Hepatotoxicity associated with illicit use of anabolic androgenic steroids in doping

R. SOLIMINI, M.C. ROTOLO, L. MASTROBATTISTA, C. MORTALI, A. MINUTILLO, S. PICHINI, R. PACIFICI, I. PALMI

Department of Therapeutic Research and Medicines Evaluation, Drug Abuse and Doping Unit, Istituto Superiore di Sanità, Rome, Italy

Abstract. – Anabolic Androgenic Steroids (AAS) abuse and misuse is nowadays a harmful habit involving both professional or recreational athletes, as well as general population. AAS are also frequently present in over-the-counter dietary supplements without being declared in the list of ingredients, leaving consumers unaware of the risks of adverse effects. Indeed, health risks of AAS consumption in pharmaceutical preparations or dietary complements seem still underestimated and under-reported. The variety of complications due to AAS misuse involves cardiovascular, central nervous, musculoskeletal and genitourinary systems of both males and females; psychiatric and behavioral effects, damages to metabolic system, skin and mainly liver. For instance, relevant concern has been raised by the AAS hepatotoxicity including adenoma, hepatocellular carcinoma, cholestasis, and peliosis hepatis.

The present review reports the information available on the hepatotoxic effects of AAS use in professional and amateur athletes.

Key Words: Anabolic androgenic steroids, Doping, Hepatotoxicity, Illicit use.

Introduction

Testosterone is the male sex hormone and the typical endogenous anabolic steroid with specific properties of stimulating muscle mass growth (anabolic aspect) and enhancing male sexual characteristics (androgenic aspect)\(^1\-^5\).

Testosterone was first isolated from bull testes in 1935 by David and co-workers\(^1\,^2\,^6\) and in the same year, it was chemically synthesized by Butenandt in Göttingen (Germany) and Ruzicka in Basel (Switzerland)\(^7\). In 1940s testosterone was supposedly used by Germans in war contexts\(^4\,^6\) and it was prescribed in psychiatry for depression and andropause until the introduction of new treatments in 1950s\(^8\).

Since then, several synthetic analogs of testosterone, known as Anabolic Androgenic Steroids (AAS) or designer steroids (e.g. methyltestosterone in 1935, nandrolone in 1950 and 1953, testosterone esters from mid-1950s, stanozolol and oxymetholone in 1959, oxandrolone in 1962) have been produced in the attempt to minimize the androgenic effects and improve the anabolic ones\(^1\,^2\,^7\-^9\). However, a successful complete separation of the anabolic and the androgenic properties has never been realized in the synthetic derivatives of testosterone\(^1\,^2\,^7\-^9\). Among those, nandrolone was the first compound which showed a partial dissociation between anabolic and androgenic properties and therefore, it started to be used in the medical practice\(^2\,^12\).

After the Second World War, the use of AAS for performance improvement started to be widely spread in the sports circles and progressively turned into a business since almost all sports showed an economic importance strictly linked to the image of the power of the countries\(^9\).

The introduction of AAS in medical practice induced elite athletes to use them “off-label” with the aim of increasing muscle mass and enhancing sports performance\(^6\), but with a dosage usually much higher than the therapeutic one, with consequent serious health risks\(^2\,^9\,^13\,^14\).

In the 1950s, the use of AAS by Soviet and USA weightlifters was reported\(^2\,^4\). During the 1960s, the Council of Europe introduced the concept of doping in sports after the deaths of a couple of competitive athletes and the spread of harmful drugs use\(^2\,^15\).

The International Olympic Committee (IOC) started doping control tests in the Olympics of 1968 and subsequently AAS were introduced in the list of prohibited substances in 1976\(^4\,^6\,^10\).

In the 1970s competitive athletes and body builders were largely using AAS\(^4\,^6\) and in 1988
the sprinter Ben Johnson was prosecuted for being found positive for anabolic steroid stanozolol at Seoul Olympics and his gold medal was withdrawn by IOC. In the 1980s the exclusive use confined to elite sport up to then dangerously shifted to amateur athletes and even to non-athletes (mostly adolescents and young men) and recreational drug users. Since 1991, in the USA, AAS have been DEA (Drug Enforcement Administration) Schedule III substances under Controlled Substances Act.

The focus on AAS misuse in sports increasingly raised to the point that today the antidoping authorities monitor and control the phenomenon both on elite and recreational athletes.

