Androstenedione

Alan David Kaye | Mark R. Jones | Jessica Kaye | Adam M. Kaye

Uses

- Testosterone replacement therapy
- Treatment of hypogonadal men
- Age-related sarcopenia
- HIV-related muscle wasting
- Increase in bone mineral density
- Prevention of age-related frailty and falls

Perioperative Risks

- Coagulopathy
- Polycythemia

Overview

- Growing sales trend of 20–30% in USA for both medical and nonmedical use of AAS.
- AAS have been available since 1996 as an OTC nutritional supplement and were banned for sale by the Anabolic Steroid Control Act in 2004.
- Estimated 10% of AAS users are teens.
- Estimated 4.9% of male and 2.4% of female adolescents in USA have used legal androgenic/anabolic steroids.
- Current estimates indicate that there are as many as 3 million AAS users in USA.
- Surveys among community weight trainers attending gyms and health clubs indicate that AAS use is between 15% and 30%.
- AAS use is positively associated with use of alcohol, illicit drugs, and legal performance enhancing substances.
- As a major precursor to testosterone that is available without a prescription, it is purported to increase strength and athletic performance. However, significant effects on muscle strength have not been found in men after androstenedione administration, except following a large dose (1500 mg/d for 12 wk) of androstenedione given to hypogonadal men.
- AAS used to increase endogenous testosterone production to enhance athletic performance and recovery from exercise, to keep RBCs healthy, and to heighten sexual arousal and function.
- Popularity related to society's preoccupation with sustaining the male libido.

Pharmacology/Mechanism of Action/Usual Dose

- As a member of a group of compounds known as AAS, these synthetic derivatives of testosterone are thought to possibly restore sex drive and boost muscle mass.
- Testosterone enters the cell by passive diffusion and is converted by 5α-reductase to 5α-dihydrotestosterone, which binds to intracellular androgen receptors.
- Increase protein anabolism and decrease protein catabolism. Nitrogen balance is improved only when there is sufficient intake of calories and protein.
- Stimulate the production of RBCs by enhancing the production of erythropoietic stimulating factor.
- Impair preadipocyte differentiation into adipocytes and reduce subcutaneous abdominal adipose tissue in nonobese women.
- Supplementation of androstenedione in the setting of a rigorous 12-wk resistance-training program resulted in a return of baseline levels of testosterone levels and significant increases in estrone and estradiol levels. No increase in measurable lean body mass or muscular strength when compared with placebo.
- Androstenedione is produced in the gonads and adrenal glands of both males and females.
- It is synthesized from dehydroepiandrosterone and then converted to testosterone by the enzyme 17 β-hydroxysteroid dehydrogenase or to estrone by the aromatase enzyme complex.
- Usual dose:
  - Androstenedione is a direct precursor of testosterone and estrone in both males and females; it may increase testosterone levels.
  - Marketing claims include increased strength, greater fat-free mass, and improved libido; recommended doses are 100–300 mg/d or 50–100 mg twice daily taken 1 h before exercise or upon awakening. Only high doses of 1500 mg/d for 12 wk confirmed to increase muscle strength.
- Contraindications:
  - Pts with steroid-dependent carcinoma of the breast, prostate gland, and endometrium.
  - Women who are or may become pregnant.
  - Pt with serious cardiac, hepatic, or renal disease.
- Adverse effects:
  - Several AAS-induced CV concerns reported include Htn, left ventricular hypertrophy, impaired diastolic filling, arrhythmias, erythrocytosis, altered lipoprotein profile, and thrombosis.
  - AAS-induced elevations in liver enzymes (alanine- and aspartate-aminotransferases).
  - Dermatologic chances such as acne, striae, alopecia, and hirsutism are possible results induced by the action of the AAS on the skin and sebaceous glands.
  - Endocrine and/or reproductive effects include a dose-dependent depression of levels of luteinizing hormone and follicle-stimulating hormone due to the negative feedback loop of the hypothalamic-pituitary-gonadal axis.
  - Feminization (gynecomastia) in males due to the aromatization of exogenous testosterone to estrogen metabolites.
  - Male users may have their endocrine suppression lead to hypogonadotrophic hypogonadism, testicular atrophy, sperm morphology, infertility, and changes in libido.
  - Female-specific side effects of AAS incl hirsutism, increased facial hair, voice deepening, clitorial hypertrophy, oligomenorrhea, reduced breast tissue, and male-pattern baldness.
  - Restoration of hypothalamic–pituitary homeostasis, endogenous testosterone, and spermatogenesis may take between 3-12 mo after using AAS.

Assessment Points

System	Effect	Assessment by Hx	Test
CV	Decreased HDL, atherosclerosis	Angina	ECG, cholesterol
GI	Cholestasis, hepatocellular tumors, hepatitis, nausea		Liver enzymes, bilirubin
HEME	Polycythemia, chronic usage, suppression of clotting factors, sodium and water retention	Easy bruising	PT, PTT Lytes
CNS	Depression, anxiety, behavioral changes, headache		

Key References: Broeder CE, Quindry J, Brittingham K, et al.: The Andro Project: physiological and hormonal influences of androstenedione supplementation in men 35 to 65 years old participating in a high-intensity resistance training program, *Arch Intern Med* 160(20):3093–3104, 2000; Dodge T, Hoagland MF: The use of anabolic androgenic steroids and polypharmacy: a review of the literature, *Drug Alcohol Depend* 114(2–3):100–109, 2011.

Perioperative Implications

- Retention of sodium, chloride, potassium, calcium, inorganic phosphate, and water.
- N/V, rarely hepatocellular neoplasms and hepatitis.
- Suppression of clotting factors II, V, VII and X; bleeding in pts on concomitant anticoagulant therapy.
- Polycythemia.
- Increased serum cholesterol, decreased HDL.
- Pts with osteolytic lesions or who are semi-ambulatory may develop nephrocalcinosis.
- In geriatric pts, high risk of prostate hypertrophy and prostate carcinoma.

Possible Drug Interactions

- Metabolic effects of androgens may decrease blood glucose level and insulin requirements.
- Androgens decreased levels of thyroxin-binding globulin, resulting in decreased total T_4 serum levels and decreased resin uptake of T_3 and T_4.
- May interfere with androgenic or estrogenic drug therapy.

β-Sitosterol

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Uses

- CHD and hypercholesterolemia.
- BPH and prostatitis.
- Gallstones.
- Enhances sexual activity.
- Prevents colon cancer.
- Boosts immune system.
- Topically for treating wounds and burns.
- Migraine headache, chronic fatigue syndrome, and symptoms of menopause.
- Asthma, allergies, bronchitis, SLE, and alopecia.
- Areas of potential application currently under investigation include the prevention of breast, ovarian, and lung cancers.