

thickening of the upper eyelid lift muscle, with greater involvement in the left orbit. These findings are compatible with inactive TAO with an expansive “white eye” phenotype, generally with a lower risk of compressive neuropathy. Discussion: In addition to normal thyroid function and mild TAO, the patient has the characteristic of presenting negative antibodies. Associated with TSH-R, factors such as IGF-1 can be found in the pathogenesis of TAO, which can generate a similar effect¹. Likewise, IGF-1 stimulates cell proliferation, and is related to neoplasms such as thyroid carcinoma². Conclusions Differentiated thyroid carcinoma should be ruled out in all patients with TAO, whether euthyroid or not. Studies confirming the relationship of IGF-1, TAO and thyroid carcinoma are necessary. References: 1. Yu et al. Thyroid-associated orbitopathy in patients with thyroid carcinoma A case report of 5 case. *Medicine* (2017) 2. Manzella et al Activation of the IGF Axis in Thyroid Cancer: Implications for Tumorigenesis and Treatment. *International Journal of Molecular Sciences*, (2019). 20 (13), 3258.

Adipose Tissue, Appetite, and Obesity OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET

Measurement Of Carotid Intima, hepatic Steatosis And Inflammatory Markers In Obese Children

MARIA CRISTINA BAZAN, MCB, Ph D.

FACULTAD DE MEDICINA, Tucuman ARGENTINA, Argentina.

MON-LB108

Measurement of carotid intima, hepatic steatosis and inflammatory markers in obese children. Elevated levels of inflammatory factors and increased mean intimal carotid thickness (IMT) would increase the risk of atherothrombotic events and contribute to the progression of cardiovascular disease in obese children. Objectives: Evaluate inflammatory factors, metabolic syndrome and non-alcoholic liver steatosis and carotid IMT as an early cardiovascular risk marker. Patients and methods: Descriptive cross-sectional exploratory study. Consider 41 obese children both sexes between 6- 12 years old. Evaluated: anthropometry and determinations of lipid and liver profile, blood glucose, insulin, HOMA, ultrasensitive CRP, fibrinogen. Hepatic ultrasound and measurement of carotid IMT with ESAOTE Mylab 50 Exdicion equipment. . Results: From 41 studied patients, 57% were female. 51% presented MS and 68% elevated triglycerides. CRP > 1 was found in 71% of cases. Hepatic steatosis was observed in 60%, which only 10% had altered transaminases. 12% presented high fibrinogen. Patients with MS had a significant positive difference in the IMTCC (X = 0.41 ± 0.12; p 0.024), HDL (X 37.89 ± 1.72; p 0.004) triglycerides (X 149.42 ± 10.69; p 0.002) in relation to patients without MS. Conclusion: CRP is an inflammatory risk factor associated with elevated BMI and MS. There was a higher prevalence of MS in our study. The increase in the average intimal thickness is significantly related to the presence of MS and RCP > 1. The determination of marker molecules of an inflammatory state and measurement of carotid IMT would contribute to the implementation of strategies to prevent cardiovascular, hepatic and metabolic risk since childhood.

Cardiovascular Endocrinology

ENDOCRINE HYPERTENSION AND ALDOSTERONE EXCESS II

Targeted Metabolomics as a Screening Tool in the Diagnosis of Endocrine Hypertension

Zoran Erlic, MD¹, Laurence Amar, MD², Casper K Larsen, PhD³, Martina Tetti, MD⁴, Christina Pamporaki, MD⁵, Cornelia Prehn, PhD⁶, Jerzy Adamski, PhD⁶, Aleksander Prejbisz, MD⁷, Marco Boscaro, MD⁸, Graeme Eisenhofer, PhD⁵, Paolo Mulatero, MD⁴, Guillaume Assié, MD⁹, Anne Blanchard, MD¹⁰, Maria-Christina Zennaro, MD, PhD¹¹, Felix Beuschlein, MD¹².

