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An Overview of the Deadly Effects of Anabolic-Androgenic Steroids: Clinical Cases and Scientific Insights

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ABSTRACT

Background: Anabolic-androgenic steroids (AAS) are widely used for performance enhancement, but their misuse, particularly in bodybuilding and professional sports, poses significant health risks. While AAS have legitimate medical applications in treating certain hormonal disorders, abuse of these substances can lead to severe and often irreversible health consequences.

Objective: The aim of this work was to highlight the health and life risks associated with AAS abuse, with a focus on the most common causes of death, based on example case reports and scientific studies.

Materials and Methods: This review was based on scientific research and case reports obtained from the PubMed database using the following key terms: “androgenic anabolic steroids,” “androgenic anabolic steroids abuse,” and combinations of these with terms such as “premature death,” “sudden cardiac death,” “suicide,” “liver injury,” “renal failure,” and “health consequences.”

Conclusion: AAS misuse can increase the risk of sudden cardiac death, stroke, suicide and other complications. Clinical research stresses the importance of awareness, education, and medical supervision to prevent these risks, emphasizing the need for regulation and informed decision-making to protect individuals from harm.

Key words: Androgenic-anabolic steroids, Androgenic-anabolic steroids abuse AAS, premature mortality, health consequences of AAS

Introduction

Anabolic androgenic steroids (AAS) are synthetic chemical substances whose structure resembles testosterone, a natural male sex hormone. They are used in medicine to treat various conditions, such as hormonal disorders, weight loss associated with chronic diseases, and delayed puberty.[1] Nevertheless, their popularity among athletes and bodybuilders is mainly due to their anabolic properties, which promote muscle mass and strength growth.[2] AAS, although commonly used in sports and bodybuilding communities, poses a serious threat to the health of users. They have numerous, often dangerous side effects that can lead to permanent damage to the body. In particular, their use is associated with various health problems, such as hormonal disorders, liver damage, heart diseases, as well as mental health issues like depression and aggression. In extreme cases, irresponsible use of anabolic steroids can lead to premature mortality.[3]

The objective of this paper is to provide a comprehensive overview of the harmful effects of anabolic steroids, with a focus on their potential to cause serious health issues and premature mortality. By examining clinical case studies and reviewing scientific research, this paper aims to highlight the risks associated with anabolic steroid use, including liver damage, cardiovascular diseases, mental health disturbances, and other long-term

consequences. The goal is to raise awareness about the dangers of anabolic steroids and emphasize the importance of informed decision-making in the context of their use.

Chemical Structure, substances, and routes of administration

Anabolic steroids are compounds classified within the steroid group, featuring a cyclic carbon structure with 17 carbon atoms. The core structural component is the steroid nucleus, made up of four fused carbon rings. Variations between different steroids occur due to the addition of various functional groups or modifications in the chemical bonds, which impact their biological activity.[4]

The most commonly used anabolic steroid in medicine and beyond is testosterone and its esters: testosterone undecanoate, testosterone enanthate, testosterone cypionate, and testosterone propionate. The second most frequently used in medical applications is nandrolone (19-nortestosterone) and its esters. Other registered synthetic derivatives of testosterone include: stanozolol, methandrostenolone (methyltestosterone), oxandrolone, mesterolone, oxymetholone, drostanolone propionate (dromostanolone propionate), metenolone (methylandrostenolone) esters, and fluoxymesterone [4]. Designer steroids are anabolic androgenic steroids (AAS) that have not been authorized for medical use but are often sold on the black market. Notable examples of designer steroids include 1-testosterone (dihydroboldenone), methasterone, trenbolone enanthate, desoxymethyltestosterone, tetrahydrogestrinone, and methylstenbolone [5].

Anabolic androgenic steroids (AAS) are commonly administered in four forms: oral tablets, injectable steroids, topical creams or gels, and transdermal patches.[4,6]

Biochemical Mechanism of Action

The action of anabolic steroids involves their binding to androgen receptors in target cells. Once bound, the hormone-receptor complex enters the cell nucleus, where it alters gene expression and promotes increased protein synthesis. This results in two key effects: anabolic and androgenic. The anabolic effect leads to increased muscle mass and improved tissue regeneration, while the androgenic effect is associated with the development of male sexual

characteristics, such as enhanced body hair growth, deepened voice, and increased libido.[7] At physiological doses, these effects support homeostasis and proper development. However, at supraphysiological doses, their effects are amplified, leading to various side effects. This has been demonstrated in numerous studies, such as a recent prospective observational study in which all 100 participants reported at least one side effect from AAS use [8].

