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Anabolic-androgenic steroids in sport

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Abstract

Introduction and objective

Anabolic-androgenic steroids (AAS) are a group of doping substances. They cause muscle hypertrophy and an increase in strength. Moreover, they may lead to dangerous side effects. Knowledge of the side effects of AAS use is necessary because in clinical practice we often encounter patients who decide to supplement with steroids. The aim of the study is to present information on the epidemiology, mechanism of action, methods of detecting AAS, the impact of the substance on the male and female body, and a description of organ side effects, highlighting: the cardiovascular system, the nervous system and the psyche.

Review methods

Literature search was conducted in the PubMed database with inclusion criteria 'free full texts' and publications date between 2015 – 2024. A total of 7272 results were found; 30 publications were ultimately included in the review.

Abbreviated description of the state of knowledge

Overusing AAS is very popular among people training at the gym. They have an anabolic effect on muscle tissue. They contribute to infertility in men and masculinization in women. Stimulation of androgen receptors above physiological doses of AAS leads to vascular changes that, in extreme cases, may lead to sudden cardiac death. Moreover, they accelerate brain aging. An increase in aggression and risky sexual behavior has been observed among people using doping. The diagnostic material used in anti-doping tests is urine and blood serum.

Summary

AAS abuse is a serious public health problem. Men who want to improve their figure and decide to use doping are particularly at risk. Due to the easy availability of steroids, society should be made aware of the negative effects of steroid use.

Keywords: anabolic-androgenic steroids, anabolic-androgenic steroids side effects, anabolic-androgenic steroids doping

Introduction

Anabolic-androgenic steroids (AAS) are a group of hormones used as doping in sports. AAS are most commonly used in cycles of 6 to 18 weeks [1]. They influence the growth of muscle mass and consequently, increase strength. They are responsible for a number of side effects such as acne vulgaris, hypertension, cardiomyopathies, gynecomastia, abnormal lipid metabolism, erectile dysfunction and dysregulation of testosterone secretion, which can lead to testicular atrophy in men [2]. Although the trade and use of these substances is banned in many countries, they can easily be purchased online [3]. There are two types of anabolic-androgenic steroids, synthetic derivatives of testosterone. The first group includes 17-alpha alkyl derivatives: e.g. oxandrolone, oxymetholone and fluoxymesterone. The second group includes derivatives of 17-beta esters, including cypionate, enanthate, testosterone heptylate and propionate, as well as nandrolone decanoate and dromostanolone [4,5]. Nandrolone phenylpropion to an androgenic steroid, which was one of the first AAS used as doping in sports already in the 1960s [5].

Objective

The use of anabolic-androgenic steroids is widespread and is a serious public health problem. The purpose of this review is to present the multi-organ adverse effects caused by the use of these substances. Greater public awareness of adverse side effects may favorably influence the decline in steroid use. The review may help to understand the effects of the above substances and facilitate clinical diagnosis when a patient is suspected of using steroids. The review also discusses the most current anti-doping methods used to detect anabolic-androgenic steroids in professional athletes.

Review methods

The literature search was conducted in PubMed databases from 2015-2024, taking into account the available free full texts. The keywords used to search the databases were “anabolic-androgenic steroids and side effects” (PubMed - 1427), “anabolic-androgenic steroids and mechanism of action” (PubMed - 3250), “anabolic-androgenic steroids and sport” (PubMed - 454), “anabolic-androgenic steroid and functioning of the cardiovascular system” (PubMed - 17). The search data are current as of 30.07.2024. In the end, we selected 30 publications that met the assumptions. Most of the papers used to create the review, were published between 2018 and 2024, we wanted the review to be as up-to-date as possible. However, we used a paper dating back to 2015 by Hughes D, as we felt that the information contained therein would be relevant to the rest of our work.

