

FEMALE-TO-MALE (FtM) TRANSSEXUAL ATHLETES

Introduction

The exclusive purpose of this medical information is to define the criteria for granting a TUE for treatment with hormones on the Prohibited List to transsexual athletes. It is not the purpose of this medical information to define the criteria for the eligibility of these athletes to participate in competitive sport, which is entirely left to the different sporting federations and organizations. Neither is there any reference made to sex verification in athletes.

Individuals who were assigned female sex at birth, and who change their body to a more masculine body, are called Female-to-Male (FtM) transsexuals. Vice versa, individuals assigned male at birth who change their body to a more feminine body are called Male-to-Female (MtF) transsexuals. Other terms used for this condition are transgender or, less often, transitioned women and men.

The individual sports federations and organizations need to decide on the eligibility of transsexual athletes in their sport, and a TUE will only be considered for eligible athletes. The hormones administered to MtF athletes (estrogen, anti-androgens) are not prohibited in sports. Only FtM athletes who take androgens require a TUE. As testosterone administration influences performance measures, it is important that the criteria for the granting of a TUE ensure that FtM athletes have physiological androgen exposure comparable with, but no more than, eugonadal men. This is best ensured by using standard testosterone doses as for androgen deficient men. At the same time, it needs to be remembered that actual levels of circulating testosterone and their determination of muscle mass and strength in males are subject to considerable inter-individual variability.

1. Diagnosis

A. Medical History

The distress that is caused by a discrepancy between an individual's gender identity and their sex assigned at birth is called gender dysphoria and may appear before, during or after puberty. More extreme gender dysphoria in childhood tends to persist into early adulthood. In about 30-40% of cases, there is no history of gender nonconforming behaviors in childhood, and an adolescent's or adult's gender dysphoria may come as a surprise to their surroundings.

Medical history will elaborate on the diagnostic workup and consequent treatment. Many individuals need both hormone therapy and surgery to alleviate their gender dysphoria, while others need only one of these treatment options and some need neither. Surgical treatment alone is rare. However, in FtM athletes, this would entail hysterectomy and/or oophorectomy.

B. Diagnostic criteria

Comprehensive DSM-V and ICD-10 criteria have been developed for gender dysphoria and transsexualism. In transsexual athletes who have undergone sex reassignment and are eligible for competition based on the rules of their respective sport, a comprehensive diagnostic process will have taken place as defined either by the medical community and/or prescribed by law in the respective country.

C. Relevant medical information

FtM athletes may be granted a TUE when they are eligible for the sport, and the respective criteria and characteristics of eligibility defined by their sport need to be documented in the TUE application. In general, the primary evaluation of a transsexual athlete who is receiving hormone treatment and/or has undergone surgery will follow the national guidelines. Reports by either mental health professionals and/or the subspecialty providing care for transsexual persons in the respective country will detail the medical history including any previous partially or fully reversible physical treatment. These reports will establish the indication for hormone treatment/surgery in persistent gender dysphoria. They should be complemented by an endocrinologist's report on initialization of hormone therapy and/or the surgeon's report documenting the oophorectomy as applicable. Prior to treatment, a full general medical assessment needs to be completed.

2. Medical best practice treatment

Androgen hormone therapy is essential for the anatomical and psychological transition process in FtM athletes. Hormones optimize male gender identity, improve quality of life, and limit psychiatric co-morbidities which have been reported to occur more often when such treatment is withheld.

A. Name of prohibited substance

The cross-sex hormone administered to FtM athletes is testosterone. Testosterone or various testosterone esters including long-acting or oral testosterone undecanoate, testosterone cypionate, enanthate or mixed

testosterone esters might be used depending on the doctor and patient preference as well as the country of residence.

B. Route

- Intramuscular: testosterone undecanoate, cypionate, enanthate or mixed esters. The treatment must be recorded by a health professional and kept available for review at any time.
- Testosterone pellets might be inserted subcutaneously and provide constant testosterone levels avoiding peaks and troughs.
- Testosterone patches, gels and creams slowly diffuse testosterone through the skin and have a daily dosing regimen avoiding peaks. There is a risk for skin contact to cause inadvertent exposure to other athletes and therefore the site of application must be covered in contact sports. A buccal testosterone tablet is also available.
- Oral administration of testosterone undecanoate is less frequently used. After absorption from the GI tract, first-pass metabolism of testosterone creates very low and unsatisfactory oral bioavailability. Oral testosterone undecanoate is absorbed via gut lymphatics but only when taken together with a fatty meal. Alkylated androgens such as 17 α -methyl testosterone are hepatotoxic and should not be used.

C. Dosage and Frequency

Regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism. The exact dosage and frequency are to be determined by the prescribing endocrinologist utilizing standard dosage regimens.