Use in Medicine

AAS can be widely used in medicine, but only a limited number is approved or proposed for therapeutic purposes, primarily in the replacement therapy of hypogonadism. Direct testosterone replacement therapy (TRT) is the only FDA-approved treatment for male hypogonadism.[9] Here are several examples: AAS can be used by pediatric endocrinologists to treat children with growth failure. However, the availability of synthetic growth hormone, which has fewer side effects, makes this a secondary treatment option [10]. Nandrolone decanoate is approved for the prevention and treatment of osteoporosis in postmenopausal women.[11] Methyltestosterone is used in low doses to treat menopausal symptoms, specifically osteoporosis, hot flashes, and to increase libido and energy, as well as postpartum breast pain, engorgement, and breast cancer in women [12,13]. Oxandrolone improves both short-term and long-term outcomes in individuals recovering from severe burns and is well-established as a safe treatment for this purpose.[14] Currently, research is underway to explore the use of AAS in developing a safe and reversible male hormonal contraceptive method. [15,16,17,18]

Androgenic-anabolic steroids in professional and amateur sports

Due to their impact on muscle mass, strength, and endurance, AAS are sometimes used in both professional and amateur sports, despite their illegal status in many disciplines.

In professional sports, AAS are used by some athletes to enhance physical performance, improve results, and shorten recovery time after intense training. They are often used in disciplines that require significant strength, muscle mass, or endurance, such as

bodybuilding, weightlifting, sprinting, and combat sports.[19] However, the use of anabolic steroids in professional sports is illegal and prohibited by most anti-doping organizations, such as the World Anti-Doping Agency (WADA). Anti-doping tests aim to detect the presence of these substances, and athletes who are caught using AAS can be penalized with disqualification, loss of medals, or a ban from competing. Furthermore, such actions are considered unethical, as they give an unfair advantage and undermine fair competition.

Among amateurs, the use of AAS is also present, though with fewer formal consequences. Amateur athletes, particularly those involved in bodybuilding, fitness, or strength sports, often use steroids to rapidly increase muscle mass and improve their physique. In this case, AAS are also used to enhance sports performance, although their health effects can be much more severe, especially when abused or used without proper supervision.

AAS can be easily obtained through local dealers or online, even though their sale—and in some cases, their use—is prohibited in many countries.[2] In Western countries, the lifetime prevalence of AAS use typically ranges from 1% to 5%, while globally, 6.4% of males and 1.6% of females report using them. [5,21,3] Among gym-goers, the rate of AAS use has been found to be as high as 70%.[22] The lack of medical supervision, the stigma surrounding their use, and the easy access to AAS—especially among individuals not involved in professional sports who may not have full knowledge about the proper use of these substances—are factors that exacerbate the global problem of AAS abuse.

Health consequences of AAS abuse

AAS are not free from side effects and have been associated with various conditions, including hormonal imbalances, gynaecomastia, testicular issues, infertility, and cardiomyopathy, as demonstrated in multiple studies [19]. This is further supported by a large retrospective cohort study conducted in 2018.[19] The study involved 545 male doping offenders (the AAS group) and compared their data with that of 5450 male control subjects. Doping sanctions occured at the average age of 26.2 years (standard deviation [SD] 6.3) for the AAS group, which was similar to the age of participants in the control group, also 26.2 years (SD 6.3). The average follow-up duration was 7.4 years (SD 2.9) in the AAS cohort and