AAS use prevalence in the general population worldwide is 6.4% for males and 1.6% for females. Abuse and misuse of AAS to boost muscles and sculpt the body also involves adolescents and young adults affected by body image disturbance or eating disorders, who use them for cosmetic purposes and showing increased masculinity.

AAS are illegally (meaning without a medical prescription) sold through the black market, websites, gyms, body building competitions, teammates, coaches, trainers and by inappropriate prescription or theft. Street names for illegally sold anabolic steroids include Gear, Winny, Deca, EQ, Tren-A, Fina, Arnolds, Juice, Pumpers, Roids, Stackers, Weight Gainers.

Overall AAS include testosterone, its synthetic derivatives, and precursors also known as prohormones (weaker formulations of AAS) like dehydroepiandrosterone (DHEA), dihydrotestosterone (DHT), 1-testosterone, 19-norandrostenedione, androstenedione, androstenediol, which are usually present in dietary supplements. Their administration can be oral, injectable (oil-based and water-based) and transdermal (testosterone cream), buccal and sublingual (i.e. tetrahydrogestrinone).

Several side effects related to AAS abuse involve mostly cardiovascular, reproductive, central nervous, and musculoskeletal systems, skin and liver. The most relevant one is undoubtedly hepatotoxicity since it has been shown that primarily the oral forms of AAS may damage liver function.

This article reviews the mechanism of action and potential hepatotoxicity of AAS abuse and misuse as a doping offense.

AAS Mechanism of Action

Synthetic AAS are compounds derived from the natural testosterone from which they differentiate because of several modifications of the basic testosterone structure. Endogenous androgens as testosterone have both skeletal muscle-building (anabolic) and masculinizing (androgenic) effects, while, as above reported, most of the synthetic AAS have been developed with the aim to separate the anabolic from the androgenic properties, preferring synthetic androgens that have preferential anabolic activity and no androgenic one. Testosterone acts as an androgen either directly by binding to the androgen receptor or indirectly by conversion to 5alpha-dihydrotestosterone (DHT). The structural modification of AAS alters the relative anabolic or androgenic activity, the binding affinity for the androgen receptor and metabolic clearance.

Testosterone and AAS pass into the blood system, through the target cell membrane, linking with intra-cytoplasmic receptors. This complex hormone-receptor is later transported into the nucleus of the cell, where it links up with DNA. It results in the production of RNA, DNA and the subsequent enhancement of proteinsynthesis (including increased amounts of actin and myosin in skeletal muscles).

The main chemical substitutions occurring to testosterone are the 17-beta-esterification and the 17alpha-alkylation. Whereas testosterone is metabolized rapidly in the body, the esterification of the 17-beta-hydroxy group makes the molecule more hydrophobic. When these esters of testosterone (i.e. testosterone enanthate, cypionate, and decanoate) are administered in an oily suspension, they are released very slowly into the aqueous plasma because of their hydrophobicity. This extends their duration of action.

Indeed, an important metabolic pathway of testosterone and its synthetic derivative is oxidation of the 17-beta-hydroxy group with the formation of the 17-keto metabolites. These polar metabolites are biologically inactive. The 17-alphal-alkylation induces the inhibition of metabolic deactivation by oxidation of the 17-beta hydroxy group in the liver, thus 17alpha-alkylated androgens can be effectively administered orally. Often the alkylation of the C-17 position of testosterone alters the relative anabolic potency about the masculinizing effects (androgenic steroids).

The mostly used oral anabolic steroids are ethylestranol, fluoxymesterone, mesterolone, methandienone, methenolone, methandrostenolone,
methyltestosterone, methenolone acetate, mibolerone, norethandrolone, oxandrolone, oxymetholone, stanozolol. The oral forms are resistant to immediate degradation and hepatotoxic, but their parenteral administration also leads to hepatic disfunction.

The injectable AAS are boldenone undecylenate, clostebol, drostanolone propionate, methenolone enanthate, nandrolone decanoate, nandrolone phenpropionate, nandrolone undecanoate, testosterone cypionate, testosterone esters blends, testosterone enanthate, testosterone propionate, trenbolone, trenbolone acetate, trenbolone hexahydrobencylcarbonate, testosterone undecanoate, stanozolol. The injectable agents have undergone esterification of the 17β-hydroxy group to make them more soluble in lipids, leading to a slower release of the steroid into circulation.