Epidemiology

It is difficult to determine the number of people using anabolic-androgenic steroids in the general population. A wide range is assumed from 1% to 15%, depending on the community [6]. It is estimated that 1-3% of US citizens take anabolic-androgenic steroids, which means that they are very popular there [7]. Other countries where AAS use is also popular include Brazil and Australia. In Asian countries, including China and Japan, their use is much less, probably because in this part of the world the male archetype is less muscular [6]. In Great Britain, according to a survey conducted in 21 gyms, as many as 8% of respondents declared that they had had contact with AAS during their lives. Currently, only 20% of people using AAS are professional athletes [7]. The overwhelming majority of people who decide to use AAS are average gym users who want to become stronger, build muscle mass and increase self-confidence in a short time. By achieving these effects, they become more convinced that the use of AAS does not cause any adverse health effects [8].

Mechanism of action. Androgen receptors (ARs) are found in unbound form in the cytoplasm of target tissue cells. ARs are activated by a ligand, free testosterone or testosterone that has been converted by the cytoplasmic enzyme 5-alpha reductase to 5α-dihydrotestosterone (DHT). Ligand-activated AR releases heat shock proteins (hsp90, hsp70 and hsp40), which were previously responsible for stabilizing the structure. AR moves to the cell nucleus, where dimerization occurs. The AR ligand binds to specific promoter regions of target genes, androgen response elements (AREs), and influences the transcription process [7,9].

Exogenous use of testosterone impairs the natural synthesis of the hormone in tissues. High levels of testosterone can antagonize receptors for glucocorticosteroids, which reduces protein catabolism, leading to an increase in muscle mass and strength. Exogenous androgens in excess stimulate the growth hormone (GH) axis and stimulate the hepatic synthesis of insulin-like growth factor 1 (IGF-1), which stimulates muscle anabolism [7]. Testosterone is converted by aromatase to estradiol and estrone [10], which are additionally responsible for the increase in bone and muscle mass [7].

AAS induce muscle hypertrophy [11]. Increased volume of type I (slow-twitch) and type II (fast-twitch) muscle fibers [12]. Angiogenesis is stimulated in them, thanks to which the muscles are better supplied with blood. The number of cell nuclei in the myocyte increases. This can lead to an increase in muscle strength. Muscle hypertrophy depends on the number of receptors and is more visible in the muscles of the arms, neck and chest, because there are more androgen receptors there [6].

The influence of androgenic steroids on the male body.

Overuse of AAS may result in hypogonadism. The use of exogenous testosterone causes a decrease in the concentration of gonadotropins. Secondarily, this leads to inhibition of endogenous testosterone production and disruption of spermatogenesis, resulting in a decrease in testicular volume and reduced sperm production. Reduced levels of gonadotropic hormones and testosterone may persist even after discontinuing AAS use [13]. Men using AAS often use post-cycle therapy. It is intended to accelerate the proper regulation of the hypothalamic-pituitary-gonadal axis (HPGA), the balance of which has been disturbed by exogenous androgenic steroids. Post-cycle therapy uses selective androgen receptor modulators (SERMs): clomiphene and tamoxifen [14], aromatase inhibitors and human chorionic gonadotropin [6].

The influence of androgenic steroids on the female body.

Testosterone is a hormone produced in both men's and women's bodies, but in men's bodies its production is much more intense. Healthy adult women should have 15x lower testosterone concentrations than men [15]. In women, the ovaries perform the function of testosterone synthesis. Testosterone is also produced by the conversion of weaker androgens, androstenedione and dehydroepiandrosterone (DHEA), this takes place in the ovaries and adrenal glands.

The main reason for women's use of AAS appears to be to improve athletic performance, especially in bodybuilding and weightlifting [16]. The effect of steroid doping is

an increase in strength and lean body mass. AAS cause masculinization. Women exposed to non-physiological, excessive doses of androgens may complain of lowered voice, clitoral hypertrophy, increased aggressive behavior and dermatological problems such as hirsutism, male pattern baldness, and acne [17].

Voice disorders are changes that may occur even with small doses of testosterone. Moreover, it is assumed that the deepening of the voice is irreversible.

While examining postmenopausal women treated with testosterone, it was noticed that hirsutism appeared slowly, within 4-6 months of starting the treatment. However, at higher-than-therapeutic doses, such as when doping, excessive male pattern hair may manifest earlier. Hirsutism that occurred as a result of using 150 mg of testosterone enanthate every 4 weeks resolved after discontinuing AAS [3].