7.3 years (SD 3.0) in the control group (P = 0.48). Over the follow-up period, seven deaths (1.3%) occurred in the AAS group and 23 deaths (0.4%) in the control group, resulting in a hazard ratio (HR) of 3.0. The AAS group had significantly more hospital visits than the control group: 5115 hospital visits among the 545 AAS users (1.26 per person-year) compared to 27,167 visits among the 5450 controls (0.68 per person-year). The median annual hospital visits were 0.81 in the AAS cohort and 0.36 in the control group (P < 0.0001, Wilcoxon rank-sum). Most of these hospital admissions (59%) were related to injuries and unspecified health examinations (ICD-10 codes S–Z), which were not the primary focus of this study. Other disorders examined in the study included: gynecomastia, with a 13-fold increase in prevalence; sexual dysfunction, with a 2.4-fold increase; and cardiomyopathy and atrial fibrillation, with a 3-fold increase. No increase in the prevalence of ischemic heart disease was observed in this group of AAS users. Furthermore, the risk of thromboembolic disorders (such as thrombophlebitis and pulmonary embolism) was found to be five times higher in the AAS group compared to the control group. Additionally, 27.3% of AAS users had filled at least one prescription for acne treatment. The incidence of neoplastic, hepatobiliary, and kidney diseases did not show a significant increase in the AAS group.

Additionally, research shows a higher rate of mortality and morbidity among AAS users. In a Swedish register-based study, researchers tracked 409 men who had tested positive for AAS and found that their mortality rate was 18 times higher than expected.[23] Another study involving 62 male powerlifters who ranked in the top five at the Finnish Championships between 1977 and 1982. Their findings indicated that this group of athletes, likely to have used AAS, experienced a mortality rate 4.6 times higher than that of the average Finnish male population.[24] Consistent with this, Rasmussen et al. found that active AAS use was linked to elevated 24-hour blood pressure and increased aortic stiffness, both of which are recognized risk factors for cardiovascular events and mortality.[25] Additionally, AAS use has been associated with a reduction in HDL cholesterol, an increase in LDL cholesterol, and secondary erythrocytosis. These factors further contribute to a heightened risk of thrombosis [26, 27].

Sudden Cardiac Death

The use of anabolic steroids creates favorable conditions for the development of heart attack risk: anabolic steroids can alter the blood lipid profile, leading to unfavorable changes in cholesterol levels, such as increased LDL and decreased HDL. They can lead to an increase in blood pressure through several mechanisms: sodium and water retention, increased sympathetic tone, increased erythropoiesis, thrombophilia, and hypertrophic cardiomyopathy.[28] The enlargement of the heart muscle can also hinder blood flow through the heart, increasing the risk of ischemia and heart attack, as well as being a source of dangerous arrhythmias.[29,30]

In a case review conducted by Torrisi, M. (2020), which gathered data from 33 cases of Sudden Cardiac Death over the years 1993-2020, the following results can be found: Out of the 33 cases, 31 (93.9%) were male and 2 (6.1%) were female. The average age was 29.79 years, with a standard deviation of 8.5 years (ranging from 13 to 54). A total of 21 cases (63.6%) involved athletes, with bodybuilding being the most common sport (13 cases, 39%). All individuals had a history of anabolic steroid (AAS) abuse or displayed a physical phenotype suggesting AAS use. The duration of AAS use was unspecified in 24 cases, while in the remaining 9 cases, the usage ranged from 3 months to several years. Heart weight as a percentage of body weight was determined in 15 cases. Anamnestic data were available in 24 out of the 33 cases (72.7%), and none of these individuals had a personal or family history of heart disease before the age of 50. The most common macroscopic finding was cardiomegaly (11 cases, 33%), based on the heart's weight relative to body weight, followed by left ventricular hypertrophy (10 cases, 30%). Dilated cardiomyopathy was detected in 3 cases (9%). Histological examination revealed fibrosis and necrosis of myocardial tissue in 21 (79%) and 17 (52%) cases, respectively. Other histological changes included atherosclerosis (7 cases, 21%), inflammatory infiltrates (4 cases, 12%), coronary stenosis (3 cases, 9%), and left ventricular apoplexy (2 cases, 6%).[31] The most recent case report in this review describes a 24-year-old male whose death was caused by a myocardial infarction due to severe coronary atherosclerosis and acute occlusive thrombosis in the left main trunk and left anterior descending artery (LAD), diagnosed as single vessel disease, attributed to anabolic steroid (AAS) use. His personal history and toxicological tests ruled out the use of other illicit substances, and there was no family history of dyslipidemia, premature atherosclerosis, or cardiovascular events.[32] More and more case reports of myocardial infarction among

young AAS abusers are being published. [33, 34, 35] Not all of them describe fatal cases, but they definitely highlight dangerous situations that could lead to death without qualified medical assistance.

