Title

MON-040 11-Oxygenated C19 Steroids in Polycystic Ovarian Syndrome

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Authors

Mody, Armaiti
Lodish, Maya
Auchus, Richard
et al.

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He was diagnosed with Hashimoto thyroiditis (thyroid peroxidase antibody level 355 IU/mL, normal <9 IU/mL). He recovered without neurological deficits and was discharged home with thyroid replacement therapy (levothyroxine 100 mcg).

Discussion: Myxedema coma occurs as a complication of undiagnosed/untreated thyroid disease. It may be precipitated by an event such as infection, drug overdose, or myocardial infarction. The mainstay of treatment is T4 replacement along with supportive therapy, and glucocorticoids to counter possible underlying adrenal insufficiency. Massive pericardial effusion due to hypothyroidism, especially resulting in cardiac tamponade, is extremely rare. The incidence of pericardial effusion in patients with hypothyroidism has significantly decreased from 30–80% to 3–6%, due to early recognition of this common disorder. Our case highlights the importance of prompt recognition of hypothyroidism as a cause of cardiac tamponade, thus allowing rapid life-saving treatment. In patient populations with limited access to health care, it should be remembered that very late and potentially fatal complications of otherwise easily treatable conditions can occur. Awareness of this may help limit morbidity and mortality.

References: Kabadi UM, Kumar SP. Pericardial effusion in primary hyperparathyroidism. Am Heart J. 1990; 120:1393.

Healthcare Delivery and Education

EXPANDING CLINICAL CONSIDERATIONS FOR PATIENT TESTING AND CARE

Inappropriate Ordering of Parathyroid Scintigraphy in an Academic Medical Center

Brad Kimura, MD[1], Jodi Nagelberg, MD[2], Sonya Koo, MD[1], Karen Clare McCowen, BSC,MBBS,MRCPI,MD[1].

[1]UCSD, La Jolla, CA, USA, [2]UC San Diego, La Jolla, CA, USA.

MON-115

Introduction: The diagnosis of primary hyperparathyroidism is a biochemical, not radiologic one. Unfortunately, many practitioners even in academic centers order parathyroid scintigraphy to "confirm a diagnosis of adenoma" or distinguish primary from secondary hyperparathyroidism. Knowing the location of single or multiple parathyroid adenomas is unnecessary unless parathyroidectomy is planned. The financial burden of nuclear imaging is substantial. The goals of this study were to determine the proportion of inappropriately ordered parathyroid scans and the cost to the health care system.

Methods: We generated a database of patients who had consulted with at least one physician at our institution and underwent parathyroid scan between December 2012 and December 2017. We focused on the subset that did not undergo parathyroidectomy. "Slicer dicer" software in our EMR was used to generate the database. Chart review extracted data on diagnoses and reasons for parathyroid scintigraphy.

Results: Over 5 years, a total of 325 parathyroid scans were performed. 171 of these did not have parathyroidectomy in our system. However, 18 underwent surgery elsewhere leaving 153 that received parathyroid scans but no surgery (47% of the total). Of the 91 cases so far analyzed of the 153 in our database, average age is 64, with 28 males and 63 females. 61 of the 91 scans (67%) were performed to confirm the diagnosis of parathyroid adenoma; 3 performed because of possible parathyroid adenoma seen on other imaging; and 24 (26%) were done supposedly to localize the adenoma for surgery. Ordering physicians were from primary care (41%), endocrinology (26%), nephrology (18%), and surgery (10%). Final diagnoses for these 91 patients were true primary hyperparathyroidism in 37 (41%), secondary hyperparathyroidism in 38 (42%), unclear in 10 and FHH in 4. In the primary hyperparathyroidism group, 19/37 met criteria for consideration of parathyroidectomy, but only 5/19 received surgical consultation. These 5 patients either refused surgery or surgeon decided against, usually because of high surgical risk.

