THE JOURNAL OF
SEXUAL MEDICINE

TRANSGENDER HEALTH

Efficacy and Safety of Gonadotropin-Releasing Hormone Agonist Treatment to Suppress Puberty in Gender Dysphoric Adolescents

Sebastian E. E. Schagen, MD,[1,2] Peggy T. Cohen-Kettenis, PhD,[3]
Henriette A. Delemarre-van de Waal, MD, PhD,[1,2,a] and Sabine E. Hannema, MD, PhD[2]

ABSTRACT

Introduction: Puberty suppression using gonadotropin-releasing hormone agonists (GnRHas) is recommended by current guidelines as the treatment of choice for gender dysphoric adolescents. Although GnRHas have long been used to treat precocious puberty, there are few data on the efficacy and safety in gender dysphoric adolescents. Therefore, the Endocrine Society guideline recommends frequent monitoring of gonadotropins, sex steroids, and renal and liver function.

Aim: To evaluate the efficacy and safety of GnRHa treatment to suppress puberty in gender dysphoric adolescents.

Methods: Forty-nine male-to-female and 67 female-to-male gender dysphoric adolescents treated with triptorelin were included in the analysis.

Main Outcome Measures: Physical examination, including assessment of Tanner stage, took place every 3 months and blood samples were drawn at 0, 3, and 6 months and then every 6 months. Body composition was evaluated using dual energy x-ray absorptiometry.

Results: GnRHa treatment caused a decrease in testicular volume in 43 of 49 male-to-female subjects. In one of four female-to-male subjects who presented at Tanner breast stage 2, breast development completely regressed. Gonadotropins and sex steroid levels were suppressed within 3 months. Treatment did not have to be adjusted because of insufficient suppression in any subject. No sustained abnormalities of liver enzymes or creatinine were encountered. Alkaline phosphatase decreased, probably related to a slower growth velocity, because height SD score decreased in boys and girls. Lean body mass percentage significantly decreased during the first year of treatment in girls and boys, whereas fat percentage significantly increased.

Conclusion: Triptorelin effectively suppresses puberty in gender dysphoric adolescents. These data suggest routine monitoring of gonadotropins, sex steroids, creatinine, and liver function is not necessary during treatment with triptorelin. Further studies should evaluate the extent to which changes in height SD score and body composition that occur during GnRHa treatment can be reversed during subsequent cross-sex hormone treatment.

J Sex Med 2016;13:1125–1132. Copyright © 2016, International Society for Sexual Medicine. Published by Elsevier Inc. All rights reserved.

Key Words: Gender Dysphoria; Gonadotropin-Releasing Hormone Agonist; Puberty Suppression; Gonadotropins; Sex Steroids

INTRODUCTION

Gender dysphoria is characterized by incongruence between the experienced gender and the sex assigned at birth. It was believed to be a rare phenomenon, but the number of individuals seeking advice and/or treatment at dedicated clinics is increasing.[1] Children can express a sense of belonging to the other sex at a very young age and might show gender role behavior typical of the experienced gender. However, studies have shown that in the children who met the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text*

Received December 31, 2015. Accepted May 9, 2016.

[1]Department of Pediatric Endocrinology, VU University Medical Centre, Amsterdam, the Netherlands;

[2]Department of Pediatrics, Leiden University Medical Centre, Leiden, the Netherlands;

[3]Department of Medical Psychology and Medical Social Work, VU University Medical Centre, Amsterdam, the Netherlands;

[a]Deceased 13 February 2014.

Copyright © 2016, International Society for Sexual Medicine. Published by Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jsxm.2016.05.004

Revision criteria for gender identity disorder, the gender dysphoria persisted into adolescence only in a minority.[2] If gender dysphoria persists or worsens at the onset of puberty, then it is very likely that it will persist into adulthood.[2]

The Endocrine Society has issued a clinical practice guideline on the endocrine treatment of gender dysphoric individuals.[3] For adolescents, pubertal development of the natal sex can be very distressing. Once irreversible characteristics of the natal sex have developed, such as breasts in natal girls and a low voice and outgrowth of the Adam's apple and jaw in natal boys, it becomes more difficult for the individual to live in the experienced gender. Therefore, treatment with gonadotropin-releasing hormone agonists (GnRHas) to suppress puberty is recommended. This gives individuals time to carefully consider their wishes regarding gender-affirming treatment without the distress caused by the development of unwanted sex characteristics. From approximately 16 years of age, individuals can be treated with sex steroids to induce the sex characteristics consistent with the gender identity.[3]

