Transsexualism in Iran

Mostafa Najafipour, MD.[1, 2]

Farzad Najafipour, MD. [3*]

1. Young Researchers and Elite Club, Ardabil Branch, Islamic Azad University, Ardabil, Iran.
2. Faculty of Medicine, Azad Ardabil University of Medical Sciences, Ardabil, Iran.
3. Endocrine Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

Corresponding author: Farzad Najafipour, MD. Endocrine Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

Email address: Farzadnajafipour@gmail.com

Table of content:

Abstract: A transsexual is a person who sex-related structures of the brain that define gender identity are exactly opposite the physical sex organs of the body. Many transgender men and women seek hormone therapy as part of the transition process. Medical therapy in transsexual

person is divided into two categories, hormone suppression therapy before 16 years and hormonal replacement therapy after 16 years. Suppression of pubertal hormones must be start when girls and boys first exhibit physical changes of puberty (confirmed by pubertal levels of estradiol and testosterone, respectively), but no earlier than Tanner stages 2–3. Pubertal development of the desired, opposite sex be initiated at the age of 16 year, using a gradually increasing dose schedule of cross-sex steroids. Exogenous testosterone is used in transgender men to induce virilization and suppress feminizing characteristics. In transgender women, exogenous estrogen is used to help feminize patients, and antiandrogens are used as adjuncts to help suppress masculinizing features. Guidelines exist to help providers choose appropriate candidates for hormone therapy, and act as a framework for choosing treatment regimens and managing surveillance in these patients. Cross-sex hormone therapy has been shown to have positive physical and psychological effects on the transitioning individual and is considered a mainstay treatment for many patients. Genital sex reassignment surgery is recommended only after completion of at least 1 year of consistent and compliant hormone treatment. Transsexual individuals should be monitored by an endocrinologist after surgery. Those who undergo gonadectomy will require hormone replacement therapy or surveillance or both to prevent adverse effects of chronic hormone deficiency.

Keywords: Hormone Therapy; Transsexualism; Cross-Sex Hormones, Gender Identity Disorders, Genital Sex Reassignment

1. Introduction

Transsexualism is defined as a persistent preference for living as a person of the opposite sex or as a strong and persistent cross-gender identification and by an inadequate sense of gender role that causes deep psychological distress and significant disability not only in the social and occupational area but also in any other important areas of functioning.[1] Transsexualism is told to somebody who has a gender identity inconsistency. For example, a person may have male sexuality, while her gender is female or vice versa. This paradox may be specific to the mind, private behavior, or social behavior.[2]

The causes of transsexualism have been studied for several years.[3] The most studied factors are biological. Some studies have found that Transsexual women's brain structure is similar to that of cisgender women's and non-cisgender men, and transsexual men is similar to cisgender men, even when controlling for hormonal use.[3,4] Researches in the past years have been confirmed earlier research finding that gender identity is influenced by brain structure. However, some of these studies are limited as they include a small number of tested individuals.[5,6]

The structural difference in the brain is also considered among gay and heterosexual men, as well as lesbian and heterosexual women. Likewise, studies such as Rametti's have found that transsexual men have male-like white matter patterns (even before using hormones), regardless of sexual orientation.[5,7] In terms of genetic factors, Hare's study reported that transsexual women have a longer androgen receptor gene than cisgender men, which is less effective at binding testosterone, potentially preventing complete masculinization of the brain.[8]

A study by Bentz found that transsexual men have a distribution of CYP17 alleles like cisgender men and unlike cisgender women.[9] One study found that 33% of identical twin pairs were both transsexual, compared to only 2.6% of non-identical twins who were raised in the same family.[10] Environmental factors have also been proposed. The failure of an attempt to raise Reiner from infancy through adolescence as a girl after his genitals were accidentally injured is cited as refuting the theory that gender identity is determined by education.[11]

Lili Elbe was a Danish transgender woman and one of the first recipients of sex reassignment surgery. Elbe was born a male and was a successful painter in that guise. She moved in 1930 and made a legal change to LiliI Elvenes and stopped painting. She died from complications including uterus transplant.[12]

