisol/corticosterone. The importance of this for optimal emotional and cognitive function in man will be described. Finally, I shall describe novel technology allowing repeated measures of glucocorticoid hormones in infants undergoing cardiac surgery without the need for blood sampling.

PL4

Abstract not available

PL5

Nutrition and the reproductive axis: Implications for the control of puberty

Manuel Tena-Sempere

University of Cordoba, Cordoba, Spain. Instituto Maimonides de Investigación Biomedica de Cordoba (IMIBIC), Cordoba, Spain. CIBER Obesity and Nutrition, Cordoba, Spain. University of Turku, Turku, Spain

Puberty is under the precise control of sophisticated regulatory networks, which integrate a large number of endogenous and environmental signals, including metabolic and nutritional cues. Thus, puberty onset is tightly bound to the state of body energy reserves, and deregulation of energy/metabolic homeostasis is often associated with alterations in the timing of puberty. However, despite recent progress in the field, our knowledge of the specific signals and central molecular mechanisms whereby puberty onset is modulated by metabolic factors remains fragmentary and incomplete.

Compelling evidence, gathered over the last fifteen years, supports an essential role of hypothalamic neurons producing kisspeptins, encoded by *Kiss1*, in the neuroendocrine control of puberty. Kiss1 neurons are major components of the hypothalamic GnRH pulse generator, whose full activation is mandatory pubertal onset. Kiss1 neurons seemingly participate in transmitting the regulatory actions of metabolic cues on pubertal maturation. However, the modulatory influence of metabolic signals (e.g.,

KARGER

E-Mail karger@karger.com
www.karger.com/hrp

cardiovascular complications, and complications of hemodialysis, and peritoneal dialysis.

Aim: Assessment of severity of renal impairment and staging of chronic kidney disease in type 1 diabetic children and adolescents using serum creatinine, renal ultrasound and renal scan.

Patients and Methods: This analytic cross sectional study was conducted on 41 children and adolescents having type 1 diabetes mellitus, aged 5 to 18 years old with duration of diabetes more than 5 years, presented at Pediatrics department, Suez Canal University Hospital, Ismailia, Egypt. Full medical history, thorough clinical examination, laboratory investigations including H A1c, serum creatinine, renal ultrasound and renal scanning were performed for assessment of chronic kidney damage.

Results: The mean age of patients was 13.9±3.03 years; 63.4% were males& 36.6% were females, The mean GFR of the studied group using radionuclear Scintigraphy was (66.1±12.08) ml/min /1.7m2 ; 14.6% of them were in stage I CKD with GFR more than 90 ml/min /1.73 m2 and 85.4% were stage II CKD . By using renal ultrasound, all of the studied population had normal renal ultrasound findings. Eighty three percent of the whole group were clinically asymptomatic. In this study, none of the studied group had elevated serum creatinine.

Conclusion: Renal Scintigraphy can be used as an accurate measure for assessment of GFR for early detection of renal dysfunction and chronic morbidity in type 1 diabetes mellitus in children and adolescents and can be used as an early predictor of chronic kidney disease better than using renal ultrasound or serum creatinine.

P3-95

Changes in the Microbiome of Pre-Type 1 Diabetic Children

Nikolina Zhelyazkova[1], *Reni Koleva*[2]

[1]Student at University of Glasgow, Glasgow, UK. [2]First Diagnostic and Consultation Center, Stara Zagora, Bulgaria

Introduction: Type 1 Diabetes (T1D) is an autoimmune disease where β-cells of the pancreatic islets are destroyed. The vast majority of T1D cases are not due to genetic predisposition, implying that the prevalence is associated with environmental, nongenetic factors. One such factor is the microbiome and its correlation with T1D has been investigated in a multitude of studies.

Aims: To investigate whether the current literature is providing evidence that there is a link between onset of T1D and the microbiome.

Methods and materials: Search for primary literature was done using PubMed Central. Changes in the gut microbial communities

Two of the main factors identified that have the capacity to change the microbial diversity are age and cessation of breastfeeding. Breastfeeding is selective for lactose degrading bacteria, while incorporation of fibre is aided by transketolase. Because of this, the fluctuations in the microbial communities during this transitional period is evident.

A positive correlation associated with predisposed T1D child was found between *Blautia*, *Ruminococcus, Rikenellaceae* and *Streptococcus* genera outgrowth even prior to disease onset. Some species within these genera are described as pathobionts, potentially causing inflammation. Significant correlation was found between increase of *Bacteroides* and anti-islet antibodies.

