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Do anabolic-androgenic steroids have performance-enhancing effects in female athletes?

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ABSTRACT

Doping with anabolic-androgenic steroids (AAS) is common among both male and female athletes and is a growing public health problem. Review of historical data of systematic state-sponsored doping programs implemented by the German Democratic Republic in elite female athletes and from clinical trials of testosterone administration in non-athlete women suggests that AAS have ergogenic effects in women. The use of AAS in female athletes has been associated with adverse effects that include acne, hirsutism, deepening of the voice and menstrual disturbances; life-threatening adverse effects such as cardiac arrhythmias and sudden death have also been reported. Therefore, detection of AAS abuse in female athletes is important to ensure fairness in competition; at the same time, the athletes should be educated regarding the adverse consequences of AAS use. Although administration of exogenous androgens have been associated with ergogenic effects, it remains unclear whether endogenous hyperandrogenism seen in some medical conditions such as disorders of sexual development (DSD), congenital adrenal hyperplasia and polycystic ovary syndrome, confers any competitive advantage. Well-designed studies are needed to determine the effects of endogenous hyperandrogenism on athletic performance in female athletes.

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1. Introduction

Over the last several decades, use of anabolic-androgenic steroids (AAS) as performance-enhancing drugs among *competitive athletes*, *recreational athletes, body-builders* and those who desire to enhance their *body image*, has substantially increased. Estimates suggest that approximately 3–4 million Americans aged 13–50 years have used AAS; and within this group, approximately 1 million developed dependence on AAS (Pope et al., 2014). AAS represent a diverse class of synthetic derivatives of testosterone and are used primarily to increase muscle mass and muscle strength, and to improve physical performance. Not surprisingly, AAS are the most common class of ergogenic drugs used by athletes participating in competitive sports and a quarter of them develop AAS dependence (Hartgens and Kuipers, 2004). Although the abuse of AAS is substantially more common in men, its prevalence is also increasing in women with an estimated lifetime prevalence of 1.6% (Nieschlag and Vorona, 2015b). As a result, use of AAS has been officially banned from competitive sports for all athletes since the mid-1970s. Although there is abundant scientific literature describing the ergogenic effects of AAS among male athletes (Hartgens and Kuipers, 2004), data regarding their effects in female athletes are limited. Even more controversial is the issue of whether endogenous hyperandrogenism in athletes with disorders of sexual development (DSD), polycystic ovary syndrome and congenital adrenal hyperplasia provides any advantage in competitive sports.

In this paper, we review; i) physiology of androgen production in women; ii) ergogenic effects of AAS use in female athletes by providing a historical overview; iii) body composition and muscle performance among women with endogenous hyperandrogenism; iv) efficacy of testosterone administration on body composition and muscle performance in non-athlete androgen deficient women (HIV, hypopituitarism and surgical menopause); and lastly, v) discuss the potential adverse effects of AAS use in women.

2. Androgen physiology in women

The ovaries and the adrenal glands are the two major sources of androgens in women (Basaria and Dobs, 2006). Testosterone is produced directly from the ovaries and also via conversion of weaker androgens, androstenedione and dehydroepiandrosterone (DHEA), which are synthesized by the ovaries and the adrenal glands, respectively. In young premenopausal women, the ovary is responsible for approximately 25% of the testosterone production, while 75% is derived from the adrenal androgens. However, in postmenopausal women, the ovary becomes a major source of testosterone production and its contribution increases to 50% (Adashi, 1994). Although the climacteric ovary is atrophic and loses its capacity to synthesize estradiol and follicles, it continues to secrete androgens under the stimulation of postmenopausal gonadotropins (Sluijmer et al., 1995; Dowsett et al., 1980; Dennefors et al., 1980).

In ovulating women, serum levels of testosterone and androstenedione gradually increase during the follicular phase and peak during the pre-ovulatory phase (Judd and Yen, 1973; Sinha-Hikim et al., 1998). Serum androstenedione level further increases during the late luteal phase; while serum testosterone concentrations do not increase further (Judd and Yen, 1973; Sinha-Hikim et al., 1998). Based on normative data from the Framingham Heart Study, median serum total testosterone levels (measured by liquid chromatography tandem mass spectrometry) in healthy, cycling women age 19–45 years were 23.7 ng/dl in the follicular phase, 34.7 ng/dl in the ovulatory phase and 28.5 ng/dl in the luteal phase (Coviello et al., 2012).

Serum testosterone concentrations are lower in older postmenopausal women compared with young, menstruating women. However, unlike the cessation of ovarian production of estrogen and follicles at natural menopause, ovarian androgen production does not cease. In fact, the steepest decline in serum testosterone and DHEAS levels occur during the early reproductive years, between the ages of 20–40, and then plateauing during menopausal transition (Cappola et al., 2007; Davison et al., 2005). Indeed, average serum testosterone levels among women in their sixties is approximately 50% compared with women in their twenties (Cappola et al., 2007; Davison et al., 2005). Thus, the decline in androgens in women appears to be more of a function of aging rather than natural menopause (Basaria and Dobs, 2006; Davison et al., 2005). In contrast to natural menopause, surgical menopause is associated with a significant reduction in serum androgen levels. Indeed, population studies show a 50% decline in circulating serum testosterone levels in women who have undergone bilateral oophorectomy compared with naturally menopausal women (Judd et al., 1974; Laughlin et al., 2000).

3. Ergogenic effects of AAS use in female athletes

The use of AAS to increase lean mass and muscle strength is common in elite female sports; indeed, androgens are the most common class of agents used for doping by elite female athletes (Bermon, 2017). However; in contrast to male athletes in who there is substantial evidence showing ergogenic benefits of AAS use, the effects of AAS on physical performance in women have not been extensively studied (Lamb, 1984; Maravelias et al., 2005; Wu, 1997). Men abusing AAS have been reported to administer androgens that are 10–100 times the therapeutic dose that is prescribed to hypogonadal men in the clinics (Penatti et al., 2011; Trenton and Currier, 2005; Wu, 1997). Limited data suggest that some female athletes have reportedly taken AAS at doses that are similar to male athletes (Franke and Berendonk, 1997). Although there is a lack of objective data, small studies that interviewed female athletes report that some women *perceived* significant improvement in their muscle mass, muscle strength and athletic performance while taking AAS compared to the period when they were not using these agents (Strauss et al., 1985).

From 1965 to 1989, the German Democratic Republic (GDR) conducted a systematic doping program where they administered AAS to elite athletes competing in the Olympic Games (Fitch, 2008; Franke and Berendonk, 1997). Evidence regarding the performance enhancing effects of AAS in elite competitive sports comes from the release of several classified government documents after the unification of Germany in 1990. Review of scientific reports, secret doctoral theses and court documents from 1966 onwards revealed that hundreds of physicians and scientists were involved in doping research and were designated as “unofficial collaborators” of the Ministry for State Security. Some of these documents suggest that administration of AAS to female athletes was highly effective in enhancing their competitive performance, particularly in sporting events that required strength and speed. The reports suggested that administration of AAS in female athletes for four years improved shot-put distance by 4.5–5 m and discus throw distance by 11–20 m; while in racing events, athletes using AAS were 4–5 s and 7–10 s faster in the 400 m and 1500 m events, respectively. Indeed, the systematic administration of androgens in female German athletes was considered a success by the GDR doping program as it resulted in many victories in female sporting events. Some of these female athletes were given doses of nandrolone and testosterone esters that were even higher than the doses that were administered to male athletes participating in similar events. The document also suggests that the physicians who were employed by the GDR in the

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