Hepatotoxicity of AAS

A relevant concern raised by the chronic administration of AAS is the toxic effect on liver.

Since the 1950s, case reports about anabolic steroids occasional effects on the liver such as cholestasis, liver tumors, and peliosis hepatis have been observed and reported in the literature. Nevertheless, the prevalence of toxic effects following AAS administration could and cannot be defined due to underreporting and lack of specific studies.

However, it seems that in some cases AAS-induced hepatotoxicity might be overestimated because rhabdomyolysis caused by heavy workouts in athletes can increase transaminases, and this occurrence may be erroneously interpreted as abnormal liver function.

Studies to evaluate hepatotoxicity, especially on a long time, on AAS abusers are difficult, usually for the unknown administered doses that are far beyond those used for therapeutic purposes. Moreover, in the case of using illicit samples of AAS, their real composition, and type of production or their concentrations are often not declared on the label, and the users do not know exactly the quality and the quantity of the substances they are assuming.

There are also ethical limitations to conducting a study since excessive and highly variable dosages cannot be proposed in clinical trials. The available scientific information mostly comes from AAS users population surveys or retrospective studies, cross-sectional surveys, and case reports as well as animal studies.

Hepatotoxicity of AAS may be correlated to individual susceptibility and genetic factors, and it is associated with an increase in infiltration of lymphocytes, neutrophils and eosinophils in liver tissue, subsequently to repeated exposure. Oxidative stress could represent a causal factor of liver toxicity due to AAS abuse. It has also been hypothesized that androgen receptor activation in hepatic cells may cause an increase in reactive oxygen species which leads to mitochondrial degeneration of hepatic cells, ultimately advancing to the clinical signs of hepatotoxicity observed with the intake of 17α-alkylated steroids. In fact, some antioxidants have been found to exhibit a hepatoprotective effect against AAS-induced hepatotoxicity. Due to the limited data, the effects of antioxidants in AAS-induced hepatotoxicity need further research.

17-Alpha-Alkylated Steroids and Liver Damage

The 17alpha-alkylated (17aa) steroids like methyltestosterone, methandrostenolone, oxymetholone, danazol, fluoxymesterone, stanozolol, norethandrolone, oxandrolone, dehydrochloromethyl-testosterone, formebolone, methandienone, testosterone (cypionate, enanthate, propionate), can be medically used for increasing weight and muscle growth in catabolic states, for treatment of aplastic anemia and bone marrow failure, as well as off-label for doping purposes. All these types of steroids have been associated with cases of liver damage such as cholestatic jaundice, peliosis hepatis, nodular regeneration, hepatic adenoma and hepatocellular carcinoma. Oxymetholone and methyltestosterone, instead, have frequently been linked to hepatocellular carcinoma. Stanozolol, either following intramuscular or oral administration, causes liver damage, in particular, inflammatory or degenerative lesions in centrilobular hepatocytes, ultrastructural alterations in the canaliculi and degenerative changes in mitochondrial and lysosomes.

On the other side, cholestasis induced by esterified testosterone and 19-nortestosterone derivatives is quite rare, although their prolonged use may increase the risk of hepatic tumors and nodular transformation, seemingly at a lower rate than the 17-alkylated testosterone.

The androgens act on intracellular androgenic steroid receptors, which are translocated to the nucleus and link androgen response elements on DNA, inducing androgen-stimulated genes in-
involved in cell growth and development. An unregulated growth stimulus to hepatocytes is the likely cause of nodular regeneration and hepatic tumors related to anabolic steroid use\textsuperscript{5}.

Other hepatic harms associated with AAS abuse include liver alterations such as subcellular changes of hepatocytes, hepatocellular hyperplasia, and general hepatic damage determined by increased liver enzymes: alkaline phosphatase, lactate dehydrogenase (LDH), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyltransferase (GGT) and conjugated bilirubin. Some growths, initially believed to be hepatocellular carcinomas, were benign hyperplastic lesions, which regressed with the discontinuation of AAS use\textsuperscript{2,40}.

A 2011 research\textsuperscript{41} conducted in Brazil on 180 non-competitive bodybuilders, 95 AAS users and 85 non-users, asymptomatic of any liver alteration, suggested that anabolic steroids could induce toxicant-associated fatty liver disease (TAFLD) in 12.6\% of the 95 AAS users. Another 2015 study\textsuperscript{42} on 182 asymptomatic recreational AAS using bodybuilders, showed that they were affected by liver injuries including hepatotoxicity, fatty liver, and liver neoplasm.