The influence of anabolic-androgenic steroids on the functioning of the cardiovascular system.

Physiological doses of anabolic-androgenic steroids may have a cardioprotective effect. Overuse of AAS may lead to changes in the cardiovascular system.

Immunochistochemical analysis of the calcified femoral artery and calcified heart valves was performed. The expression of androgen receptors was detected in the tested materials. Then, in vitro tests were carried out on mice. 9 days of testosterone therapy resulted in an increase in vascular calcifications in rodents. The study concluded, excessive stimulation of androgen receptors led to calcification, which induces cell damage and leads to loss of vascular elasticity. [8].

It has been shown that approximately 3% of people using AAS are diagnosed with acute myocardial infarction at a young age. The pathophysiology of the development of acute myocardial infarction in young people using doping is multifactorial [18]. These factors include: damage to coronary vessels, progressive atherosclerosis, thrombosis and narrowing of blood vessels [19]. Atherosclerosis develops due to an increase in low-density lipoprotein (LDL) and a decrease in high-density lipoprotein (HDL). It has also been shown that people using doping experience an increased development of atherosclerotic plaques in coronary vessels compared to people not using AAS. There is evidence that the physiological level of testosterone in the blood has a vasodilating effect on blood vessels, while in people using doping, vasoconstriction is observed, mainly caused by an increase in the concentration of norepinephrine, angiotensin II and thromboxane in the circulating blood [18].

In extreme cases, the described changes may lead to Sudden Cardiac Death (SCD) [20]. Excessive growth of the heart muscle induced by doping may lead to the occurrence of heart rhythms that pose a direct threat to the patient's life. Moreover, it was noticed that the occurrence of SCD is related to the direct cardiotoxicity of the AAS used [21].

Anti-doping tests.

Abuse of anabolic-androgenic steroids is a common practice among athletes around the world. That is why many sports federations require that athletes be subjected to anti-doping tests. The World Anti-Doping Agency (WADA), under the leadership of the International Olympic Committee (IOC), coordinates the fight against the use of prohibited chemicals in sports [22]. In 1974, the IOC declared anabolic steroids a banned group [23]. The organization's goals are education and prevention of people in the risk group [22]. Another key function of WADA is to support high-quality diagnostic tests aimed at detecting constantly emerging analogues of doping substances used by athletes who want to illegally improve their sports results in various types of sports competitions [24].

Urine as a matrix contains relatively high concentrations of AAS or their metabolites, in addition to being a non-invasive method [25]. There are several analytical methods around the world that enable the detection of AAS and their metabolites in urine. The methods used in diagnostics are: gas or liquid chromatography combined with mass spectrometry (GC-MS/MS and LC-MS/MS). The basic diagnostic material is a urine sample taken from the athlete. The collected sample is searched for metabolites of substances banned by WADA using the methods described above. This is not an ideal research material due to the inability to supervise the athlete's urine sample. Another obstacle is the inability to collect a urine sample in some situations immediately after completing a sports competition.

Blood serum may be an additional diagnostic material. Steroid esters can be detected in the serum, which are not detectable in the urine of a person using doping.

The developed LC-MS/MS method is highly effective in detecting exogenous steroids in blood serum. It is an alternative or complementary method of anti-doping tests, where the test material is a sample of the athlete's urine [26].

There are indications for the use of AAS in athletes. In such a situation, the detection of specific prohibited substances in given athletes is not treated as doping. The Food and Drug Administration (FDA) approves the use of testosterone enanthate in men with primary hypogonadism and in boys with delayed puberty. It also allows the use of testosterone

enanthate, undecanoate and testosterone cyponate if the athlete is diagnosed with hypogonadotropic hypogonadism.

The use of AAS in aplastic anemia, renal failure and growth disorders is not an indication justified by the FDA for the detection of banned substances in athletes [5].

Impact on the nervous system and psyche.

