

Approach to transgender individuals

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Background

Trans-sexualism is the desire to be a member of the opposite sex during normal somatic sexual development. In this study, we would like to share our endocrinological approach and general clinical features of the patients with gender identity disorder.

Patients and methods

General and clinical features of 63 patients who were referred to Endocrinology Department between October 2012 and March 2014 were investigated retrospectively. In the beginning of the therapy, and later periodically, the patients were physically examined and their basal hormones and biochemical data were evaluated.

Results

Forty-eight (76.2%) patients constituted the female-to-male (FtM) group, and 15 (23.8%) patients constituted the male-to-female (MtF) group. The mean age was 25.0±4.6 in the FtM group and 24.9±5.9 in the MtF group. In the FtM group, 28 patients used testosterone preparations as cross-sex hormone, whereas 20 did not. Five (10.4%) patients had already used this preparation before they applied to us. Seven patients underwent mastectomy and four underwent oophorectomy. Penile prosthesis was implanted in one patient with reconstructive surgery. In the MtF group, nine patients used estradiol preparation. In the MtF group, three patients underwent breast implant surgery. Reconstructive surgery or orchiectomy was not performed.

Conclusion

The cross-sex hormone therapy provides the development of secondary sex characteristics and must also be given as a replacement therapy after gonadectomy.

Keywords:

gender identity disorder, hormone therapy, sex-reassignment, trans-sexualism

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Introduction

Sex identity can be described as a person's fundamental sense of being a man, woman or of indeterminate sex [1]. Trans-sexualism is the desire to be a member of the opposite sex during normal somatic sexual development [2]. The diagnosis of gender identity disorder (GID) is specified by the Clinic of Psychiatry. The cases are assessed in terms of the persistency of this desire and other mental disorders. The rate of male-to-female (MtF) trans-sexuals to female-to-male (FtM) ones is 3 : 1 in the western countries. In this study, we would like to share our endocrinological approach and general clinical features of the patients with GID at Ege University, Department of Endocrinology.

Patients and methods

General and clinical features of 63 patients who were diagnosed with GID in Psychiatry Department and referred to Endocrinology Department between October 2012 and March 2014 were investigated retrospectively. As for our hospital policy, the patients with GID are taken to

therapy groups for 2 years by Psychiatry Department. In the beginning of the therapy and later periodically, the patients are physically examined and their basal hormones and biochemical data are evaluated. After 1 year of therapy, cross-sex hormone replacement treatment starts. In the patients with cross-sex hormone treatment, regular liver function test, complete blood count, and hormone profiles are obtained. However, the laboratory parameters before and after cross-sex hormone treatment of our patients were not statistically compared due to the low number of cases in our study.

Results

Forty-eight (76.2%) individuals constituted the FtM group, and 15 (23.8%) individuals constituted the MtF group. The mean age was 25.0±4.6 years in FtM group

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and 24.9±5.9 years in MtF group. Polycystic ovary syndrome existed in 16.7% of the FtM group. Basic laboratory and basal hormone values are shown in Table 1. In the FtM group, 28 patients used testosterone preparations as cross-sex hormone, whereas 20 did not. Five (10.4%) patients had already used this preparation before they applied to us. Seven patients underwent mastectomy and four underwent oophorectomy. Penile prosthesis was implanted in one patient with reconstructive surgery.

In the MtF group, nine patients used estrogen preparation. The patients had usually preferred estradiol valerate, estradiol cypionate, and depot progesterone preparations in injection form as hormone therapy, and six had used antiandrogen before they were referred to us. Hormone usage rate was 60% before their applications. In our clinic, estradiol patch or 17β estradiol is preferred for estrogen therapy. In the MtF group, three patients underwent breast implant surgery. Reconstructive surgery or orchiectomy was not performed (Table 2).

Discussion

Trans-sexualism is a GID defined as a persistent conflict between one's biological sex and desired sex. One perceives inappropriateness of the individual's biological sex and desires to live and be accepted as a member of the opposite sex [3].