During the reign of Mohammad Reza Pahlavi, the transsexualism were severely punished or even killed and they were wrong with gays and lesbians.[13] After the revolution of Ayatollah Rohollah Khomeini, they were treated well[14] and at 1980s transsexuals patients were recognized by the government and permitted to experience sex reassignment surgery. Maryam Khatoon Molkara was the first transsexualism in Iran who had been assigned male at birth but identified as female. Before the revolution, she had longed to become physically female but could not afford surgery and wanted religious authorization.[15] In 1975, she began to write letters to Khomeini, who was to become the leader of the revolution and was in exile. After the revolution, she was fired, forcedly injected with male hormones, and institutionalized. She was later released with help from her connections and continued to lobby many other leaders. Later she went to see Khomeini, who had returned to Iran. During this visit, she was subjected to beatings from his guards. Khomeini, however, did give her a letter to authorize her sex reassignment operation, which she later did in 1997.[16] Due to this fatwa, issued in 1987, transgender women in Iran have been able to live as women until they can afford surgery, have surgical reassignment, have their birth certificates and all official documents issued to them in their new gender, and get married to men.[17] As of 2008, Iran carries out more sex change operations than any other nation except Thailand. The government provides up to half the cost for those needing financial assistance, and a sex change is recognized on the birth certificate.[18]

Khomeini's original fatwa has since been reconfirmed by the current leader of Iran, Ayatollah Ali Khamenei, and is also supported by many other Iranian clerics.[17] However, there is still a great deal of stigma attached to the idea of transgender and gender reassignment in ordinary Iranian society, and most transgender people, after completing their transition, are advised to maintain discretion about their past.[16] Once a transgender individual has undergone sex reassignment,

that person legally becomes the new sex. All legal documents, such as birth certificates and passports, are also changed accordingly.[18]

Laws regarding changes to the legal status of transsexual people are different from country to country. Some authorities allow an individual to change their name, and sometimes, their legal gender, to reflect their gender identity. Within the US, some states allow adjustments or complete replacement of the original birth certificates.[15] In Iran authorities allow transsexual patients to change their name.[15, 19]

Estimates of the prevalence of transgender people are different in countries and highly dependent on the specific case definitions used in the studies, with prevalence rates varying by orders of magnitude.[20] The most prevalence is from the Amsterdam and it suggests a prevalence of 1:10,000 among allocated males and 1:30,000 among allocated females.[21] Although there is no accurate and direct study on the prevalence of gender Identity disorders have been done, a variety of clinical papers published in the past 24 years provide estimates ranging from 1:7,000 to 1:40,000 in assigned males and 1:30,000 to 1:100,000 in assigned females.[22] A 2008 study of the number of New Zealand passport holders who changed the sex on their passport estimated that 1:3,000 birth-assigned males and 1:22,000 birthassigned females were transsexual.[23] The most recent systematic review of prevalence of transsexualism found estimates per 100,000 population of 9.2 for surgical or hormonal gender confirmation therapy and 6.8 for transgender-related diagnoses.[24]

The prevalence of Gender Identity Disorder in a cross-sectional study in Tehran from 2002 to 2009 with a diagnosis of Gender Identity Disorder was done. in this time period was calculated based on the ratio of the total number of identified subjects to the total population aged between 15 and 44 years old. The prevalence of Gender Identity Disorder was 1:141,000 and the sex ratio of male to female Gender Identity Disorder was 0.96:1. The sex ratio of Gender Identity Disorder near 1:1 in Iran may indicate that fewer male Gender Identity Disorder subjects seek help in Iran than other countries.[25]

2. Hormone therapy

Since 1975 more than 800 articles have been published about transsexualism. Before that, few peer-reviewed articles have been published about endocrine treatment of transsexual persons. Sex reassignment is a multidisciplinary treatment. It requires five processes: diagnostic assessment, psychotherapy or counseling, real-life experience, hormone therapy, and surgical therapy.[26]

One of the first and most important hormone replacement therapy for transsexual patients is cross-sex hormonal therapy. This treatment is used for preoperative preparation, which makes patients experience secondary characteristics of the opposite. On the other hand, after sex change surgery, person is not able to produce sex hormones naturally and hormone therapy must be used lifelong. Cross-sex hormonal therapy is given as one of two types, based on whether the goal of treatment is feminization or defeminization.[27] Hormone therapy should be performed in a transsexual person to overcome his or her secondary characteristic and create new secondary traits and adapts his appearance to the desire sex. The goal of hormone therapy in transgender people is to get the person closer to his true self.[27, 28]

Unfortunately, some transgender people choose to self-administer hormone replacement medications. The reason is the lack of knowledge of doctors or because no doctor is available.[29] Others self-administer because their doctor will not prescribe hormones without a letter from a psychotherapist stating that the patient meets the diagnostic criteria and is making an informed decision to transition.[29,30] Many therapists require at least three to six months of continuous psychotherapy before they will write such a letter.

Medical therapy in transsexual person is divided into two categories: 1- hormone suppression therapy before 16 years. 2- Hormonal replacement therapy after 16 years.