AAS have the ability to cross the blood-brain barrier. They bind to androgen receptors, which are abundant in the brain stem, hippocampus, cerebral cortex, amygdala, hypothalamus and striatum. Excessive stimulation of receptors caused by the external supply of androgenic steroids may accelerate brain aging processes, lead to cognitive dysfunction and be responsible for psychosocial disorders.

In 2017, a study using Magnetic Resonance Imaging (MRI) was conducted, in which the thickness of the cerebral cortex was compared between weightlifting athletes using steroid doping and a group of non-exercising people. The results of the study indicate thinning of the cerebral cortex of athletes using doping compared to non-training people [27]. In addition to a reduction in the volume of the cerebral cortex, the reduction of gray matter may lead to another structural dysfunction of the brain, a reduction of the putamen. Long-term use of AAS leads to neurochemical and functional changes in the central nervous system [28]. Scientific literature reports that above-physiological doses of AAS may contribute to neuronal apoptosis, contributing to the development of neurodegenerative processes.

Over the years, it has been proven that the use of AAS increases aggressive behavior. Several publications present cases of men who had no criminal history before using AAS and were not prone to violence and aggression. However, while using AAS, they attempted or committed murder.

High serum testosterone levels have been shown to be associated with risky behavior and reactive aggression [29]. People who use AAS may experience emotional uplifts called "steroid rage", these are sudden attacks of aggression provoked by subliminal stimuli [30]. In 2020, a study was conducted on a group of bodybuilders, which showed that the use of AAS increases the likelihood of engaging in risky sexual behavior and the development of psychopathic traits. It was also noticed that people who have considered supplementation with anabolic steroids have greater psychopathic tendencies and problems in dealing with emotions than people who have never considered AAS supplementation. The authors of the above study warn against drawing clear conclusions because it requires further observations and recommend continued research [27].

Conclusions

Anabolic-androgenic steroids are very popular in various settings. Epidemiological data indicate that some gym-goers have been exposed to AAS, which means that access to these substances is not difficult. Currently, the vast majority of doping users are non-professional athletes. The desired effect of AAS use, which is the main motivation of those who choose to use doping, is faster gains in strength and muscle mass. Muscle hypertrophy occurs most visibly in areas with abundant receptors for androgens. AAS also cause a number of systemic side effects that those who choose to use doping are often unaware of. Supra-physiological doses of AAS have far-reaching consequences, acting destructively on organs. Table 1 summarizes the adverse effects of anabolic-androgenic steroids on specific organ systems.

Organ system	Side effects
Skin	▫ Acne vulgaris
Metabolism	▫ Dyslipidemia, increased LDL levels and decreased HDL levels
Cardiovascular system	▫ Increased development of atherosclerotic plaques in coronary vessels ▫ Vasoconstriction ▫ Vascular calcification ▫ Reduced vascular elasticity ▫ Hypertension ▫ Cardiomyopathies ▫ Acute myocardial infarction ▫ Sudden cardiac death (SCD)
Nervous system	▫ Accelerate brain aging ▫ Cognitive dysfunction ▫ Psychosocial disorders ▫ Development of neurodegenerative diseases
Female sexual system and sex characteristics	▫ Masculinization ▫ Lowered voice ▫ Clitoral hypertrophy ▫ Hirsutism ▫ Male pattern baldness
Male sexual system	▫ Erectile dysfunction ▫ Testosterone secretion disorders ▫ Testicular atrophy

Table 1. Abuse of anabolic-androgenic steroids and their adverse effects on various organ systems.

AAS, due to their anabolic effects on tissues, are used as illegal doping in sports. The vast majority of sports federations check athletes for banned substances. The most common diagnostic material used is urine collected from the athlete. The diagnostic methods used to analyze the sample are gas or liquid chromatography combined with mass spectrometry (GC-MS/MS and LC-MS/MS). Urine is checked for the presence of AAS and their metabolites. Unfortunately, steroid esters cannot be detected in urine. The method that makes this possible is the analysis of the athlete's blood serum. It is a complementary or alternative method to urinalysis.

Disclosure

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