Table 1 Basal biochemical and hormonal measurements

	FtM	MtF
FPG (mmol/l)	4.9±0.07	5.14±0.17
B. insulin (pmol/l)	115.29±36.11	61.12±20.14
ALT (μkat/l)	0.32±0.03	0.38±0.09
TG (mmol/l)	1.03±0.09	1±0.11
Total cholesterol (mmol/l)	4.25±0.12	4.43±0.15
HDL (mmol/l)	1.41±0.06	1.19±0.15
LDL (mmol/l)	2.29±0.11	2.67±0.26
TSH (μIU/ml)	1.8±0.1	1.9±0.3
DHEAS (μmol/l)	7.18±0.51	^a
PRL (pmol/l)	32.1±2.2	^a
F. testosterone (nmol/l)	0.012 (median)	^a
T. testosterone (nmol/l)	1.49 (median)	^a
FSH (IU/l)	8.4±2.3	^a
LH (IU/l)	10.1±1.8	^a
E2 (pg/ml)	396.4±45.1	^a

ALT, alanine transaminase; B. insulin, basal insulin; DHEAS, dehydroepiandrosterone sulfate; FPG, fasting plasma glucose; FSH, follicle-stimulating hormone; F. testosterone, free testosterone; FtM, female-to-male; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LH, luteinizing hormone; MtF, male-to-female; PCOS, polycystic ovary syndrome; PRL, prolactin; TG, triglycerides; TSH, thyroid-stimulating hormone; T. testosterone, total testosterone. ^aBasal E2 and testosterone levels were not evaluated because of the cross-sex hormone usage before the first visit.

Individuals with GID are sometimes accompanied by psychiatric comorbidities. Thus, possible GID cases and their parents should be evaluated by a psychiatrist as regards general and psychosocial development. The GID is diagnosed by a psychiatry specialist according to Diagnostic and statistical manual of mental disorders, 4th ed., text revised (DSM-IV-TR) and International Classification of Disease-10 (ICD-10) criteria. ICD-10 declares that GID is disparity between biological and desired sex of the individual and the constant desire for living and be accepted in opposite sex. The individual with GID seeks for hormonal therapy and sex-reassignment surgery to provide adjustment of body to the desired sex [4]. The term 'Gender Identity Disorder' in DSM-IV-TR was replaced with 'Gender Dysphoria' in DSM-V published in 2013 [5].

The statement of 'trans-sexualism' was first reported by Hirschfeld. The Harry Benjamin International Gender Dysphoria Association was founded in 1979 and this association reported the standards of the treatment and follow-up of GID for the first time in 1979. The European Society of Endocrinology, European Society of Pediatric Endocrinology, Lawson Wilkins Pediatric Endocrine Society, and World Professional Association of Transgender Health published a guideline related to endocrinological treatment of transgender individuals [6]. Gender dysphoria can be identified as a discomfort or distress, which is caused by a difference between a person's sex identity and that person's sex assigned at birth. Although trans-sexual,

Table 2 Features of our female-to-male and male-to-female trans-sexual patients

	n (%)
FtM patients	
Total	48 (76.2)
Age	25.0±4.6
PCOS	16.70
The rate of cross-sex hormone use before admission	10.4
The number of cross-sex hormone treatment receivers (testosterone preparation users)	28
Mastectomy	7
Oophorectomy	4
Penile prosthesis	1
MtF patients	
Total	15 (23.8)
Age	24.9±5.9
Estradiol use	9
Antiandrogen use	6
The rate of cross-sex hormone use before admission	60%
Breast prosthesis	3
Orchiectomy	0

FtM, female-to-male; MtF, male-to-female; PCOS, polycystic ovary syndrome.

transgender, and gender-nonconforming people may experience gender dysphoria at times, many people who receive treatment will find a sex role and expression that is comfortable for them [7].

Olyslager and Conway [8] reported that the rate of trans-sexualism was 1/500 according to the data of sex-reassignment surgery. Rate of MtF trans-sexuals was 1/3.639 and that of FtM trans-sexuals was 1/22.714 according to the prevalence studies performed in New Zealand [9]. Forty-eight of our 63 (76.2%) patients were FtM trans-sexuals; 15 (23.8%) of them were MtF trans-sexuals (Tables 1 and 2). FtM trans-sexuals were more in number in our study population when compared with the literature data. Differences in cultural issues could be a reason for the diversity in the ratio of trans-sexuals. MtF trans-sexuals in our country take their hormone medications and sex-reassignment surgery without the support of Social Security Institution.