Gut integrity was also compromised in pre-T1D cases, as butyrate producing bacteria were low. Butyrate is especially important as it maintains the gut epithelial stability and ensures bacterial localisation. Additionally, there was an observation of increased production of triglycerides and branched-chain amino acids from *Blautia* and *Ruminococcus*.

Discussion: Cessation of breastfeeding and age are linked, as reduction in breastmilk and incorporation of solid foods on the basis on age of the child, which in turn induces the changes in the microbiome. The presence of *Blautia*, *Ruminococcus, Rikenellaceae* and *Streptococcus* in pre-T1D children cannot only cause gut inflammation but also induce permeability of the gut, which can be aided by the reduced number of butyrate, during which microorganisms can reside in the intraperitoneal space, causing increase in inflammation. Moreover, the increase of triglycerides pre- and post-T1D onset increases the unpredictability of hypoglycaemia. The positive correlation between *Bacteroides* and anti-islet antibodies advances the further destruction of β-cells and aiding disease onset.

Conclusion: It is evident that the gut microbiome has an effect on T1D onset and progression, with these findings highlight the importance of understanding the microbiome of T1D, which can potentially aid treatment, diagnosis and perhaps even prevention.

Fat, Metabolism and Obesity

P3-96

Assessment of cardiac function in obese children and adolescents with metabolic syndrome

Athanasia Tragomalou[1], *Evangelia Kosti*[1], *Konstantina Sveroni*[1], *Sofia Loukopoulou*[2], *Maria Binou*[1], *Georgia Kourlaba*[3], *Marina Papadopoulou*[1], *Penio Kassari*[1], *Evangelia Charmandari*[1,4]

[1]Outpatient Clinic For the Prevention and Management of Overweight and Obesity, Division of Endocrinology, Metabolism and Diabetes, First Department of Pediatrics, National and Kapodistrian University of Athens Medical School, "Aghia Sophia" Children's Hospital, Athens, Greece. [2]Department of Pediatric Cardiology, "Aghia Sophia" Children's Hospital, Athens, Greece. [3]EVROSTON LP, Chatzigianni Mexi 5, Athens, Greece. [4]Division of Endocrinology and Metabolism, Center of Clinical, Experimental Surgery and Translational Research, Biomedical Research Foundation of the Academy of Athens, Athens, Greece

Background: Obesity in childhood and adolescence is often associated with dyslipidemia, hypertension, insulin resistance, inflammation, and disturbances in adipocytokine secretion, which lead to endothelial dysfunction and the development of atherosclerotic cardiovascular disease.

Aim: To determine the prevalence of metabolic syndrome (MS) among obese children and adolescents attending our outpatient childhood obesity clinic, and to evaluate their cardiovascular function.

Methods: One thousand four hundred (n=1400) obese children and adolescents attending our 'Out-patient Clinic for the Prevention and Management of Overweight and Obesity in Childhood and Adolescents' were evaluated and screened in order determine those fulfilling the International Diabetes Federation (IDF) criteria for MS. The study was approved by the local Committee on the Ethics of Human Research. Written informed consent was obtained in all cases by a parent/guardian. All participants underwent clinical examination and standard anthropometric measurements were obtained by a single trained observer. A fasting blood sample for baseline hematological, biochemical and endocrinologic investigations was obtained at 08:00h, and was followed by an oral glucose tolerance test. All subjects underwent echocardiography, ultrasound of the carotid arteries to determine carotid intima-media thickness (cIMT), and a liver ultrasound scan to determine hepatic steatosis.

Results: Seventy seven (n=77) children and adolescents [mean age ± SD: 13.1 ± 1.9 years; 46 males (59,7%), 31 females (40,3%); 12 prepubertal (14,5%), 65 pubertal (85,5%)] were identified as having MS. Plasma glucose concentrations were 86.7 ± 9.2 mg/dL, serum insulin 34.1 ± 15.8 µIU/mL, HbA1C 5.3% ± 0.2%, cholesterol 159.8 ± 30.9 mg/dL, triglycerides 141 ± 63.6 mg/dL, HDL 39.7 ± 8.5 mg/dL, LDL 92.3 ± 27.8 mg/dL, ApoA 125.6 ± 18.7 mg/dL, ApoB 90.9 ± 22.4 mg/dL, Lp(a) 16.99 ± 24.84 mg/dL. The cIMT of the left and right carotid arteries were 0.7 ± 0.2 mm (normal range: 0.49 ± 0.03 mm). Interventricular septal end diastole (IVSd) and systole (IVSs) were 8.8 ± 1.6 mm and 9.9 ± 2.5 mm, respectively. Left ventricular internal diameter end diastole (LVIDd) and systole (LVIDs) were 47 ± 4 mm and 28.8 ± 4.4 mm, respectively, while left ventricular posterior wall end diastole (LVPWd) and systole (LVPWs) were 9,1 ± 2.6 mm and 14.4 ± 4.1 mm, respectively. Hepatic steatosis was identified in 67 (87%) of the participants.

