cascade of mistreatment with serious consequences. The case presented highlights the challenges encountered in taking care of such patients. It is necessary to understand the pre-testing probability to reach a precise conclusion. Factitious disorder or sample contamination can be yet another challenge in the differential diagnosis of Cushing's work up.

(1)
Raff H Measurement of Late-Night, Salivary Cortisol and Cortisone by LC-MS/MS to Assess Preanalytical Sample Contamination with Topical Hydrocortisone. Clinical Chemistry 58:5 (2012)

Reproductive Endocrinology

CLINICAL STUDIES IN FEMALE REPRODUCTION I

Comparison of Estradiol by Mass Spectrometry Versus Immunoassay in Women Undergoing Menopause: Study of Womens Health Across the Nation (SWAN)

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SAT-027

Serum estradiol (E2) concentrations in midreproductive women are easily measured using a variety of conventional immunoassays (IA). However, when women approach and traverse menopause, E2 eventually drops below levels where IA lacks sufficient sensitivity to accurately measure E2. Liquid chromatography and tandem mass spectrometry (LC/MS/MS) has become the standard method for assessing steroid hormones, especially when circulating concentrations are low. We evaluated the relationship between IA and LC/MS/MS E2 measurements in a cohort of women taken from the Study of Womens Health Across the Nation (SWAN) to assess the degree of agreement between the two methods and to determine the level of E2 at which IA becomes unreliable.

Methods: 315 serum samples that had been previously measured for E2 using IA were re-analyzed using LC/MS/MS performed by one of the authors (RA). In this original set, E2 levels that were below the limit of assay detection (LLD, 6 pg/ml) were interpolated as a random number between 0 and the LLD. Agreement between all 315 samples was assessed using both Pearson and Spearman correlation. The analysis was repeated excluding the subset of specimens that were below the lower limit of detection (LLD) for the IA E2 assay (6 pg/ml; N=176), and a third set of correlations was obtained for specimens that measured <15 pg/ml by IA but were above the 6 pg/ml LLD (N=82).

Results: The overall dataset (N=315) demonstrated excellent agreement between IA and LC/MS/MS with a Pearson's r and Spearmans r of 0.98 AND 0.60, respectively. When the subset of 176 samples above the LLD were assessed, Pearson's r was 0.98 and Spearman's r was 0.81. In contrast, when specimens measuring 6–15 pg/ml by IA were compared to LC/MS/MS, Pearson's r was -0.03 and Spearman's r was 0.09, indicating a complete loss of relationship between the two methods.

Conclusions: The IA used by SWAN (England, Clin Chem 2002; 48: 1584) and LC/MS/MS demonstrate excellent correlation for E2 measurements above 15 pg/ml. However, circulating concentrations of E2 below 15 pg/ml were not accurately measured using IA.

Reproductive Endocrinology

FEMALE REPRODUCTION: BASIC MECHANISMS

NALCN Expression Is Regulated by Progesterone and Estrogen in Human Myometrial Smooth Muscle Cells

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MON-011

During pregnancy, the uterus transitions from a quiescent state to a highly contractile, excitable state. Both ion channels and hormones are essential for this transition. We recently identified that the Na^+ leak channel, non-selective (NALCN) contributes to a leak current in human MSMCs and mice lacking NALCN have prolonged and dysfunctional labor. Additionally, NALCN levels change throughout mouse pregnancy suggesting regulation by hormones of pregnancy, specifically estrogen and progesterone. Here, we tested the hypothesis that P4, a pro-quiescent hormone, and E2, a pro-contractile hormone, regulate NALCN expression and current in the myometrium. In a human immortalized myometrial cells (HM6ERMS2), using qPCR we measured a 2.3 fold decrease and a 5.6 fold increase in NALCN mRNA expression in the presence of E2 and P4, respectively. These findings were also confirmed when NALCN protein expression were measured by immunoblot. Conversely, treatment with the ER antagonist, ICI 182,780, significantly increased NALCN mRNA expression, while treatment with the PR antagonist RU486 significantly decreased NALCN mRNA expression suggesting E2 and P4 work through their respective receptors to regulate NALCN. P4 differentially regulates myometrial activity depending on which progesterone receptor is activated: PRA, promotes contractility, whereas PRB promotes quiescence. Thus to study the effect of each PR, we used a human myometrial cell line stably expressing PRA or PRB, and measured similar increases in NALCN mRNA expression in both cell lines treated with P4. To determine the functional consequences of E2 and P4, we measured NALCN-dependent leak current in MSMCs using whole cell patch clamping. We observed that E2 significantly inhibited while P4 significantly enhanced NALCN current. Finally, we identified estrogen response and progesterone response elements (ERE and PRE) in the NALCN promoter and showed that the PREs contributed to P4 regulation while the ERE did not contribute to the regulation of NALCN expression using luciferase based promoter assays. Overall, our findings show that NALCN is upregulated by P4, the

pro-quiescent hormone, and downregulated by E2, the pro-contractile hormone. This data reveals a new mechanism by which NALCN is regulated in the myometrium and may suggest a novel role for NALCN during pregnancy. Further investigation into these novel roles can provide an insight into potential targets to modulate uterine quiescence and contractility.

