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Original Article

Physiologic Response to Gender-Affirming Hormones Among Transgender Youth

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ABSTRACT

Purpose: The purpose of this study was to examine the physiologic impact of hormones on youth with gender dysphoria. These data represent follow-up data in youth ages 12–23 years over a two-year time period of hormone administration.

Methods: This prospective, longitudinal study initially enrolled 101 youth with gender dysphoria at baseline from those presenting consecutively for care between February 2011 and June 2013. Physiologic data at baseline and follow-up were abstracted from medical charts. Data were analyzed by descriptive statistics.

Results: Of the initial 101 participants, 59 youth had follow-up physiologic data collected between 21 and 31 months after initiation of hormones available for analysis. Metabolic parameters changes were not clinically significant, with the exception of sex steroid levels, intended to be the target of intervention.

Conclusions: Although the impact of hormones on some historically concerning physiologic parameters, including lipids, potassium, hemoglobin, and prolactin, were statistically significant, clinical significance was not observed. Hormone levels physiologically concordant with gender of identity were achieved with feminizing and masculinizing medication regimens. Extensive and frequent laboratory examination in transgender adolescents may be unnecessary. The use of hormones in transgender youth appears to be safe over a treatment course of approximately two years.

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IMPLICATIONS AND CONTRIBUTIONS

This prospective, observational data suggest the safety of cross-sex hormone use among youth with gender dysphoria over a treatment course of at least two years. The findings reported here may help improve provider and caregiver comfort moving forward with hormonal therapy for minors and young adults with gender dysphoria.

Over the past seven years, there has been a significant increase in the number of youth presenting for care related to gender dysphoria in gender-specific clinics, and in primary care settings [1–3]. Gender dysphoria is widely understood as the persistent distress that arises as the result of an incongruence

between one's assigned sex at birth (male or female) and one's experienced gender (male, female, both, or neither). Many youth with gender dysphoria seek medical intervention (pharmacological and/or surgical) to bring their phenotypic presentation into closer alignment with their gender of identity. Because there is a paucity of data related to the impact of gender-affirming hormones in youth, providers, caretakers, and community members experience trepidation about the safety and efficacy of their use in transgender adolescents. This article describes the physiologic impact of gender-affirming hormones among adolescents seeking phenotypic gender transition after approximately two years of gender-affirming hormone treatment.

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Background

Although the presence of primary sex characteristics is often described as a source of distress for transgender youth, the development of “incorrect” secondary sex characteristics during endogenous puberty is the cause of great suffering for many. Some youth describe feeling confused by sexually incongruent development, some feel betrayed by their bodies, and many experience heightened levels of anxiety, depression, and sometimes suicidal thoughts and attempts [3]. The past decade has improved access to care for many youth, but the scarcity of skilled and knowledgeable medical providers has continued to make access to care challenging for transgender youth throughout the country. The dearth of available data regarding medical protocols and outcomes contributes to a lack of continuity about hormone administration, timing, doses, and expected response. Dutch investigation indicates that hormone treatment in adolescence followed by gender confirmation surgery is effective in mitigating gender dysphoria [4]. Despite these findings, there remains an ongoing concern among providers and parents about the safety of hormone use among youth with gender dysphoria.

In 2006, the use of gonadotropin-releasing hormone (GnRH) analogs for suppression of endogenous puberty was introduced by a team of professionals in the Netherlands, and significantly altered the landscape of transgender youth care [5]. For those youth who present early enough for care, having endogenous puberty placed on hold allows them an opportunity to explore gender, learn more about exogenous hormones, and get a deeper understanding of the challenges of navigating the world as an individual of transgender experience [6]. However, most youth are presenting for care well into, or even beyond their endogenous pubertal development. Most youth presenting well into endogenous puberty desire hormones to bring their bodies into closer alignment with their gender.

Feminizing hormones

The use of gender-affirming hormones in transgender adults for the purpose of phenotypic gender transition is well documented, and demonstrates both efficacy and safety [7,8]. Weinand and Safer reviewed published longitudinal data examining the impact of hormones in transgender adults. Among transfeminine adults (those assigned male at birth who identify somewhere along the feminine spectrum) who were administered feminizing hormones for phenotypic changes, a small risk of venous thrombotic events ranging between 1% [8] and 8% [9] was reported depending on the type of estrogen used in the treatment protocol and other existing risk factors (smoking, proximity to surgery, hypercoagulable states). Other cardiovascular events reported were also rare. Among these studies, findings consistently describe no increased cancer risk for transfeminine individuals undergoing hormone therapy. Changes in physiologic measures for transfeminine individuals include mixed results about changes in lipid profile [10]. Liver function tests and hematocrit did not change with feminizing hormone use [10,11]. An increase in prolactin levels, enlarged pituitary glands, and prolactinomas (six cases) has been reported with feminizing hormone therapy [7,12]. Increased mortality among the transfeminine population is a result of AIDS-related complications, suicide, substance abuse, and cardiovascular disease [13].

Masculinizing hormones

Among adult transmasculine individuals (those assigned female at birth who identify somewhere along the masculine spectrum of gender) who underwent hormone therapy with testosterone, there was no reported increase in cardiovascular disease, cancer, or reproductive tract sequelae. Hemoglobin and hematocrit increased in those taking testosterone, but remained within normal male range. Increased insulin resistance and fasting glucose were both noted as sequelae for transmasculine individuals taking hormones. A higher rate of polycystic ovary syndrome diagnoses among pre-hormone transmasculine individuals may contribute to some of these findings in that cohort [14]. Finally, there has been no increase in mortality noted for transmasculine individuals taking testosterone. Overall, the authors concluded that gender-affirming hormone therapy is safe, with careful monitoring for potential complicating factors [7].

Present study

Little has been reported about transgender adolescents and their response to hormone therapy. A recent retrospective article by Jarin et al. reported the minimal impact of hormone treatment on 116 adolescents aged 14–25 years with gender dysphoria who were treated over time. Jarin et al. demonstrated that among adolescents treated for a period of 1–6+ months, the only findings were an increase in hemoglobin, hematocrit, and body mass index, and a lowering of high-density lipoprotein levels in those using testosterone for masculinization. Among those using estrogen for feminization, lower testosterone and alanine aminotransferase (ALT) were reported [15]. These findings are consistent with data from adults undergoing phenotypic gender transition with exogenous hormones, and indicate short-term safety of hormone use. The results from this retrospective study are useful for helping to allay some of the concerns that providers and parents have about safety. This study is limited by its retrospective design, and the challenges faced by many trying to collect data from adolescents—sporadic follow-up, frequent relocation, and inconsistent medication adherence.

The Center for Transyouth Health and Development at Children’s Hospital in Los Angeles is the largest clinic dedicated to the care of transgender and gender non-conforming children, adolescents, and young adults in the United States. The center currently provides services for approximately 925 youth between the ages of 3 and 25 years, and provides multidisciplinary care that includes mental health, medical intervention, advocacy, and referral resources for transgender and gender non-conforming youth and their families. The center has been providing gender-affirming hormones for adolescents and young adults since 1993. Growth of the clinic numbers has been unprecedented, and demand has far outpaced capacity.

This article offers preliminary results from a prospective study examining the physiologic impact of gender-affirming hormones in a cohort of adolescents aged 12–24 years with gender dysphoria over approximately two years of hormone use.

Methods

Self-identified transgender youth between the ages of 12 and 24 years presenting consecutively for care at the center

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