Adipose Tissue, Appetite, and Obesity

OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET

Hydroethanolic Extract of Lampaya Medicinalis Phil. (Verbenaceae) Decreases Intracellular Triglycerides and Proinflammatory Marker Expression in Fatty Acid-Exposed HepG2 Hepatocytes

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Background: Non-alcoholic fatty liver disease (NAFLD) is the most common hepatic chronic disease worldwide. NAFLD is characterized by an abnormal triglyceride (TG) accumulation (steatosis) in the liver, that may lead to hepatic inflammation (1). DGAT2 is a key enzyme that catalyzes the final step of TG synthesis and whose expression is elevated in NAFLD (2). FABP4 is a transporter of intracellular lipids and its levels are related with inflammation, characterized by a high expression of proinflammatory cytokines such as TNF-α, IL-6 and IL-1β. Palmitic acid (PA, C16:0) and oleic acid (OA; C18:1) are two of the most abundant fatty acids that participate in the formation of TGs in hepatic cells *in vivo* and *in vitro* (3). *Lampaya medicinalis* Phil. *(Verbenaceae)* is a small bush that grows in the "Puna atacameña" in the North of Chile. The infusion from leaves and aerial parts of the plant has been used by local ethnic groups to treat and cure inflammatory diseases (4). The aim of this study was to assess *in vitro* the effect of the hydroalcoholic extract of *Lampaya medicinalis* (HEL) against OA/PA-induced steatosis and proinflammatory marker expression in HepG2 hepatocytes.

Methods: HEL (0.01, 0.1, 1, 10 μg/mL) cytotoxicity potential (48 h) was evaluated by Trypan blue exclusion. Cells were exposed for 48 h to 1 mM OA/PA (2:1) in the presence or not of 0.01 or 10 μg/mL HEL. Intracellular TGs were assessed with Oil Red O staining and quantified with Nile Red reagent by fluorimetry. mRNA expression of *DGAT2, TNF-α, IL-6* and *IL-1β* was evaluated by qRT-PCR. FABP4 content was assessed by Western blot. The levels of TNF-α and IL-6 in the culture media were analysed by ELISA.

Results: HEL was not cytotoxic at any concentration assessed (n=4; $p>0.05$). The increased content of TG induced by OA/PA was reduced in the presence of HEL (n=7; $p<0.05$), showing a strong consistency with Oil Red O staining. The increase in the protein content of FABP4 as well as the increment in mRNA expression of *DGAT2, TNF-α, IL-6* and *IL-1β* induced by OA/PA were lower in cells co-exposed to HEL (n=6-9; $p<0.05$). The incubation with HEL+OA/PA reduced proinflammatory cytokine levels in culture media compared to cells exposed to OA/PA alone (n=6-7; $p<0.05$).

Conclusion: HEL reduces the OA/PA-induced increase in intracellular TG, DGAT2 and proinflammatory cytokine expression and FABP4 content, as well as the levels of secreted proinflammatory cytokines in HepG2 cells. These findings suggest a protective role for HEL against OA/PA-induced steatosis and inflammation, and therefore that *Lampaya medicinalis* may represent a promising therapeutic tool for pathologies such as NAFLD.

References: (1) Gluchowski L, et al. Nat Rev Gastroenterol Hepatol. 2017;14(6):343-355. (2) Perry, et al. Nature. 2014;510(7503):84-91. (3) Cunningham P, et al. J Nutr. 2009;139(4):636–639. (4) Morales G, et al. Biol Res. 2014;47:6.

Neuroendocrinology and Pituitary

NEUROENDOCRINOLOGY AND PITUITARY

Post-Surgical Metabolic Outcomes in Adult-Onset Craniopharyngioma: A Single Pituitary Center Experience

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Background:

Craniopharyngiomas, while benign, have the highest morbidity of all pituitary tumors. Hypothalamic obesity (HO), one of the most devastating consequences, is commonly studied in the pediatric population, but few data are available on weight and other metabolic outcomes in adult-onset craniopharyngiomas (AOCP).

Methods:

We conducted a retrospective chart review of 49 adult patients with AOCP who underwent surgery between 1/2014 and 5/2019 at an academic pituitary center. Weight, BMI, metabolic diseases (type 2 diabetes, hypertension, hyperlipidemia, cardiovascular disease, OSA), and pituitary hormone deficiencies were recorded pre-surgery and at last follow up and analyzed using paired t-tests or McNemar's test.

Results:

Median age was 56 years (51% women), 45% had >1 surgery (range 1-5), and 49% had radiotherapy. Of 72 total surgeries, 54% were craniotomies and 68% of surgeries resulted in subtotal resections. Median follow up was 25 months. Median BMI was 29.2 and 30.5 kg/m^2 at baseline and at last follow up, respectively. Weight was higher at last follow up (mean increase 2.7 kg; $p=0.043$), with an average of 4% weight gain. Patients with baseline normal and overweight BMI had significant weight gain (mean increase 5.1 kg, $p=0.045$; mean increase 5.5 kg, $p=0.015$ respectively), while those who were obese at baseline did not (mean increase 2.0 kg, $p=0.302$). The proportion of patients with obesity (BMI>30) increased from 37% to 53% ($p=0.008$). 31% of patients had >5% weight gain, with mean