¹Klinik für Endokrinologie, Diabetologie und Klinische Ernährung, Universitätsspital Zürich, Zurich, Switzerland,

²Université de Paris, PARCC, INSERM and Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Unité Hypertension artérielle, Paris, France,

³Université de Paris, PARCC, INSERM, Paris, France, ⁴Division of Internal Medicine and Hypertension Unit, Department of Medical Sciences, University of Torino, Torino, Italy,

⁵Department of Medicine III, Universitätsklinikum Carl Gustav Carus, Dresden, Germany, ⁶Helmholtz Zentrum München, Research Unit Molecular Endocrinology and Metabolism, Neuherberg, Germany, ⁷Department of Hypertension,

Institute of Cardiology, Warsaw, Poland, ⁸UOC Endocrinologia, Dipartimento di Medicina DIMED, Azienda Ospedaliera-

Università di Padova, Padova, Italy, ⁹INSERM U1016,

Institut Cochin, Université de Paris and CNRS UMR 8104 and Department of Endocrinology, Center for Rare Adrenal

Diseases, Assistance Publique-Hôpitaux de Paris, Hôpital Cochin, Paris, France, ¹⁰Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Centre d'Investigations

Cliniques, Paris, France, ¹¹Université de Paris, PARCC, INSERM and Assistance Publique-Hôpitaux de Paris, Hôpital

Européen Georges Pompidou, Service de Génétique, Paris, France, ¹²Klinik für Endokrinologie, Diabetologie und Klinische

Ernährung, Universitätsspital Zürich, Zurich, Switzerland and Medizinische Klinik und Poliklinik IV, Klinikum der

Universität München, LMU München, Zurich, Switzerland.

SUN-LB97

Arterial hypertension [HT] is a global epidemic that requires adequate treatment to reduce cardiovascular morbidity and mortality. Secondary causes of HT and specifically endocrine hypertension [EHT] (primary hyperaldosteronism [PA], pheochromocytoma/paraganglioma [PPGL] and Cushing syndrome [CS]) can potentially be cured by surgery or treated by targeted medication. However, diagnosis of EHT requires expertise in test selection and interpretation of test results. The availability of experts outnumbers its demand. Thus, preselecting tools are necessary to identify patients who require further referral to an expert. Since targeted metabolomics [TM] is a new method showing promising results in profiling cardiovascular diseases and endocrine conditions associated with HT, we tested the ability of TM in discriminating primary hypertension [PHT] from EHT cases. The study included 282 adult patients (52% female; mean age 49 years) from the European multicentre consortium ENSAT-HT (www.ensat-ht.eu). Of these, 59 were diagnosed with PHT and 223 with EHT (40 CS, 107 PA and 76 PPGL). TM was performed on stored blood samples with a mass spectrometry based approach using the AbsoluteIDQTM p180 Kit (BIOCRATES Life Sciences, Austria). In total, 188

metabolites were determined, of which 155 were eligible for statistical analyses according to established selection criteria. To identify relevant discriminating metabolites, a series of univariate and multivariate analyses were applied. Since the distribution of the patients between the clinical entities was different according to sex ($p < 0.001$) and age ($p = 0.001$), analyses were also performed separately for each sex and age group (cut-off 50 years). Thereby, we identified 4 common metabolites (C18:1, C18:2, spermidine, ornithine) from the comparison of PHT with each endocrine hypertension subgroup (CS, PA, PPGL) separately. The ROC curve for discrimination between PHT and EHT built upon these 4 metabolites had an area under the curve (AUC) of 0.79 (95%CI 0.73-0.85). In the comparison of PHT and EHT as a common group 38 metabolites were identified. Using the top 15 metabolites from the latter comparison (C3-DC, C9, C16, C16:1, C18:1, C18:2, arginine, aspartate, glutamate, ornithine, spermidine, lysoPCaC20:4, PCaaC38:6, PCaaC40:6, PCaaC42:1) the AUC was 0.86 (95%CI 0.81-0.91). We conclude that TM is associated with distinct metabolic pattern in PHT and EHT and is a promising pre-screening tool for identifying EHT patients.

Diabetes Mellitus and Glucose Metabolism

LIPIDS, OBESITY AND METABOLIC DISEASE

Metformin Attenuates Sodium Retention and Blood Pressure in Hypertensive Diabetic Mice by Reducing the Phosphorylation of Renal NCC and Its Association With the Actin Cytoskeleton

Mohammed F. Gholam, MBBS¹, Alina Waleed, BS¹, Kubra M. Tuna, MD², Morgan Carson-Marino, MS³, Kevin M. Chacko, BS¹, Zeeshan S. Malik, BS¹, Whitney C. Schramm, BS¹, Juliana V. Pena Lopez, BS¹, Abdel A. Alli, PhD, MPH¹.

