Neuroendocrinology and Pituitary

PITUITARY TUMORS II

Prolactin Response to Metformin in Cabergoline-Resistant Prolactinomas: A Prospective Study

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MON-LB60

Introduction: Prolactinomas are the most frequent pituitary-secreting tumors. Medical therapy with cabergoline (CAB), a dopamine agonist (DA), is the first line treatment, but 10% of prolactinomas are resistant to CAB. Recently, *in vitro* studies have shown anti-tumoral activity of metformin and other biguanids in human prolactinomas[1], which prompted us to investigate that possibility *in vivo*. Aim: To evaluate the effect of metformin (MET) on Prolactin (PRL) secretion in patients with CAB resistant prolactinomas. Design and Setting: Prospective interventional study in a single referral center. Subjects: Ten patients (7 M; mean age: 44 ± 12y) with CAB resistant (PRL: 148 ± 125ng/ml; range: 38 - 386) prolactinomas (all macroadenomas) and metabolic syndrome on maximally tolerated CAB doses (4.3 ± 1.2 mg/week; range: 2.0-7.0) for ≥ 6 months (45 ± 39mo; range: 6-120). Intervention: Oral extended release metformin (p.o.) was prescribed according to patient's tolerance (mean dose: 1.3 ± 0.4 g; range: 1.0-2.0). Main Outcome Measurements: Serum PRL (Elecsys, Roche, Indianapolis, USA), body weight (BW), fasting glycemia (FG) and HbA1C were evaluated before and at two time points during metformin treatment (30-60 and 120-180 days). Results: BW, FG, and/or HbA1C reductions were observed in 9/10 patients and mean FG decreased significantly (P=0.04). No significant changes were observed in serum PRL levels during metformin treatment [134 ± 124 ng/ml *vs* 138 ± 132 ng/ml *vs* 144 ± 129 ng/ml, before, at 30-60 days and at 120-180 days, respectively (P=0.499, mixed-effects analysis with the Geisser-Greenhouse correction)]. Individually, two patients exhibited a ≥ 50% decrease in PRL levels at a single timepoint (one at 30-60 days, with a further increase at 120-180 days and the other at 120-180 days). Conclusion: Metformin, at usual doses, did not inhibit prolactin secretion in patients with cabergoline-resistant prolactinomas. The discrepancy between our results and *in vitro* studies is not clear, but may be related to the much higher concentrations of metformin used *in vitro*[1] as compared to the serum concentrations observed in patients during metformin treatment[2]. References: [1]Gao J *et al.* Metformin inhibits growth and prolactin secretion of pituitary prolactinoma cells and xenografts. J Cell Mol Med. 2018 22:6368-79; [2] Frid A *et al.* Novel assay of metformin levels in patients with type 2 diabetes and varying levels of renal function: clinical recommendations. Diabetes Care 2010 33:1291-3.

Pediatric Endocrinology

PEDIATRIC GROWTH AND ADRENAL DISORDERS

Adult Growth Hormone Deficiency Transition Care From Pediatric to Adult Services: Insights From a US Advisory Board

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SAT-LB11

Background: Transition care of patients with childhood-onset GH deficiency (CO-GHD) who were treated with GH during childhood remains an ongoing challenge with substantial variation in coordination of care, clinical assessment, and management among pediatric and adult services. Despite the availability of clinical guidelines providing a framework for transition care of adolescents with CO-GHD, many patients discontinue therapy during the transition phase. **Methods:** A panel of pediatric and adult US endocrinologists with extensive experience in treating transition patients convened in October 2019 as part of an advisory board to address current clinical unmet needs and to share learnings based on a structured transitional plan to strive for optimal management of these patients. **Results:** It is acknowledged that pediatric endocrinologists play a crucial role in initiating the transition process, which involves close communication and direct collaboration between pediatric and adult services to reduce delays in identifying patients and resuming GH therapy in adulthood; adult endocrinologists need to increase their awareness of the importance of potential benefits and extent of long-term safety of GH therapy in adult patients. There is also a need for consensus guidelines or a white paper that focuses on transition care and endorsed by pediatric and adult organizations. Because not all patients with CO-GHD will have persistent GHD as adults, there is a need to improve the identification and timely retesting of those who will require continuity of GH therapy into adulthood. An increase in accessibility for retesting and guidance on appropriate GH dosing once persistent GHD is confirmed are other important factors. Certain subpopulations of pediatric patients (e.g., cancer survivors; patients with congenital hypopituitarism, optic nerve hypoplasia, treated sellar masses, and traumatic brain injury) should be prioritized in determinations of when and how retesting should be performed. The viewpoints of both pediatric and adult endocrinologists were presented at this meeting, and comprehensive considerations and suggestions were discussed. **Conclusion:** Transition care of patients with CO-GHD requires a collaborative multidisciplinary approach to ensure continuity of care between pediatric and adult services and to improve bone health and reduce long-term cardiometabolic risks. The major challenge is to effectively ensure that

transition patients are retested and offered adult GH therapy without delay. Current guidelines should be more focused on transition patients, addressing key areas of uncertainty as evidenced by variable clinical practices. A clearly structured transition protocol is vital, and these insights provide useful, practical guidance to clinicians to establish best practices when transitioning adolescents with persistent CO-GHD to adult services.