Conclusions: The prevalence of MS in our large cohort of obese children and adolescents was 5.5%. Our findings demonstrate increased cardiovascular risk in children and adolescents with MS.

P3-97

Metabolic Syndrome in adults with congenital adrenal hyperplasia due to 21-hydroxylase deficiency

Imen Gargouri[1], *Faten Hadjkacem* [1], *Wajdi Safi*[1], *Dorra Ghorbel*[1], *Rekik Nabila*[1], *Charfi Nadia*[1], *Thouraya Kamoun*[2], *Mouna Mnif*[1], *Mohamed Abid*[1]

[1]Department Of Endocrinology, Hedi Chaker Hospital, Sfax, Tunisia. [2]Department Of Pediatrics, Hedi Chaker Hospital, Sfax, Tunisia

Introduction: 21-Hydroxylase deficiency is the most frequent form of congenital adrenal hyperplasia (CAH) which is a common autosomal recessive disorder characterized by impaired adrenocortical and adrenomedullary function, and adrenal hyperandrogenism. Chronic glucocorticoid therapy and excess androgen exposure in patients with CAH may predispose them to developing a metabolic syndrome in adulthood.Our objective is to evaluate the metabolic syndrome in adulthood in a Tunisian cohort.

Subjects and Methods: We underwent a prospective study of 26 patients over 16 years of old with CAH.

Results: The cases included 26 patients (M: 11, F: 15) with CAH due to 21-hydroxylase deficiency with a mean age of 27.4 years (16.5-48 years). Eighteen patients had the classical CAH form and the remaining 8 patients had the non-classical form. The mean body mass index was 26,9 ± 4,27 kg/m2 (20,3-34,8 kg/m2). The most commonly used drug was hydrocortisone which was used by 21 cases. Five cases had been managed on dexamethasone alone. The mean body fat mass was 17,88 ± 9,8 kg (6-39,3kg) 24,8 ± 10,65 % of body mass (10,9 - 41,6 %). Eight patients suffered from obesity. Mean fasting serum glycaemia was 4,82 ± 0,52 mmol/l (3,85-5,54 mmol/l). Eighteen patients (78.2%) had a normal glucose tolerance, whereas 4 patients (17.4%) had impaired glucose tolerance and only one patient had diabetes. A hypercholesterolemia was observed in one patient, a combined hyperlipidaemia in another one and finally a low HDL-cholesterol in 5 patients. Hepatic cytolysis was noticed in one patient with a hepatic steatosis in abdominal ultrasound. Hypertension was confirmed in two patients.

At the end of this metabolic assessment and according to the criteria of theNCEP-ATPIII, the metabolic syndrome was confirmed in a single patient associating android obesity, diabetes and hypoHDLemia.

Conclusion: The risk of developing a metabolic syndrome appears to be considerably increased in case of HCS. All the compounds of metabolic syndrome have been identified during 21-OH deficiency, such as obesity, hyperleptinemia, dyslipidemia, insulin resistance and increasing body fat requiring screening in this population to prevent the complications of those comorbidities.

P3-98

High allostatic load in children with excess of weight

Valeria Calcaterra[1], *Chiara Montalbano*[2], *Federica Vinci*[3], *Corrado Regalbuto*[4], *Giulia Casari*[4], *Annalisa De Silvestri*[2], *Hellas Cena*[4], *Daniela Larizza*[1]

[1]University of Pavia and IRCCS Policlinico S. Matteo, Pavia, Italy. [2]IRCCS Policlinico S. Matteo, Pavia, Italy. [3]University of Pavia, Pavia, Italy. [4]University of Pavia, Pavia, Italy

Objective: Allostatic load (AL) refers to the physiological response that occurs in chronic stress burden, Excessive weight gain is an important source of physiological stress promoting chronic low-inflammation state detrimental for health. We estimated AL score among a pediatric population, in order to define a correlation between cumulative biological dysregulation and excess weight.

Methods: We enrolled 164 children and adolescents (11.89 ± 3.89). According to body mass index (BMI) threshold, the subjects were classified as normal weight BMI<75th percentile; overweight BMI 75-95th percentile; obese BMI>95th percentile. Data based on 16 biomarkers were used to create the AL score. A dichotomous outcome of high AL, was defined for those who had >4 dysregulated components.

Results: High AL was noted in 88/164 subjects (53.65%), without significant difference in sex distribution (p =0.07) and pubertal status (p=0.10).