Treatment with GnRHa has been shown to improve psychological well-being in several domains.[4] However, physical outcome has not been very well studied. The Endocrine Society guidelines describe that testicular volume decreases and slight development of sex characteristic regresses,[3] but little evidence is available to support these statements.[5] This makes it difficult to counsel individuals on what they can expect. In addition, it is recommended to measure gonadotropins and sex steroids every 3 months during treatment and monitor liver enzymes and renal function.[3] However, the necessity of these frequent measurements is uncertain. A consensus statement on the use of GnRHa in children states there is insufficient evidence for any specific short-term monitoring scheme.[6] GnRHas have been used for many years for the treatment of children with precocious puberty and no side effects on liver or kidney function have been reported, but adolescents might respond differently.

AIM

We set out to describe the changes in Tanner stage, testicular volume, gonadotropins, and sex steroids during GnRHa treatment of gender dysphoric adolescents to evaluate the efficacy of this treatment. In addition, we report on the yield of monitoring liver enzymes and renal function and on changes in body composition.

METHODS

Subjects and Protocol

Gender dysphoric adolescents seen at the Centre of Expertise on Gender Dysphoria at the VU University Medical Centre (Amsterdam Netherlands) from 1998 through 2009 were invited to participate in a study on brain development, brain functioning, growth, and metabolic aspects of their treatment. These adolescents were diagnosed as described in existing guidelines,[3] were eligible for treatment fulfilling *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* criteria for gender identity disorder,[7] had lifelong extreme gender dysphoria, were psychologically stable, and were living in a supportive environment. The design of the study was observational and prospective. Treatment consisted of intramuscular injections of the GnRHa triptorelin 3.75 mg (Decapeptyl-CR, Ferring Pharmaceuticals, Copenhagen, Denmark), at 0, 2, and 4 weeks, followed by injections every 4 weeks. Individuals were seen at 3-month intervals. The duration of treatment with GnRHa alone depended on when the individual reached the age at which cross-sex hormone therapy could be added. Only individuals who had been treated for at least 3 months were included in this study.

Fifty-five male-to-female (MtF) and 73 female-to-male (FtM) adolescents started treatment according to this protocol. Twelve subjects were excluded from analysis because no baseline data were available (n = 4), treatment duration was shorter than 3 months (n = 2), or they were already being treated with medication that affects the hypothalamus-pituitary-gonadal axis at baseline (an antiandrogen, n = 1; a GnRHa provided elsewhere, n = 2; or a progestin, n = 3). Data from 49 MtFs and 67 FtMs were analyzed. None of the subjects in this study discontinued the GnRHa treatment.

Ethical Approval

Medical ethical approval was granted by the local medical ethics committee and informed consent was obtained from all participants and their parents or guardians. The study was placed on the International Standard Randomized Controlled Trial Number register and ascribed the registration number ISRCTN 81574253 (http://www.controlled-trials.com/isrctn/).

MAIN OUTCOME MEASURES

Physical Examination

Tanner stage was determined by the same examiners at each visit and based on breast development in FtMs and testicular volume and genital development in MtFs.[8,9] Testicular volume was determined using a Prader orchidometer. Weight and height were measured using an electronic scale and a wall-mounted stadiometer (SECA, Hanover, MD, USA), with weight measured to the nearest 0.1 kg and height to the nearest 0.1 cm. Height SD score (SDS) was calculated using Dutch reference data[10] and body mass index (BMI) SDS was calculated using reference data from Cole et al.[11]

Laboratory Investigations

After 0, 3, and 6 months of treatment and every 6 months thereafter, blood was drawn for measurement of luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, estradiol, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, γ-glutamyl transferase, and creatinine. The

Download English Version:

https://daneshyari.com/en/article/4269088

Download Persian Version:

https://daneshyari.com/article/4269088

Daneshyari.com