¹Department of Physiology and Functional Genomics and Department of Medicine Division of Nephrology, Hypertension, and Renal Transplantation, University of Florida, Gainesville, FL, USA, ²Graduate Medical Education, University of Central Florida, College of Medicine and Internal Medicine Residency Program, Ocala Regional Medical Center, Ocala, FL, USA, ³Department of Pharmaceutics, University of Florida, College of Pharmacy, Gainesville, FL, USA.

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Metformin is the first-line drug in the treatment of type 2 diabetes mellitus. The aim of this work was to evaluate the efficacy of metformin treatment in reducing blood pressure and investigate the molecular mechanism using a preclinical animal model. Adult male and female diabetic db/db mice with a blood glucose of greater than 300 mg/dl were salt-loaded (8% NaCl) for 10 days to induce hypertension. The mice were subject to metabolic cage studies for 24 hour urine collections in order to measure urinary electrolytes, albumin, and creatinine. Blood pressure was measured weekly by the tail-cuff method to assess the effect of metformin or vehicle given by oral gavage (dose of 60 mg/kg of body weight per day). At the end of the study the mice was euthanized and the left kidney was formalin-fixed and paraffin-embedded for immunohistochemistry

while the right kidney was homogenized for Western blotting. Western blotting showed attenuation of total NCC and phospho-NCC in diabetic db/db mice given an oral gavage of metformin (Pearson correlation coefficient: $0.9470 \pm 2.52e^{-3}$) compared to vehicle (Pearson correlation coefficient: $0.9800 \pm 2.86e^{-3}$). Immunohistochemical analysis showed less co-localization of the actin cytoskeleton protein filamin and phosphorylated NCC in the metformin treated group compared to the control group. Taken together, we show metformin decreases sodium retention and blood pressure by reducing the density of renal NCC at the luminal membrane and the association between NCC and the actin cytoskeleton.

Diabetes Mellitus and Glucose Metabolism

LIPIDS, OBESITY AND METABOLIC DISEASE

Regulation of ENaC by Exosomal Lipids in the Diabetic Kidney

Kubra M. Tuna, MD¹, Hunter G. Ramsay, BS², Mohammad-Zaman Nouri, PhD³, Nancy D. Denslow, PhD³, Abdel A. Alli, PhD, MPH².

¹Graduate Medical Education, University of Central Florida, College of Medicine and Internal Medicine Residency Program, Ocala Regional Medical Center, Ocala, FL, USA, ²Department of Physiology and Functional Genomics, University of Florida, College of Medicine, Gainesville, FL, USA, ³Department of Physiological Sciences and Center for Environmental and Human Toxicology, University of Florida, Gainesville, FL, USA.

SAT-LB127

Effective treatment of hypertension (HTN) in patients with diabetes may help to significantly reduce the risk of those patients developing additional complications including vascular disease and diabetic nephropathy. Blockers of the renin-angiotensin system including angiotensin converting enzyme inhibitors and angiotensin receptor blockers are not always effective in treating HTN in diabetic patients. Therefore, the aim of this study was to use an animal model of type 2 diabetes to investigate a novel mechanism of diabetes associated HTN involving exosomal lipids in the upregulation of epithelial sodium channel (ENaC) activity in the kidney. We performed metabolic cages studies using male and female hypertensive (salt-loaded induced) diabetic db/db mice and healthy age-matched wild-type control mice in order to isolate and characterize urinary exosomes from each group by nanoparticle tracking analysis, Western blotting, and transmission electron microscopy. Our mass spectrometry based lipidomic studies identified key lipids that were differentially expressed in the kidney derived exosomes from the hypertensive diabetic mice compared to control mice. Sphingomyelin quantification assays showed total sphingomyelin content was elevated in the exosomes from the hypertensive diabetic mice compared to the control group. Single channel patch clamp studies showed urinary exosomes enriched in sphingomyelins from hypertensive diabetic mice compared to controls increase ENaC activity (at the level of channel density and open probability) in cultured distal tubule renal epithelial cells. Moreover, exogenous application of sphingomyelin-6 to cultured mouse cortical