Thromboembolic complications and Stroke.

Stroke, including both ischemic and hemorrhagic types, can be triggered by changes in blood pressure, increased blood clotting, and other risk factors that are amplified by anabolic steroid (AAS) use.[36] Additionally, some reports suggest that long-term AAS use may elevate serum homocysteine levels [37], though the precise mechanism behind this effect remains unclear. This is also recognized as a risk factor for ischemic stroke, as highlighted in the subsequent case report [38]. The article presents a case of a man in his 40s who suffered a large ischemic stroke in the left middle cerebral artery (MCA) area, along with multifocal thrombosis in both venous and arterial systems outside the cranial region. The patient was also diagnosed with a pulmonary embolism through CT pulmonary angiography and a right popliteal artery thrombus via lower limb ultrasonography. Anabolic androgenic steroid (AAS) use is emphasized as an important risk factor, especially in young stroke patients with elevated serum homocysteine levels. The stroke was caused by a hypercoagulable state induced by high plasma homocysteine, likely due to chronic AAS use combined with the homozygous MTHFR c.677 C > T thermolabile variant, folate deficiency, and vitamin B12 deficiency.

Mental disorders and Suicide

Anabolic steroids, in addition to their impact on the physical aspects of the body, also have a significant effect on mental health. Their use can lead to the development of

depression, suicidal thoughts, and aggression, which may contribute to the risk of suicides. The etiology and pathomechanism of these disorders are multifactorial and complex [39]. Risk factors for suicidal behavior linked to AAS abuse include hormonal imbalances, heightened aggression, and impulsivity. Anabolic steroid use is often associated with high expectations regarding body image and athletic performance. When these goals are not met, or when physical and mental health issues arise, problems with self-esteem and body image may occur. Studies show that prolonged AAS use can alter brain structures responsible for regulating emotions and behavior [39]. Additionally, AAS can cause insomnia, which negatively impacts mental health. Sleep deprivation worsens mood, leads to exhaustion, and can contribute to depression.[40] Chronic sleep disturbances may also increase the risk of suicidal thoughts. Long-term anabolic steroid use can result in addiction, with individuals experiencing emotional "lows" after completing a steroid cycle. The rise in hormone levels followed by a sudden drop after discontinuing use can cause rapid mood swings [39]. Increased aggression, body image changes, and emotional struggles can create difficulties in interpersonal relationships, leading to feelings of isolation and loneliness. These relationship issues can further deteriorate mental health, potentially contributing to the development of depression [41].

A large study summarized 8 cases of suicides or suicide attempts among AAS users.[41] The participants were men, aged 21 to 33, who were otherwise physically healthy and had been using AAS for several years. The study concluded that long-term AAS use appears to increase the risk of suicide in multiple ways. One suicide occurred in a person experiencing major depression after discontinuing AAS, while others were impulsive, linked to a combination of depression and poor impulse control during active AAS use. All subjects had psychiatric issues prior to AAS use, but the mental and behavioral changes caused by steroid use led to psychosocial complications, which ultimately contributed to suicides.

Liver injury and hepatotoxicity

Anabolic steroids, particularly those taken orally (such as C17-α alkylated steroids), can have a harmful impact on the liver. The liver is forced to metabolize these substances intensively, leading to overloading and damage to hepatocytes.[42] Anabolic steroids can

also cause cholestasis and jaundice. Prolonged use of AAS can lead to liver cell damage, potentially causing hepatitis, and in severe cases, liver failure. As a result, the liver may become unable to properly eliminate metabolic waste, leading to its accumulation in the body and further damage.[43,44] Anabolic steroids affect lipid metabolism, which can lead to fat accumulation in the liver, causing fatty liver and increasing the risk of cirrhosis.[2,45]

Anabolic steroids, especially when used in high doses over long periods, can elevate the risk of developing both benign and malignant liver tumors, such as hepatoma [46], as they may cause mutations in liver cells. Regular users of anabolic steroids may have a 2-3 times higher risk of liver cancer compared to those who do not use these substances [47].