Intramuscular administration of testosterone cypionate, enanthate or mixed testosterone esters every two to four weeks may result in fluctuating blood testosterone levels with peaks and troughs. The recommended standard doses are a maximum dose of 100-125 mg weekly, or 200-250 mg every two to three weeks. More stable and physiological levels are achieved with long-acting testosterone undecanoate, which is well suited for FtM athletes competing at the elite level. The standard dosing regimen requires a loading dose (1000 mg) during initiation of treatment and then four 1000 mg doses per year. Optimal clinical results may require individual dose titration around the 12 week dose interval, ranging between 10-14 weeks, according to clinical effects and trough serum levels.

For injectable testosterone, the dosage should be monitored with trough serum testosterone levels. The testosterone product, dosage

and timing of the previous treatment with injectable testosterone products must be recorded and submitted for annual review or for dosage changes.

Transdermal application of testosterone through daily changed patches, gel or creams is self-administered by the athlete and therefore carries a risk of overdosing which might be difficult to detect due to the short half-life of the hormone. Testosterone gel can be monitored by serum testosterone levels at any time. Any change in product, dosage or treatment schedule of testosterone should be approved by the ADO.

Oral testosterone undecanoate administration is usually twice or thrice daily with meals.

In one study, subcutaneous testosterone pellets implanted every six months achieved stable and physiological blood testosterone levels comparable to the three-monthly testosterone undecanoate injections.

D. Recommended duration of treatment

The continuing need for testosterone is self-evident in FtM athletes as there is no hormone-producing organ, and therapy is life-long unless contraindications occur (for TUE validity see 7).

3. Other non-prohibited alternative treatments

FtM athletes require hormonal treatment with testosterone, for which there is no non-prohibited alternative.

4. Consequences to health if treatment is withheld

In transsexual athletes, hormones help to optimize real-life gender role congruent with identity, improve quality of life, and limit psychiatric co-morbidities. It has been shown that psychiatric co-morbidities do occur more often when hormonal treatment is withheld.

In the period after surgery, androgen therapy is essential for completion of the anatomical and psychological transition process in FtM athletes. Thereafter, hormonal treatment is essential to maintain the male gender characteristics and the physical appearance of the transsexual athlete. There is an increased risk of bone density loss after oophorectomy if testosterone therapy is interrupted or insufficient.

5. Treatment monitoring

To control for the secondary effects of receiving long-term hormone therapy, any transsexual athlete needs permanent thorough medical monitoring by experienced primary care and specialized health care providers with documentation that testosterone treatment achieves complete transition.

It is the athlete's responsibility to provide the TUEC with a complete record of testosterone prescriptions of oral, gel or buccal testosterone products and date, dosage and name of medical personnel administering injections of testosterone.

Frequent testing of serum testosterone including unannounced urine and blood testing as ordered by ADO (at least 1-2 times per year) should be required and related to injection timing or gel application. Treatment should use standard testosterone doses which should return the trough testosterone to mid-normal levels.

6. TUE validity and recommended review process

Hormone replacement with testosterone is usually continued lifelong, unless medical contraindications arise.

TUE validity should be for ten (10) years, with a mandatory requirement for annual follow-up reports including testosterone dosing regimens and levels to be submitted to the TUEC as above.

7. Any appropriate cautionary matters

Absolute contraindications to testosterone therapy include pregnancy (not applicable in case of FtM after surgery) and untreated polycythemia with a hematocrit of 55% or higher.

Baseline laboratory values including hematocrit are important to both assess initial risk and evaluate possible future adverse events. All FtM athletes need to be carefully monitored for cardiovascular and diabetes risk factors even though testosterone has not been shown to increase risk in healthy patients, it might do so in those with risk factors. Lipid profiles might be affected and should be regularly assessed.

8. References

1. World Professional Association for Transgender Health. The Standards of Care. 7th version. Int J Transgenderism. 2011;13:165-232. Available from: http://www.wpath.org/site_page.cfm?pk_association_webpage_menu=1351
2. Gooren LJ. The significance of testosterone for fair participation of the female sex in competitive sports. Asian J Androl. 2011 Sep;13(5):653-654. doi: 10.1038/ aja.2011.91. Epub 2011 Jul 4.
3. Fennell C, Sartorius G, Ly LP, Turner L, Liu PY, Conway AJ, Handelsman DJ. Randomized cross-over clinical trial of injectable vs. implantable depot testosterone for maintenance of testosterone replacement therapy in androgen deficient men. Clin Endocrinol (Oxf). 2010 Jul;73(1):102-109.
4. Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA, Gooren LJ, Meyer WJ III, Spack NP. Endocrine therapy of transsexual persons: An endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2009 Sept; 94(9): 3132-3154.
5. Gooren LJ. Olympic sports and transsexuals. Review. Asian J Androl. 2008 May; 10(3):427-432.
6. Handelsman DJ, Gooren LJ. Hormones and sport: physiology, pharmacology and forensic science. Asian J Androl. 2008 May;10(3):348-350.
7. Devries MC. Do Transitioned Athletes Compete at an Advantage or Disadvantage as compared with Physically Born Men and Women: A review of the Scientific Literature (May 18, 2008). Available from http://www.caaws.ca/e/wp-content/uploads/2013/02/Devries_lit_review2.pdf
8. Gooren LJ, Bunck MCM. Transsexuals and competitive sports. Review. Eur J Endocrinol. 2004;151(3):425-429.
9. International Olympic Committee. Statement of the Stockholm consensus on sex reassignment in sports. 2003. Available from: http://www.olympic.org/Documents/ Reports /EN/en_report_905.pdf.