3. Hormonal suppression therapy before 16 years

In both sexes, the hypothalamus produces gonadotropin releasing hormone to stimulate the pituitary gland to produce luteinizing hormone and follicle stimulation hormone. These in turn cause the gonads to produce sex steroids such as androgens and estrogens.[31] In adolescents of either sex with relevant indicators, gonadotropin releasing hormone analogues such as Decapeptyl can be used to stop undesired pubertal changes for a period without

inducing any changes toward the sex with which the patient currently identifies.[31,32] Gonadotropin releasing hormone analogues work by initially overstimulating the pituitary gland, then rapidly desensitizing it to the effects of gonadotropin releasing hormone. After an initial surge, over a period of weeks, gonadal androgen production is greatly reduced.[33, 34]

There is considerable controversy over the earliest age at which it is clinically, morally, and legally safe to use gonadotropin releasing hormone analogues, and for how long. Most physicians permit it from Tanner stage 2 but do not allow the addition of hormones until age 16, which could be five or more years later. Sex steroids have important functions in addition to their role in puberty, and some skeletal changes (such as increased height) that may be considered masculine are not hindered by gonadotropin releasing hormone analogues.[27, 33, 34]

Gonadotropin releasing hormone analogues are often prescribed to prevent the reactivation of testicular function when surgeons require the cessation of estrogens prior to surgery.[27,34] Suppression of pubertal hormones must be start when girls and boys first exhibit physical changes of puberty (confirmed by pubertal levels of estradiol and testosterone, respectively), but no earlier than Tanner stages 2–3.[27, 35] The protocol of suppression of pubertal development can be applied to adolescents in later pubertal stages. In contrast to effects in early pubertal adolescents, physical sex characteristics, such as breast development in girls and lowering of the voice and outgrowth of the jaw and brow in boys, will not regress completely. Irreversible and undesirable sex characteristics in female puberty are large breasts and short stature and in male puberty are Adam's apple; low voice; male bone configuration such as large jaws, big feet, and hands; tall stature; and male hair pattern on the face and extremities.[36, 37]

Suppression of pubertal development and gonadal function is accomplished most effectively by gonadotropin suppression with gonadotropin releasing hormone analogues and antagonists. Analogues suppress gonadotropins after a short period of stimulation, whereas antagonists immediately suppress pituitary secretion.[38, 39]

Because no long-acting antagonists are available for use as pharmacotherapy, long-acting analogues are the currently preferred treatment option.[34,39] During treatment with the gonadotropin releasing hormone analogues, slight development of sex characteristics will regress and, in a later phase of pubertal development, will be halted.[27,34,40] In girls, breast

development will become atrophic, and menses will stop; in boys, virilization will stop, and testicular volume will decrease.[27, 34, 40]

Depomedroxyprogesterone will suppress ovulation and progesterone production for long periods of time, although residual estrogen levels vary. In high doses, progestins are relatively effective in suppression of menstrual cycling in girls and women and androgen levels in boys and men. However, at these doses, side effects such as suppression of adrenal function and suppression of bone growth may occur.[41-43] Antiestrogens in girls and antiandrogens in boys can be used to delay the progression of puberty.[44] Their efficacy, however, is far less than that of the gonadotropin releasing hormone analogues.[44]

Measurements of gonadotropin and sex steroid levels give precise information about suppression of the gonadal axis. If the gonadal axis is not completely suppressed, the interval of gonadotropin releasing hormone analogue injections should be shortened. During treatment, adolescents should be monitored for negative effects of delaying puberty, including a halted growth spurt and impaired bone accretion.[45]

4. Cross-sex hormone therapy

For transsexual people, hormone replacement therapy causes the development of many of the secondary sexual characteristics of their desired sex. However, many of the existing primary and secondary sexual characteristics cannot be reversed by hormone replacement therapy. For example, hormone replacement therapy can induce breast growth for transsexual women but can only minimally reduce breasts for transsexual men.[46] Hormone replacement therapy can prompt facial hair growth for transsexual men, but cannot regresses facial hair for transsexual women. Hormone replacement therapy may, however, reverse some characteristics, such as distribution of body fat and muscle, as well as menstruation in transsexual men.[32, 46-48]

5. The hormone regimen for male to female

Hormone replacement therapy of the male-to-female type is a form of hormone therapy that is used to change the secondary sexual characteristics to feminine.[32, 46, 48]

The hormone regimen for male to female transsexual individuals is more complex than the female to male regimen. Physical changes that may occur in the first 3– 6 months of estrogen and antiandrogen therapy include decreased libido, decreased facial and body hair, decreased oiliness of skin, breast tissue growth, and redistribution of fat mass. Breast development is generally maximal at 2 year after initiation of hormones.[48-50]

