Reproductive Endocrinology
TRANSGENDER CARE

Stability of Weekly Intramuscular Estradiol Cypionate in a Transgender Woman

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Background: Transgender women often take estrogen with or without an antiandrogen to achieve the physical and physiological changes of estrogen. Estradiol may be administered through intramuscular (IM) injection weekly or every other week (1). It is thought that weekly IM estradiol may be more stable than every other week administration. The objective of this case was to evaluate the levels of IM estradiol cypionate when administered weekly.
Clinical Case: A 38-year-old transgender woman with a past medical history of gender dysphoria, type 2 diabetes mellitus, hyperlipidemia, obstructive sleep apnea compliant with continuous positive airway pressure, class 3 severe obesity, anxiety, depression and a non-smoker, presented for evaluation for hormone replacement therapy (HRT). The patient wished to begin IM estradiol because she heard it was most effective. She was started on estradiol cypionate 0.5 mL (2.5 mg) IM every Sunday along with spironolactone 100 mg daily. Approximately one month later, her estradiol was 65.8 pg/mL on a Saturday, total testosterone by LC-MS/MS was suppressed to 7 ng/dL (male: 300-1080 ng/dL, female: 9 - 55 ng/dL), FSH <0.3 mIU/mL (1.5-12.4), LH <0.3 mIU/mL (1.7-8.6). We increased her estradiol cypionate to 0.8 mL (4 mg) IM every Sunday to achieve goal estradiol levels up to 100-200 pg/mL. Approximately 2 months later, estradiol was up to 160 pg/mL on a Thursday. FSH and LH remained suppressed. Spironolactone was stopped. Patient gave her estradiol dose every Sunday between 4:15-7 PM. She injected on the lateral thigh switching sides every week. At the patient's request, blood was drawn on distinct days of the week going further from the day of injection as data collection progressed. The data we received: Monday: 153 pg/mL, Tuesday: 164 pg/mL, Wednesday: 147 pg/mL, Thursday: 122 pg/mL, Friday: 134 pg/mL, Saturday: 167 pg/mL. All labs were drawn between approximately 9:30-10:15 AM.
Conclusion: Our patient wanted to see just how stable weekly IM estradiol cypionate was. We found she was able to stay within target physiologic estrogen levels, 100-200 pg/mL, throughout the week. Overall mean +/- standard deviation levels for the six samples taken between injections were 148 +/- 17 pg/mL (range: 122-167). This case provides reassurance to clinicians concerned IM estradiol may cause supraphysiologic estradiol levels.
References: 1. Wylie C Hembree et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline, The Journal of Clinical Endocrinology & Metabolism, Volume 102, Issue 11, 1 November 2017, Pages 3869-3903, https://doi.org/10.1210/jc.2017-01658

Reproductive Endocrinology
TRANSGENDER CARE

The Role of the Endocrinologist in the Gender Adequacy Process and the Barriers for Adequate Transgender Health Care

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The transgender universe comprises a wide range of individuals who do not identify with the gender role related to their birth sex, presenting distinct gender identities that transcend the binary concept of female and male. The follow-up of this population requires specific knowledge and training for its demands and peculiarities. Hormone therapy is a key point in the process of gender adequacy, and despite the increase in demand for specialized health services, there are still many barriers to full and free of prejudice health care. This is a descriptive and exploratory study about the characteristics of the professional training of the doctors involved in transgender health care, in particular the endocrinologist, and to enable an overview of the doctor-patient relationship and medical follow-up in the context of transsexuality in the Federal District. For this purpose, questionnaires were used for physicians: endocrinologists, family and community physicians, urologists, and psychiatrists; and transgender people residents of the Federal District. This study shows that most of the professionals involved in the process of gender adequacy, in particular the endocrinologist, do not present confidence or knowledge to accomplish it, and prejudice is still presented in a striking way in health care. In Federal District, services are not adequately structured for the care of this population, both from the perspective of doctors and transgender people. Moreover, in this sample, it was observed that the higher degree of specific knowledge in the subject increases the sensation of confidence of the professional to treat transgender people but does not correlate with the prejudice.

Reproductive Endocrinology
TRANSGENDER, DSD, AND TURNER SYNDROME

Copy Number Variations Are More Frequent on Chromosome 14 as Compared to X Chromosome in Suspected Turner Syndrome Girls - A Chromosomal Microarray Analysis

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Introduction: Turner syndrome(TS) is defined by complete/partial monosomy of X chromosome in association with classic clinical manifestations. Conventional karyotyping is the gold standard test for diagnosis of TS. However it is labour intensive and inaccurate for detecting mosaicism, marker chromosomes and sub-microscopic deletions/duplications. TS is characterized by heterogeneous phenotypes despite identical karyotypes and precise genotype-phenotype correlations have not yet been deciphered. Presence of TS specific features in absence of X chromosome abnormality, evokes the hypothesis of possible autosomal involvement. Here, we report detailed Chromosomal microarray (CMA) analysis of 47 girls with clinically suspected TS, using Affymetrix CytoScan 750K array. **Materials and Methods:** The clinical diagnosis