Appendix

Background information on transsexual athletes and performance

Since the second half of the 20th century, medical therapies allow transsexual men and women to change their sex. Some definitions aid in understanding this condition. According to the WHO, sex refers to the biological and physiological characteristics that define men and women, and gender refers to the socially constructed roles, behaviors, activities, and attributes that a given society considers appropriate for men and women. Further, gender identity is a person's sense of being a woman or man. The sex and gender identity of a person do not always comply, which may result in gender dysphoria. This term refers to the distress that is caused by a discrepancy between a man's or woman's gender identity and that man's or woman's sex assigned at birth.

Psychological treatment trying to change a person's gender identity to become compliant with their sex assigned at birth has been attempted without success. Such treatment is no longer accepted and considered unethical. Before any physical interventions, extensive exploration of psychological, family, and social issues should be undertaken.

The prevalence of Female-to-Male (FtM) and Male-to-Female (MtF) transsexualism is difficult to ascertain. Prevalence figures for transsexualism reported in ten studies from different countries over a period of about 40 years ranged from 1:11'900 to 1:45'000 for MtF transsexuals and 1:30'400 to 1:200'000 for FtM transsexuals. There is a trend to higher prevalence rates in more recent studies, possibly corresponding with the increasing acceptability of the condition and the availability of clinical care.

From the perspective of (competitive) sports, it is important that there is not one single biologic characteristic for the ultimate determination of sex in current medical practice. Chromosomal sex was abandoned as the criterion for fair competition in sports in 2000. Before, transgender and athletes with Disorders of Sexual Development (DSD) had been precluded from participation. Sex differences are the result of differences in testosterone and estrogen levels. Testosterone increases muscle mass and strength, bone size, mineral and hemoglobin content. Based on numerous studies demonstrating the performance enhancing abilities of androgens, the use of exogenous androgens (and of drugs which raise endogenous androgen levels like human chorionic gonadotropin and anti-estrogens) is prohibited in sports. Previous use and/or present exposure to androgens are criteria for unfair competition in general, and not only between men and women.

Therefore, transsexual athletes present a unique challenge to sport governing bodies having to decide on their eligibility to compete against

athletes who are natal men and women when transition is made after puberty. The question to be decided by a sport is whether a woman or a man who has undergone normal physical pubertal and post-pubertal development in one sex, with prolonged exposure to sex-corresponding levels of sex hormones, can fairly compete as a member of the other sex.

The importance of the distinction whether the transition is being made prior or after puberty is also reflected in the IOC consensus statement 2003. It confirmed the previous IOC recommendation that any “individuals undergoing sex reassignment of male to female before puberty should be regarded as girls and women (female). This applies as well for female to male reassignment, who should be regarded as boys and men (male).”

The consensus recommends that individuals undergoing sex reassignment from male to female after puberty (and the converse) be eligible for participation in female or male competitions, respectively, under the following conditions:

- Surgical anatomical changes have been completed, including external genitalia changes and gonadectomy.
- Legal recognition of their assigned sex has been conferred by the appropriate official authorities.
- Hormonal therapy appropriate for the assigned sex has been administered in a verifiable manner and for a sufficient length of time to minimize gender-related advantages in sport competitions.

The IOC stated that eligibility should begin no sooner than two years after gonadectomy. This remains the position of the IOC to date. Different from the IOC, the National Collegiate Athletic Association does not insist on gonadectomy or external genitalia changes, and requires only one year of hormone therapy and only for MtF, but not FtM athletes, to achieve eligibility. In FtM athletes, it is considered that endogenously produced estrogens do not provide a competitive advantage.

There is no compelling scientific evidence on the speed at which changes induced by cross-sex hormone treatment occur over time. A number of studies suggest that most changes occur within the first year. Using standard doses, testosterone administration to FtM transsexuals increased hemoglobin and hematocrit content within one year of hormone supplementation, with no further increase beyond one year.

No difference in hemoglobin levels between FtM transsexuals and natal men has been observed thereafter when standard testosterone doses were used. Maximal muscle cross-sectional area statistically did not differ between FtM transsexuals and natal men. The only difference that was shown to persist

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after one year of testosterone administration was a higher amount of subcutaneous fat in FtM transsexuals, as compared with natal men.

However, studies on cross-sex hormone administration have only been carried out in transsexual individuals, but not in athletes. The only study meant to address the issue of transsexual individuals in competitive sport used a retrospective design in a non-athletic population. Further, no study has examined the effects of cross-sex hormones on any objective measures of athletic performance (maximal aerobic capacity, time trials). No trial has been conducted in transsexual athletes as compared with natal men and women athletes.