High doses of a less potent estrogen – estradiol, are recommended during the first ten or so years of hormone replacement therapy, with or without an orchiectomy or genital reassignment. After that period, dosages can be reduced.[50, 51]

Most published clinical studies report the use of an antiandrogen in conjunction with an estrogen.[51] The antiandrogens shown to be effective reduce endogenous testosterone levels, ideally to levels found in adult biological women, to enable estrogen therapy to have its fullest effect. Two categories of these medications are progestins with antiandrogen activity and Gonadotropin releasing hormone agonists.[32, 51, 52] Spironolactone has antiandrogen properties by directly inhibiting testosterone secretion and by inhibiting androgen binding to the androgen receptor.[53]Cyproterone acetate, a progestational compound with antiandrogenic properties is widely used.[27, 52]Flutamide blocks binding of androgens to the androgen receptor, but it does not lower serum testosterone levels; it has liver toxicity, and its efficacy has not been demonstrated.[27]

Venous thromboembolism may be a serious complication. A 20-fold increase in venous thromboembolic disease was reported in a large cohort of Dutch transsexual subjects.[54, 55] This increase may have been associated with the use of ethinyl estradiol.[56] Thus, the use of synthetic estrogens, especially ethinyl estradiol, is undesirable because of the inability to regulate dose by measurement of serum levels and the risk of thromboembolic disease. Deep vein thrombosis occurred in 1 of 60 male to female transsexual persons treated with a gonadotropin releasing hormone analogue and oral estradiol.[32, 57]

Studies looking at the effects of estrogen on cardiovascular disease in transgender women are not very conclusive, but do show that there may be a trend toward an increased risk of heart disease, which should be further studied. Use of oral ethinyl estradiol appears to be strongly associated with cardiovascular events.[58]

Monitoring of male to female transsexual persons on cross-hormone therapy must be done. Evaluate patient every 2–3 months in the first year and then 1–2 times per year afterward to monitor for appropriate signs of feminization and for development of adverse reactions. Every 3 months serum testosterone and estradiol are measured. Serum testosterone levels should be 55 ng/dl and serum estradiol should not exceed the peak physiological range for young healthy females, with ideal levels 200 pg/ml.[59-61] For individuals on spironolactone, serum electrolytes (particularly potassium) should be monitored every 2–3 months initially in the first year.[60, 61] Routine cancer screening is recommended such as in non-transsexual individuals (breasts, colon, prostate).[62] Consider densitometry testing at baseline if risk factors for osteoporotic fracture are present (e.g. previous fracture, family history, glucocorticoid use, prolonged hypogonadism). In persons at low risk, screening for osteoporosis should be conducted at age 60 and in those who are not compliant with hormone therapy.[63, 64]

6. Hormone replacement therapy of the female-to-male

Hormone replacement therapy of the female-to-male type is a form of Hormone therapy that is used to change the secondary sexual characteristics to masculine.[65] The purpose of this form of hormone replacement therapy is to cause the development of the secondary sex characteristics of the desired sex, such as voice deepening and a masculine pattern of hair, fat, and muscle distribution. It cannot undo many of the changes produced by naturally occurring puberty, which may necessitate surgery.[65]

Similar to androgen therapy in hypogonadal men, testosterone treatment in the female-to-male individual results in increased muscle mass and decreased fat mass, increased facial hair and acne, male pattern baldness, and increased libido.[66] Specific to the female-to-male transsexual person, testosterone will result in clitoromegaly, temporary or permanent decreased fertility, deepening of the voice. Cessation of menses may occur within a few months with testosterone treatment alone, although high doses of testosterone may be required. If uterine bleeding continues, addition of a progestational agent or endometrial ablation may be considered.[67, 68]Gonadotropin releasing hormone analogues or depot medroxyprogesterone

may also be used to stop menses before testosterone treatment and to reduce estrogens to levels found in biological males.[27, 59, 69]

Physical changes that are expected to occur during the first 3 months of initiation of testosterone therapy include cessation of menses, increased libido, increased facial and body hair, increased oiliness of skin, increased muscle, and redistribution of fat mass. Changes that occur within the first year of testosterone therapy include deepening of the voice, clitoromegaly, and, in some individuals, male pattern hair loss.[59, 69]

A standard monitoring plan for individuals on testosterone therapy must be done. Key issues include maintaining testosterone levels in the physiological normal male range and avoidance of adverse events resulting from chronic testosterone therapy, particularly erythrocytosis, liver dysfunction, hypertension, excessive weight gain, salt retention, lipid changes, excessive or cystic acne, and adverse psychological changes.[61, 69]