of TS was based on recommendations by clinical practice guidelines from 2016 Cincinnati International TS meeting. Peripheral venous sample was collected in EDTA tubes and DNA was extracted using Qiagen-DNAeasy Blood and Tissue kit (Cat No. 69504). DNA samples were then hybridized to the Affymetrix CytoScan 750K array as per manufacturer's instructions. The data obtained was analysed using Chromosomal Analysis suite software and public genomic databases- ISCA, OMIM, DGV, DECIPHER. For bioinformatic analysis, all the genes (172) implicated in TS were retrieved from DisGeNET database. A TS-interactome of 4033 genes was then constructed from these genes and their first-degree neighbours from complete human interactome. Thereafter compilation was done based on CMA results and a protein-protein interaction network of 316 nodes was constructed. **Results:** Mean age of study cohort was 15.8 ± 3.64 years with short stature being the most common presenting phenotype (91.4%). CMA analysis detected copy number variations (CNVs) on chromosome 14 in 42 (89.3%) of 47 cases while X chromosome CNVs were present in only 28 (59.5%) cases, with all patients clinically qualifying as TS. Total 445 CNVs were discovered on X chromosome and 64 CNVs were found on Chromosome 14 exhibiting either CNV gain at 14q32.33 or CNV loss at 14q11.2 or both. The 30 cell karyotype was available for 27 patients and was found to be false negative in 7 (14.8%) patients. Also, 6 out of 47 cases had Y chromosome translocation detected on CMA that failed detection by karyotype. On enrichment analysis, thirty KEGG pathways were found to be enriched by the overlapping genes between TS-interactome and the interactome constructed by genes located within 14q11.2, and 14q32.33 67% of genes (212) in this network overlap with TS-interactome.
Conclusions: CMA is a superior diagnostic modality for TS than karyotyping. Functional interactomes between Chromosome X and Chromosome 14 on enrichment analysis reveal novel pathways underlying phenotypic manifestations.

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Development of Repository From a Pediatric Gender Clinic

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Objectives: With the publication of updated guidelines for care of transgender and gender non-conforming individuals, there has been an increase in the presence of gender diversity in both mainstream media and medical literature. Several gaps currently exist in medical knowledge regarding long term effects of gender-affirming therapies. There is a lack of standardization in study design, patient sampling, and outcome measures, and most studies are retrospective. Here we describe the creation of both a retrospective and prospective repository of patients who presented to the Massachusetts Medical School-Baystate Medical Center (UMass-Baystate) pediatric gender program.
Methods: Baystate Medical Center is located in western MA and is a tertiary referral center. A pediatric gender clinic was created in 2014. A repository containing both retrospective and prospective data was approved by the UMass-Baystate IRB to include patients ages 2 to 24 years of age who presented to our gender clinic. Retrospective data was obtained using the McKesson billing database. Sociodemographic, clinical and behavioral health data were collected. We are consenting individuals as they present to the clinic for the prospective component. Those that have consented fill out a survey at each visit. The repository has been approved to follow outcome data for 25 years.
Results: To date, we have 218 individuals in the repository, 75 of which are in the prospective component. Age of presentation ranged from 6 yrs to 24 yrs with an average age of 15 yrs. 62% identified as transmale, 31% as transfemale and the remainder as gender fluid or other. 75% have been prescribed gender affirming hormone therapy (56% GnRH agonist therapy, 20% estrogen, 58% testosterone). Of those being followed prospectively, 76% identified as white, 19% Hispanic. 79% were satisfied or very satisfied with their care.
Conclusions: Here we describe the demographic and clinical characteristics of patients that have presented to our gender clinic since 2014. The creation of our gender repository will allow us to assess sociodemographic, clinical and behavioral health outcomes of treatment, including metabolic parameters, bone health, and mental health outcomes in our pediatric population. Future projects include assessment of the change in cardiovascular risk in individuals on gender-affirming hormone therapy.

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TRANSGENDER, DSD, AND TURNER SYNDROME

Evaluation of Enzymatic Activity of Various HSD17B3 Mutants Using Androgen Receptor-Mediated Transactivation

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17β-Hydroxysteroid dehydrogenases (17β-HSDs, HSD17B) catalyze the reduction of 17-ketosteroids and the oxidation of 17β-hydroxysteroids to regulate the production of sex steroids. Among HSD17B family, 17β-HSD type 3 (HSD17B3) is expressed in testicular Leydig cells and contributes to development of male sexual characteristics by converting androstenedione (A4) to testosterone (T). Mutations of HSD17B3 genes cause a 46,XY disorder of sexual development (46,XY DSD) as a result of low T production. Therefore, the evaluation of HSD17B3 enzymatic activity is important for understanding and diagnosing this disorder. Although various amino acid substitutions of HSD17B3 have been reported in previous studies, the enzymatic activities of these proteins were often not defined. This is probably due to the difficulties that such enzymatic activities have been evaluated by quantifying the conversion of A4 into T using radioactive isotopes and liquid chromatography-mass spectrometry-mass spectrometry (LC-MS/MS). We adapted a method that easily evaluates enzymatic activity of HSD17B3 proteins by quantifying the conversion from A4 to T using androgen