Conclusion: 47% of parathyroid scans at an academic institution were performed in patients who did not undergo parathyroidectomy. Many parathyroid scans were ordered inappropriately to "confirm" a diagnosis of primary hyperparathyroidism, leading to unnecessary charges and resource waste. Physician charges for sestamibi scans range from $237-$1942, depending on whether planar imaging, SPECT, or SPECT-CT is used; hospital charges are $1165-$3211. We propose to change the ordering system for parathyroid imaging to clarify that this is not a method to diagnose parathyroid adenoma, rather a tool to optimize surgical planning when the diagnosis is secure.

Reproductive Endocrinology

REPRODUCTIVE ENDOCRINOLOGY: REPRODUCTIVE FUNCTION AND DYSFUNCTION ON DEVELOPMENT

11-Oxygenated C19 Steroids in Polycystic Ovarian Syndrome

Armaiti Mody, MD[1], Maya Beth Lodish, MD[1], Richard Joseph Auchus, MD,PhD[2], Heather Gibson Huddleston, MD[1].

[1]UCSF, San Francisco, CA, USA, [2]University of Michigan, Ann Arbor, MI, USA.

MON-040

Background: Polycystic ovarian syndrome (PCOS), an endocrine and reproductive disorder consisting of hyperandrogenism, menstrual dysfunction and ovarian changes, affects 6–20% of reproductive aged women worldwide. While hyperandrogenemia is traditionally determined by evidence of elevated testosterone (T), this hormone can be difficult to accurately measure in women with relatively lower circulating levels compared to men. Recent studies have suggested that four adrenal androgens known as 11-oxygenated C19 steroids (11OxyAs), specifically 11-ketotestosterone (11KT), may be good alternative markers for hyperandrogenism in PCOS. Using a multiethnic population seeking evaluation for PCOS symptomatology, we sought (1) to investigate the utility of 11OxyAs to differentiate women with and without NIH PCOS relative to classical androgens such as T, androstenedione (A4) and DHEAS levels, and (2) to evaluate the relationship of 11OxyAs to clinical findings of androgen excess.

Methods: Using the University of California, San Francisco PCOS Tissue Bank, serum samples from 131

women seen for a PCOS evaluation were selected sequentially and identified as PCOS or non-PCOS (controls) based on meeting NIH criteria at the time of evaluation. In addition to obtaining gonadotropin and metabolic profiles, classical androgens and 11OxyAs were measured using mass spectrometry. The relationship of these androgens to modified Ferriman-Gallwey (mFG) scores and ovarian morphology were also assessed.
Results: Out of 131 women selected, 83 met NIH PCOS criteria at the time of evaluation and 48 did not (controls). Age and BMI did not differ among the two groups. As expected, total T, A4 and LH were all significantly higher in NIH PCOS. A trend towards higher HOMA-IR levels was also seen in NIH PCOS, but this did not reach statistical significance (3±3.9 mg/dL vs. 1.9±1.7 mg/dL, $p = 0.12$). No difference was seen in all four 11OxyAs between NIH PCOS and controls. Unlike previous studies, we also did not find mean 11KT levels to exceed that of T in both controls (T 393±143 pg/mL vs. 11KT 389±206 pg/mL) and PCOS (T 530±245 pg/mL vs. 11KT 388±201 pg/mL). In addition, no relationship was seen between HOMA-IR and 11β-hydroxyandrostenedione (11OHA4) or 11-ketoandrostenedione (11KA4) levels. Within PCOS, DHEAS and A4 were noted to have a weak but inverse relationship to BMI (r^2 0.05 $p = 0.05$; r^2 0.08 $p = 0.007$), whereas no correlation was seen between any of the four 11OxyAs or T and BMI. Lastly, 11OxyAs, T, and A4 levels did not predict mFG scores or polycystic ovarian morphology.
Conclusions: 11OxyAs levels were not statistically higher among women with NIH PCOS compared to at risk women who did not meet NIH criteria. There was no significant relationship between these androgens and mFG scores or ovarian morphology. Further studies are necessary to show the utility of 11OxyAs levels as a marker for hyperandrogenism or metabolic risk.

