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MON-006

The softgel, vaginal 17β-estradiol (E2) insert (TX-004HR) significantly improved the maturation index of the vaginal epithelium, dyspareunia and vaginal dryness in menopausal women with vulvar and vaginal atrophy (VVA) and moderate to severe dyspareunia, without histological changes to the endometrium (Constantine G et al, *Menopause* 2017;24:409-416). The 4-µg and 10-µg E2 doses were FDA approved as Imvexxy® (TherapeuticsMD, Boca Raton, FL), for the treatment of moderate to severe dyspareunia, a symptom of VVA, due to menopause. The progesterone receptor (PR) is an estrogen-regulated gene with expression that is very sensitive to E2 exposure (Xiao CW and Goff AK, *J Reprod Fertil*.1999;115:101-109). Endometrial PR expression in the biopsies of women using the softgel vaginal 4-µg E2 insert was used as a marker of E2 exposure to determine whether sufficient E2 applied with the vaginal insert reaches the endometrium to upregulate PR expression. Our hypothesis posits that there would be insufficient E2 from the 4-µg E2 insert to stimulate an increase in endometrial PR expression.

In this post hoc analysis of the REJOICE trial, endometrial biopsies from 25 women who had a normal baseline biopsy, an on-therapy biopsy after study day 70, and tissue readings from all pathologists were randomly selected from the 4-µg E2 vaginal insert and placebo groups. Endometrial tissue sections were stained to visualize PR expression using PgR1294 (Agilent; Santa Clara, CA). Cell staining was quantified using a trainable feature-recognition algorithm and mean expression levels between baseline and week 12 were analyzed by 2-sided t-tests.

Acceptable PR expression results were available for 22 women in the 4-µg E2 group (three had insufficient tissue for analysis) and 25 women in the placebo group. For the 4-µg E2 group, mean ± SD (pmol/mg) PR expression was 0.455 ± 0.203 at baseline and 0.506 ± 0.226 at week 12. For the placebo group, mean PR expression was 0.579 ± 0.196 at baseline and 0.563 ± 0.213 at week 12. Mean PR expression levels at baseline and week 12 were not significantly different from each other within the 4-µg E2 (P=0.438) or placebo (P=0.783) group. No meaningful difference in endometrial PR expression was observed with the vaginal 4-µg E2 insert at week 12. These data support our hypothesis and the assertion that low-dose, local vaginal E2 exposure with the insert placed in the lower part of the vagina, does not pose an endometrial safety issue in postmenopausal women.

Adrenal

ADRENAL PHYSIOLOGY AND DISEASE

The Intra-Individual Variability of 11-Ketotestosterone and 11β-Hydroxyandrostenedione.

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SUN-208

Background

Emerging evidence has suggested the 11-oxygenated steroids may be important in the diagnosis and monitoring of hyperandrogenism. Two in particular, 11-ketotestosterone (11KT) and 11β-hydroxyandrostenedione (11OHA4) have been implicated in polycystic ovary syndrome, congenital adrenal hyperplasia, precocious puberty and castration resistant prostate cancer. Despite the interest in these analytes, some of their more fundamental properties have yet to be determined. At present, no data is available that quantifies the biological variation of 11KT and 11OHA4 within individuals over time, this may be important as we look to establish normative reference ranges for these potentially useful analytes.

Objective

Here we sought to define the intra-individual variability of 11KT and 11OHA4 in serum using LC-MS/MS.

Method

Blood was collected from 18 healthy volunteers (8 males, 10 females) on the same day each week over a 10 week period using standard venepuncture technique. After collection, the samples were centrifuged within 1 hour, aliquoted and stored at -20°C (-4°F) prior to analysis. All samples from individual volunteers were analysed by LC-MS/MS in triplicate within the same batch so as to limit analytical variability.

Results

The mean analytical coefficient of variation (CV%) for the triplicate analysis was 3.2% for 11KT and 3.7% for 11OHA4. No significant difference was observed between the variability of 11KT concentrations in the male and female cohorts; total intra-individual variation for 11KT was 18.0%. Concentrations of 11OHA4 were more variable in the male cohort when compared to the female cohort. This was reflected by differences in their respective intra-individual variations of 32.5% vs 24.8%.

Summary

Intra-individual variation is an important consideration when interpreting patient results. Concentrations of 11KT were tightly regulated in both the male and female cohorts with no clear demarcation between the two groups. Although concentrations of 11OHA4 were prone to greater variation over the 10 week period, considerable overlap was observed between the male and female subjects. Our data suggests that 11KT and 11OHA4 concentrations are not significantly affected by the menstrual cycle.

Neuroendocrinology and Pituitary

HYPOTHALAMIC-PITUITARY DEVELOPMENT AND FUNCTION

Pituitary Developmental Defects Caused by Haploinsufficiency for the Transcription Factor SIX3 Are Worsened by POU1F1 Deficiency.

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SAT-288

Advances in genomic technologies are revolutionizing the practice of medicine by delivering molecular diagnoses that can be informative for prognosis and treatment of genetic