Adipose Tissue, Appetite, and Obesity

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

Metformin-Induced Weight Loss in Patients With or Without Type 2 Diabetes/Prediabetes

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MON-LB102

Background: Metformin is the first-line pharmacologic treatment for type 2 diabetes (T2DM). Its use has been associated with significant weight loss in patients with obesity with or without T2DM. However, it is unknown whether weight loss outcomes differ with metformin monotherapy in patients with excess weight and euglycemia compared to patients with T2DM/prediabetes (PreDM).

Methods: This is a retrospective study of new patients with overweight/obesity seen at an academic weight management center between 4/1/14-4/1/16. Patients who received metformin as a sole pharmacotherapy were identified, and data pertaining to demographics, medications, comorbidities, and weight changes during 1-year follow-up were obtained from their electronic medical records. Mean and categorical weight losses were compared between patients with and without T2DM/PreDM. We also assessed the rate of metformin discontinuation due to side effects, lack of efficacy or other reasons in the entire cohort.

Results:

Of 1056 patients who were prescribed metformin for weight loss over the 2-year study period and had at least 2 office visits, 99 (9.38%) discontinued the medication due to the following reasons: side effects 59 (60%), lack of efficacy 15(15%) or other reasons 25(25%). A total of 254 patients received metformin as a sole pharmacotherapy for weight loss and had 6 and/or 12-month follow-up visits. In this cohort, the mean age was 53 ± 14 years, 66% were women. The mean BMI was 35 ± 7 kg/m^2. The average percent weight loss at 6 and 12 months were similar in patients with euglycemia compared to patients with T2DM/PreDM (6.12% ± 5.68 vs 6.36% ± 6.52 p=0.73 at 6 months; 7.13% ± 6.42 vs 7.23% ± 7.74 p=0.93 at 12 months). The proportion of patients who experienced ≥5% weight loss was similar in both groups at 6-month (54.04 vs 54.55%, p=0.94) and 12-month follow-up visits (63.95 vs 55.42%, p=0.26). The proportion of patients who experienced ≥10% weight loss was also similar in both groups at 6-month (25.81 vs 27.72%, p=0.81) and 12-month follow-up visits (33.72 vs 30.12%, p=0.62).

Discussion: Among patients with obesity, metformin as a sole pharmacotherapy for weight loss achieved significant and comparable weight reduction in patients with or without T2DM/PreDM. Further studies are needed to evaluate the long-term weight loss in patients with euglycemia.

Adrenal

ADRENAL CASE REPORTS III

Adrenocortical Carcinoma: A Case Report

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MON-LB037

Adrenocortical Carcinoma: a case report

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Introduction:

Unilateral adrenal tumors are relatively common; adrenal incidentaloma has a prevalence of 4% on CT imaging. These masses are classified by their functional and malignant potential. We present here a case of adrenocortical carcinoma (ACC), a rare and often aggressive tumor that accounts for 2% of all adrenal incidentalomas. ACC has a worldwide incidence of disease of 0.5-2 cases per million population per year. While some instances of ACC are associated with hereditary conditions, most cases are sporadic mutations.

Case:

A 44-year-old male with a past medical history of hypertension, polysubstance use, and anasarca presented with a one-year onset of abdominal swelling. This was associated with a 16 pound weight loss over the prior 4 months and bilateral lower extremity swelling for the previous 3 weeks. Of note the patient had been detained in an adult corrections institution for over 5 years. Review of systems was negative for night sweats, nausea, vomiting, headaches, confusion, or palpitations. CT of the abdomen demonstrated a large mass involving the left adrenal gland measuring 28 x 27 x 31 cm, with punctate and delayed calcifications. Also noted were numerous bilateral lung nodules, and multiple liver lesions. Bilateral lower extremity ultrasound revealed a DVT involving the left gastrocnemius vein. A heparin drip was initiated and the patient was transitioned to Xarelto. CT scan of the chest demonstrated gastroesophageal junction lymphadenopathy, right hilar lymphadenopathy, numerous lung metastases and a prominent lesion in the left lower lung. Laboratory studies included both a low and high dexamethasone suppression test demonstrating a cortisol level 24 mcg/dL, metanephrines < 0.2 nmol/L, low testosterone 2.1 ng/dL (free) and 54 ng/dL (total), and DHEA 7.1 ng/mlL. Aldosterone <4.0 ng/dL and ACTH < 5 pg/mL. Biopsy for the adrenal mas was consistent with cortical neoplasm. Surgery recommend against debulking due to wide-spread metastases. Oncology recommended chemotherapy; a regimen of mitotane, etoposide, doxorubicin, and cisplatin, with glucocorticoid replacement in 28-day cycles x 6 through venous port.