Diabetes Mellitus and Glucose Metabolism

DIABETES TECHNOLOGY AND ADVANCES IN CLINICAL TRIALS

Efficacy and Safety Comparison Between U100 Regular Human Insulin and U100 Rapid Acting Insulin When Delivered by a 24 Hour Wearable Insulin Delivery Device in Type 2 Diabetes

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OR30-02

Introduction: Increasing insulin prices have led to a renewed debate to determine if Rapid Acting Insulin (RAI) analogs offer an advantage over less expensive Regular Human Insulins (RHI). The steep increase in the cost of RAI has led to rationing of insulin or the total discontinuance of therapy by many patients due to cost. For many, RHI provides a more affordable option for insulin therapy when compared to RAI, especially if the limitations of the insulin profile can be overcome by delivering RHI through continuous subcutaneous insulin infusion (CSII) using a wearable insulin delivery device. To our knowledge, no data exists in a type 2 diabetes (T2D) population comparing RAI to RHI when delivered via CSII. **Methods:** This 14 week multi-center prospective, randomized parallel, non-inferiority study in a T2D population compared the efficacy and safety of RAI versus RHI when delivered by V-Go®, a 24-hr wearable patch-like insulin delivery device that provides a preset continuous basal rate of insulin and on-demand bolus dosing. This study was conducted in a real-world practice setting under usual standard of care. Glucose lowering agents were to remain stable unless removal warranted due to documented clinically significant hypoglycemia and the only specific guidance for insulin titration was to down-titrate if blood glucose levels were consistently lower than target range. Patients administering RAI with V-Go were randomized 1:1 to continue RAI or to switch to RHI. Primary endpoint assessed non-inferiority for the between group net difference in HbA1c derived from a mixed model analysis. Between group differences from baseline for insulin total daily dose (TDD) and hypoglycemia (based on 7 point glucose profiles) were evaluated as secondary endpoints. **Results:** One hundred thirteen patients (59 RHI and 54 RAI) were evaluated. Baseline characteristics were similar between cohorts. The mean change in HbA1c with RHI was -0.60% from a baseline of 8.41% vs -0.38% from a baseline of 8.33% with RAI (estimated treatment difference [ETD]: -0.22%; 95% confidence interval [CI] -0.67% to 0.22%; non-inferiority margin<0.4% and p=0.007). The mean change in TDD with RHI was 0.8 U/day from a baseline of 61.0 U/day vs 1.8 U/day from a baseline of 61.3 U/day with RAI (ETD: -1.04 U/day; 95% CI: -3.18 U/day to 1.11 U/day; p=0.92). The absolute change in percent of patients reporting hypoglycemia (≤ 70 mg/dL) from pre-randomization to post-randomization was +5.08% with RHI vs + 5.56% with RAI (ETD: -0.48%; 95% CI: -10.6% to 9.1%; p=0.91). Severe hypoglycemia was not reported in either cohort. **Conclusion:** Patients with T2D administering RAI with V-Go can safely switch to RHI maintaining similar glycemic control.

Thyroid

THYROID CANCER CASE REPORTS I

Poorly Differentiated Thyroid Cancer Arising from a Hyperfunctioning Nodule Treated with I-131

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SUN-478

Thyroid nodules are a common clinical problem with an incidence of up to 1% in men and 7–15% of cases representing thyroid cancer. Current American Thyroid Association guidelines do not recommend cytologic evaluation of hyperfunctioning nodules as they rarely harbor malignancy. We present a case of a hyperfunctioning nodule which years after ablation was diagnosed as a poorly differentiated thyroid cancer.

A 38 year old male had a 4cm thyroid nodule discovered in 1994. Nuclear Medicine (NM) imaging revealed a warm nodule though patient was euthyroid. Biopsy was benign with good sample. Nodule was followed with serial ultrasound (US) and TSH. In 2008 he became hyperthyroid. Scan showed hot nodule and he was given 27.3 mCi I-131 with normalization of the TSH. In 2013 patient again developed hyperthyroidism. NM imaging showed a hot nodule. After 29.5 mCi I-131 he became hypothyroid requiring levothyroxine. Intermittent US showed stability. In early 2019 nodule was 3.7cm, solid and hypoechoic but more heterogeneous. Despite TIRADS recommendation that nodule no longer be followed by US, FNA was performed and revealed Bathesda IV cytology. Gene classification with Thyroseq revealed a TERT mutation. On total thyroidectomy pathology demonstrated a 4.5cm poorly differentiated carcinoma thought to be of follicular origin. Tumor was partially encapsulated with multiple areas of vascular invasion and extensive tumor necrosis. Tumor was present at inked margin but no extrathyroidal extension was noted. There was a <1mm metastasis noted in 1 peri-isthmus lymph node. One month post operatively thyroglobulin was 123.5 ng/mL. I-123 whole body scan demonstrated bilateral uptake in the region of the thyroid suggesting adenopathy; there were similar findings on FDG-PET scan but no adenopathy was identified on US or the CT portion of the