increase in BMI of 4.1 kg/m^2 (p<0.0001) and mean weight gain of 13.1 kg (p<0.0001). 24.5% had an increase in the total number of metabolic diseases (p=0.07). Of 43 patients who were overweight or obese at last follow up, obesity was addressed in 51%, most commonly through lifestyle counseling (49%) and adjustment of hormone replacement in response to weight gain (23%). Two patients had bariatric surgery within one year of pituitary surgery. The proportion of patients with ≥3 hormone deficiencies increased from 18% to 55% (p=0.0003). At last follow-up, only one patient had GHD, diagnosed by low age-adjusted IGF-1 level. 14 of 15 patients with ≥3 hormone deficiencies had normal age-adjusted IGF-1 levels and one patient had normal GH provocative testing.
Conclusion:
Weight significantly increased after surgery for AOCP, with mean weight gain of 4%. 31% of patients had a marked increase in BMI and weight, suggesting possible HO. GHD is likely under-diagnosed in AOCP, and IGF-1 may not be a sensitive tool. Obesity-directed treatment is under-utilized in this patient population.

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RARE CAUSES AND CONDITIONS OF OBESITY: PRADER WILLI SYNDROME, LIPODYSTROPHY

Mediastino-Abdominal Lipomatosis: Deep Accumulation of Fat Mimicking a Respiratory Disease

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SUN-605

Introduction: Multiple systemic lipomatosis (MSL) is a rare disorder with unknown etiology. It is characterized by the massive development of non-encapsulated lipomas in subcutaneous tissues. Lipomatosis of the face, head, neck, extremities, abdomen, and pelvis have been reported in the literature. Case: We report a case of a 65 years old female (BMI: 34 kg/m2) with past medical history of hypertension, hyperlipidemia(DLD) diabetes mellitus type 2 and sleep apnea that was brought into emergency room (ER) for worsening shortness of breath. In the ER, she was having an oxygen saturation of 75% and required intubation. The patient was afebrile, with a BP of 120/75 mm Hg and a heart rate of 70/minute. Trans-thoracic echocardiogram revealed normal ejection fraction and normal pulmonary pressure with no wall motion abnormality. CXR showed no infiltration or consolidation. CT angiogram (CTA) ruled out pulmonary embolism but it was notable for large deposits of fat involving the abdomen and thorax, with invasion into the mediastinum and the space between the liver and diaphragm. Mesenteric fat was increased. Tissue was biopsied, which confirmed the diagnosis of fatty invasion. Discussion: Abdominal lipomatosis is characterized by massive enlargement of the abdomen due to intraperitoneal and retroperitoneal fatty deposits. Phenotypically patients can appear to be thin or obese, however, it is more common in the overweight population like our patient. Mediastinal lipomatosis is a benign cause of mediastinal widening, however patients can develop respiratory symptoms like exertional dyspnea due to compression of airways. MSL affects white caucasian between 25-60 years old and it is associated with DLD, impaired glucose tolerance, hyperuricemia, macrocytic anemia, and peripheral neuropathy. The pathophysiology is not fully understood, some theories stated that it is related to defective lipid mobilization in lipomatocytes, other suggested disorder in the mitochondria of brown fat. Conclusion: CT and MRI of the abdomen and chest are very helpful in the diagnosis of MSL but a tissue biopsy is what makes the final diagnosis. There is no definitive treatment; the recommendations are a healthy lifestyle including a low-fat diet, abstinence from alcohol and exercise. In severe cases, surgery is recommended.

Adrenal

ADRENAL CASE REPORTS I

Diagnostic Dilemma: An Adrenal Incidentaloma in a Young Adult

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SAT-199

Introduction:
In an adult endocrine clinic, the majority of patients referred for evaluation of an adrenal incidentaloma are older than 30 years of age. It is important to be reminded that a patient may be diagnosed with an adrenal mass at any age but the etiology may vary depending on the age at presentation.
Clinical case:
An 18 year-old African American female with no significant past medical problems presented with a 2 month history of flank and abdominal pain associated with nausea and vomiting. An abdominal CT scan and a dedicated adrenal CT showed a right adrenal mass measuring 2.2 x 2.6 cm. The noncontrast Hounsfield units were 23, enhanced Hounsfield units 210, and delayed Hounsfield units 72. The calculated washout was 44%, not consistent with an adrenal adenoma. An MRI of the abdomen showed a 2.5 cm right adrenal nodule. The lesion did not demonstrate significant loss of signal between in and out of phase imaging, therefore the characteristics were not consistent with a lipid rich adenoma. Laboratory tests included an ACTH of 31 pg/mL (6-48 pg/mL), cortisol 8.7 ug/mL at 10:57 am (7-9 am 5.27-22.45 ug/mL), aldosterone 10.1 ng/dL (6-48 ng/dL), renin 2.2 ng/mL/hr (upright 0.5-4.0 ng/mL/hr), DHEA-sulfate 129 ug/dL (44-248 ug/dL), plasma free metanephrine 0.10 nmol/L (0.00-0.49 nmol/L), and plasma free normetaneprhine 0.41 nmol/L (0.00-0.89 nmol/L). The 24-hour urine norepinephrine, epinephrine, and metanephrine were all normal, however the 24-hour urine dopamine was elevated, 824 ug/24 hrs (52-480 ug/24 hrs). Subsequently, plasma dopamine, norepinephrine, and epinephrine were all within the reference range. The patient had a robotic-assisted right adrenalectomy removing a 5.7 x 3.5 x 1.7 cm gland, weighing 16.3 grams. The pathology demonstrated a ganglioneuroma within the right adrenal gland measuring 2.2 x 2.0 x 2.7 cm, negative for neuroblastoma or blastic components. Focal hemorrhage