Pediatric Endocrinology

PEDIATRIC SEXUAL DIFFERENTIATION, PUBERTY, AND BONE BIOLOGY

Low-Dose Infigratinib Treatment Does Not Lead to Changes in Phosphorous Preclinically in Mice

Maribel Reyes, PhD[1], Uma Sinha, PhD[2], Gary Li, PhD[1], David Martin, PhD[1].
[1]QED Therapeutics, San Francisco, CA, USA, [2]BridgeBio Pharma, Palo Alto, CA, USA.

SUN-098
Background: Infigratinib (BGJ398) is a potent and selective FGFR1-3 inhibitor under evaluation for the treatment of achondroplasia, the most common form of disproportionate short stature. Low doses of infigratinib were shown to be effective in improving skeletal abnormalities in a mouse model of achondroplasia [Demuynck et al. 2019; Komla-Ebri et al. 2016]. At higher doses in adult patients (e.g. 10-100-fold the dose shown to have efficacy in preclinical models of achondroplasia) infigratinib appears to be associated with elevation in phosphorus, an effect known to be associated with FGFR1 inhibition. Specifically, FGFR1 inhibition leads to decreases in FGF23, which, in turn, leads to decreased excretion of phosphate by the kidneys. We sought to understand the relationship between lower doses of infigratinib and changes in phosphorus in preclinical animal models. **Methods:** Changes in phosphorus were tested at multiple doses in three different species - mouse, rat, and dog - across five different studies. Infigratinib was given orally at doses ranging from 0.03 mg/kg to 30 mg/kg. Both PK and PD (i.e., phosphorus) data was available in all species. Measurement days ranged from day 10 to week 12, although PK/PD measurements occurred within 1 day of each other. All animals were treated in accordance with AVMA guidelines. **Results:** No significant dose-phosphorus relationship was observed in rats and mice treated with doses of infigratinib ranging from 0.03 mg/kg to 5 mg/kg. A dose-phosphorus and exposure ($AUC_{0\text{-}24}$)-phosphorus relationship was observed at doses of infigratinib ≥10 mg/kg across transgenic mouse, rat, and dog studies. At low doses, the exposure ($AUC_{0\text{-}24}$)-phosphorus relationship showed a shallow slope with linear regression analysis in rats and mice. **Conclusions:** These findings from five studies in three different species indicate that the exposure-phosphorus relationship is consistent. Importantly, no relationship was observed between dose and phosphorus levels in rats and mice treated with infigratinib at or below 5 mg/kg. Despite the fact that infigratinib is a FGFR1, 2 and 3 inhibitor, low doses of infigratinib shown previously to exert a significant effect in improving skeletal abnormalities in an achondroplasia mouse model, do not seem to result in meaningful changes in phosphorus. These experiments demonstrate that at doses of infigratinib much lower than used in oncology - like those being considered for use in clinical studies of achondroplasia - infigratinib is less likely to cause hyperphosphatemia. Infigratinib will be evaluated in global clinical studies in children with achondroplasia in 2020.

Tumor Biology

TUMOR BIOLOGY: DIAGNOSTICS, THERAPIES, ENDOCRINE NEOPLASIAS, AND HORMONE DEPENDENT TUMORS

Preoperative Hematological Parameters Associated with Recurrence or Regrowth of Meningiomas

Carolina Garcia Soares Leães Rech, MD, PhD[1], Ricardo Kunde Minuzzi, MD[1], Camila Batista de Oliveira Silva, MsC[2], Bruna Araújo, Undergraduate student[2], Tainá Mafalda, Undergraduate student[2], Nelson Pires Ferreira, MD, PhD[1], Miriam da Costa Oliveira, MD,PHD[1], Júlia F Semmelmann Pereira-Lima, MD, PhD[1].
[1]Neuroendocrinology Center Santa Casa of Porto Alegre, Porto Alegre, Brazil, [2]Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil.

SUN-130
Preoperative Hematological Parameters Associated with Recurrence or Regrowth of Meningiomas
Abstract: Meningiomas represent the most frequently diagnosed intracranial tumors. Inflammation and immune processes may play an important role in therapeutic response as well as in anti- and pro-tumor modulating function. In tumors, inflammatory markers have been able to provide useful prognostic information for treatment or clinical evaluation of patients. The aim of this study was to investigate preoperative hematological markers concerning