Biological and psychosocial factors may have a role in the etiology of trans-sexualism. Zhau *et al.* [10] has shown that there is a similarity of the bed nucleus of the stria terminalis (BNST) region in the brain between female and MtF trans-sexuals. BNST is a heterogeneous and complex limbic forebrain structure, which plays an important role in controlling autonomic, neuroendocrine, and behavioral responses. In men, the BNST volume is twice as large as that in women. A MtF trans-sexual has BNST volume similar to that of female [10]. Exposure to androgens in prenatal period could lead to the development of male gender identity. The possibility of being trans-sexual in girls with congenital adrenal hyperplasia is higher but the rate of trans-sexuality is 1–3% [11]. The hormone levels of our cases were compatible with their biologic sexes. There were a few studies in the literature indicating the association of polycystic ovary disease with FtM trans-sexuality [12,13]. The rate of polycystic ovary disease was 16.7% in our FtM trans-sexual patients (Table 2).

The GID could be together with psychiatric problems. For this reason, patients should be evaluated with their parents as regards their psychosocial developments. Before hormonal drug therapy, diagnosis should be made by a psychiatry specialist in line with the ICD-10, DSM-IV, and DSM-V criteria. Approach to this group of patients should be multidisciplinary, including a psychiatrist, an endocrinologist, a gynecologist, and a urologist. After GID was diagnosed, possible side effects of hormonal should be explained to the patients [6].

After the evaluation by a psychiatry specialist, the real life experience (RLE) period, in which the individual lives according to the desired sex before irreversible hormonal and surgical therapies, begins. After that, endocrinologist starts cross-sex hormone therapy if there is no contradictory state. Hormone therapy is started at least 3 months after the RLE period. GID could be evaluated more accurately after pubertal signs begin. In the light of clinical evidence, hormonal therapy is not recommended for those under 16 years of age. The reversible and irreversible effects of hormone therapy should be explained and information about fertility should be given.

The aim of cross-sex hormone therapy is to provide regression of secondary sex characteristics of original sex. Besides, this type of therapy causes the features of desired sex to build. Cross-sex hormone therapy has some unwanted side effects such as thromboembolism and breast cancer. Thus, follow-up at regular intervals becomes very important in this respect [1].

Our cases were enrolled into a group therapy after personal interview by the psychiatry team. After this process, the patients were sent to Endocrinology Department for the hormone therapy. At the beginning of group therapy, physical examination and basal hormonal and biochemical evaluations were performed. After a year of group therapy, cross-sex hormone therapy was started. The patients were followed-up for the measurement of liver function test, lipid profile, complete blood count, and hormone levels.

It was witnessed that MtF patients were taking estrogens such as estradiol valerate and estradiol cypionate injection by themselves without a prescription. Unnecessarily, they also used progesterone pills. In our practice, oral or patch estradiol was used as replacement. Spironolactone (100–200 mg/day) and cyproterone acetate (50–100 mg/day) were preferred as antiandrogen therapy. Sex-reassignment surgery was recommended for patients over 18 years who lived RLE period, completed group therapy, and were taking cross-sex hormone therapy without any complications [14]. In our country, the status of trans-sexuals in the Turkish Civil Code was arranged according to the Article 40. According to this article, any person who wants to alter his or her sex may invoke to be given permission for alteration of sex by applying to court in person. However, the applicant must be 18 years of age and unmarried. Besides, he/she must be in trans-sexual nature and prove indispensability of sex alteration

in respect to his/her mental health and his/her permanent infertility through a report of a board of health provided from a medical education and research hospital. When an official health report confirming the sex alteration surgery has been conducted properly in line with its purpose, the court may decide to make the required correction in the civil status of the patient [15].

Studies by Asscheman *et al.* [16] did not show an increase in mortality rates in individuals receiving cross-sex hormones compared with the general population; however, they reported higher rates of completed suicide and death due to AIDS in MtF trans-sexual individuals. In addition, no increased morbidity/mortality was seen in FtM trans-sexual individuals.

Although cross-sex hormone therapy provides secondary sex characteristics, it also has a role in hormone replacement therapy after gonadectomy. Trans-sexual individuals should be followed-up for cardiovascular, bone health, and side effects of hormone therapy.

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Conflicts of interest

There are no conflicts of interest.

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