Despite these reports, there is no consensus in the scientific community regarding the actual risk of severe liver damage caused by AAS use. In controlled trials, clinical signs of liver damage due to AAS use are relatively uncommon. For example, in a double-blind, randomized controlled trial, only one of 61 HIV patients receiving a high dosage of 100–150 mg of oxymetholone (a 17α-alkylated anabolic steroid) daily developed jaundice over 16 weeks [48]. Similarly, in two other double-blind, randomized controlled trials, hemodialysis patients who were administered 100 mg of oxymetholone daily for 24 weeks showed no signs of liver damage [49, 50]. Additionally, the HAARLEM study found no acute or subacute clinical signs of liver damage, even though 67% of participants reported using oral AAS [8].

However, the situation is different in cases of AAS abuse. Several case reports document instances of toxic hepatitis, which can be fatal due to AAS overdose. One such report details a fatal overdose of stanozolol in a previously healthy 35-year-old amateur bodybuilder.[51] The patient presented with general malaise, jaundice, and a history of hematemesis after taking stanozolol orally for three months. Upon admission, his liver function tests showed significant abnormalities, and he died within 48 hours despite symptomatic treatment. During the autopsy, sub-massive liver cell death, areas of macro-vesicular fat accumulation, and signs of acute liver injury with a cholestatic pattern were observed. Chemical analysis confirmed the presence of stanozolol in the blood, liver, and kidneys. The cause of death was attributed to hepatic necrosis resulting from the stanozolol overdose.

Renal failure and nephrotoxicity

There is significant evidence indicating the nephrotoxic effects of AAS, including sodium and water retention, which increases blood volume and pressure.[52] This poses a serious risk to the kidneys, as their blood vessels, particularly the glomeruli, are highly sensitive to elevated blood pressure. Chronic hypertension can damage these vessels, potentially leading to glomerulonephritis and chronic kidney disease. Anabolic steroids also boost protein synthesis in the body, resulting in higher production of nitrogenous metabolites like urea and creatinine. Additionally, AAS stimulate red blood cell production, leading to polycythemia. This increase in red blood cells raises blood viscosity, making it more difficult for blood to flow through the vessels, including those in the kidneys.[53]

Although these concerns exist, the majority of studies do not classify AAS use as the direct or main cause of fatal kidney failure. Rare case reports that associate premature death with kidney damage from AAS generally involve renal failure caused by hepatotoxicity, such as acute bile nephropathy [54], or the toxic effects of high AAS doses. Additionally, a few studies have linked AAS use to focal segmental glomerulosclerosis (FSGS) [55, 56].

Conclusion

Anabolic-androgenic steroids (AAS) pose significant health risks that extend far beyond their intended use in medical treatments. Despite their therapeutic potential in managing certain hormonal disorders, their misuse, particularly in the realms of bodybuilding and professional sports, can lead to severe and often irreversible health consequences. The abuse of AAS has been linked to a range of harmful effects, including cardiovascular diseases, liver damage, kidney failure, and mental health disturbances, such as aggression, depression, and suicidal tendencies. Furthermore, the misuse of these substances, often without medical supervision, exacerbates the risks of sudden cardiac death, stroke, and thromboembolic complications, highlighting the dangerous consequences of AAS abuse. In addition to the physical toll, the mental health implications of AAS use—especially the psychological dependence and mood swings—demonstrate the complex nature of steroid addiction.

Clinical case studies and scientific research consistently emphasize the long-term dangers of anabolic steroid abuse, urging a need for increased awareness and education regarding their risks. The widespread availability and use of AAS, particularly among non-professional athletes and gym-goers, further exacerbate the problem, often leading to irreversible damage before proper medical intervention can occur. To mitigate these risks, it is essential to promote informed decision-making, responsible use, and the need for adequate medical supervision for those considering AAS. Through public health efforts, greater regulation, and education on the dangerous effects of AAS, we can reduce the prevalence of misuse and safeguard the well-being of individuals at risk.

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