Monitoring of female to male transsexual persons on cross-hormone therapy must be done. Evaluate patient every 2–3 months in the first year and then 1–2 times per year to monitor for appropriate signs of virilization and for development of adverse reactions.[59] Measure serum testosterone every 2–3 months until levels are in the normal physiological male range. For testosterone enanthate, the testosterone level should be measured midway between injections. If the level is more than 700 ng/dl or less than 350 ng/dl, adjust dose accordingly.[60]For parenteral testosterone undecanoate, testosterone should be measured just before the next injection. During the first 3–9 months of testosterone treatment, total testosterone levels may be high, although free testosterone levels are normal, due to high sex hormone binding globulin levels in some biological women.[61, 70] We Measure complete blood count and liver function tests at baseline and every 3 months for the first year and then 1–2 times a year. Consider bone mineral density testing at baseline if risk factors for osteoporotic fracture are present (e.g. previous fracture, family history, glucocorticoid use, prolonged hypogonadism). In individuals at low risk, screening for osteoporosis should be conducted at age 60 and in those who are not compliant with hormone therapy.[71] If cervical tissue is present, an annual pap smear is recommended by the American College of Obstetricians and

Gynecologists and if mastectomy is not performed, then consider mammograms as recommended by the American Cancer Society.[72]

7. Surgery for sex reassignment

Sex reassignment surgery for male-to-female involves reshaping the male genitalia into a form with the appearance of, and, as far as possible, the function of female genitalia.[73]

The genital sex reassignment surgery is recommended only after completion of at least 1yr of consistent and compliant hormone treatment. The surgery should be delayed until the age of 18.[27, 73]

Sex reassignment surgeries available to the male-to-female transsexual persons consist of gonadectomy, penectomy, and creation of a vagina.[74, 75]The skin of the penis is often inverted to form the wall of the vagina. The scrotum becomes the labia majora. Cosmetic surgery is used to fashion the clitoris and its hood, preserving the neurovascular bundle at the tip of the penis as the neurosensory supply to the clitoris. Most recently, plastic surgeons have developed techniques to fashion labia minora. Endocrinologists should encourage the transsexual person to use their tampon dilators to maintain the depth and width of the vagina throughout the postoperative period until the neovagina is being used frequently in intercourse. Genital sexual responsivity and other aspects of sexual function should be preserved after genital sex reassignment surgery.[75]

Sex reassignment surgeries available to the female to male transsexual persons have been less satisfactory. Sex reassignment surgeryfrom female to male includes a variety of surgical procedures for transgender men that alter female anatomical traits to provide physical traits more appropriate to the trans man's male identity and functioning. Many transsexual men considering the option do not opt for genital reassignment surgery; more frequent surgical options include bilateral mastectomy and hysterectomy and bilateral salpingo-oophorectomy.[76]Genital reconstructive procedures use either the clitoris, which is enlarged by androgenic hormones, or rely on free tissue grafts from the arm, the thigh and an erectile prosthetic. In either case, the urethra can be rerouted through the phallus to allow urination through the newly constructed penis. The labia major are united to form a scrotum, where prosthetic testicles can be inserted.[76, 77]

8. Conclusions

Suppression of pubertal hormones with gonadotropin releasing hormone analogue must be start when girls and boys first exhibit physical changes of puberty (confirmed by pubertal levels of estradiol and testosterone, respectively), but no earlier than Tanner stages 2–3. Hormone therapy for pubertal development (opposite sex) must be initiated at the age of 16yr, using a gradually increasing dose of cross-sex steroids. For the induction of puberty, we use a similar dose of induction of puberty in these hypogonadal transsexual adolescents as in other hypogonadal individuals. The transsexual adolescent may be sensitive to high doses of cross-sex steroids, causing abnormal breast shape in girls and cystic acne in boys.

We suggest that treatment with gonadotropin releasing hormone analogues be continued during treatment with cross-sex steroids to maintain full suppression of pituitary gonadotropin levels and, thereby, gonadal steroids. When puberty is initiated with a gradually increasing schedule of sex steroid doses, the initial levels will not be high enough to suppress endogenous sex steroid secretion. The estrogen doses used may result in reactivation of gonadotropin secretion and endogenous production of testosterone that can interfere with the effectiveness of the treatment. Gonadotropin releasing hormone analogue treatment is advised until gonadectomy.

Acknowledgement

Special thanks to Endocrine Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

Financial support and sponsorship

This work was supported in part by the Endocrine Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

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