**Dietary Supplements Induced-Liver Injury**

Dietary supplements induced-liver injury (DILI) (i.e. hepatocellular hepatitis, spontaneous hepatic rupture, cholestatic hepatitis, hepatocellular adenoma and carcinoma, peliosis hepatitis and focal nodular hyperplasia) has been associated with products containing AAS such as androstenedione, dehydroepiandrosterone, desoxymethytestosterone, stanozolol, methasterone, methylthiostanol\textsuperscript{42}.

Herbal and dietary supplements related liver toxicity range from 2\% to 16\% of all cases of hepatotoxicity identified in Western countries Registries. It is worth to note that in the Spanish DILI Registry the cases of hepatotoxicity due to AAS has recently increased: from 5 cases in 1994-2009 to 15 cases in 2010-2013 (from 1\% to 8\% of the total cases) with a mean age of 32 years\textsuperscript{42,43}. Hepatocellular damage was the most frequent liver injury followed by cholestatic injury\textsuperscript{43}. Dietary supplements containing methylpentithiostanol, known to induce hepatotoxicity, were seized in Spain and withdrawn in 2013\textsuperscript{43}. The exact mechanism of toxicity is unclear, but the genotyping of patients with cholestatic hepatitis due to AAS suggests that these substances could inhibit biliary transporter proteins such as ATP8B1/ABCB11, similarly to cases of benign intrahepatic cholestasis type 1 or 2\textsuperscript{44}. In the USA, a total of 10 AAS DILI cases involved young men who took these products unsupervised. The principal drug responsible for liver injury was methasterone\textsuperscript{43}.

The oral designer steroid methasterone, also known as methyldrostanolone, is an example of the hepatotoxicity associated with the consumption of 17-alpha alkylated steroids. This steroid was sold in the USA as a dietary supplement until 2012 and is a methylated (17-alpha alkylated) version of the injectable steroid drostanolone\textsuperscript{44}.

Many designer AAS remain available in over-the-counter dietary supplements that are legally sold in countries, where specific compounds have been prohibited. Currently, unscheduled designer steroids include: dimethazine (17aa oral androgen with high potential for hepatotoxicity, studied in humans in Italy for its anabolic effects, and detected in dietary supplements); methylepitostanol (17aa oral androgen with high potential for hepatotoxicity, detected in dietary supplements); methoxygonadrel (progesterin related to levonorgestrel, effects of oral consumption unknown); methylclostebol (17aa oral androgen with high potential for hepatotoxicity, detected in dietary supplements); methylstenbolone (17aa oral androgen with high potential for hepatotoxicity, detected in dietary supplements); metabolan/trestione (closely related to MENT/trestolone, strong androgen)\textsuperscript{44}.

**Cholestasis**

Cholestasis due to the C-17 substituted androgens is not well established, but high doses of those compounds cause a similar cholestasis in some animal models, and may be due to reduced bile salt transporter proteins and disruption of intrahepatic microfilaments\textsuperscript{5,24,40}.

The development of cholestatic jaundice is predictable and related to dose and treatment duration: it may occur in a low percentage of patients assuming 17aa steroids like methyltestosterone, danazol, methandrostenolone, stanozolol or oxymetholone\textsuperscript{2,5,8}. Cholestatic jaundice is usually transient and can be completely healed upon discontinuation of AAS\textsuperscript{8}. Bland cholestasis due to anabolic steroids use may occur in patients, who do not report anabolic steroids consumption or who are taking herbal or a dietary supplement, containing anabolic steroids not declared on label, as a mean to increase muscle strength\textsuperscript{8}. 

---

\textsuperscript{5} R. Solimini, M. C. Rotolo, L. Mastrobattista, C. Mortali, A. Minutillo, S. Pichini, R. Pacifici, I. Palmi
Liver Peliosis

Prolonged use of oral anabolic steroids has been linked to vascular changes in the liver referred to as peliosis hepatis. Peliosis hepatis is a rare syndrome, firstly noted in 1952, in which blood-filled enlarged sinusoids and cysts form in the liver. These lesions can be asymptomatic. The liver may be enlarged, deep red in color and fragile. Peliosis hepatis typically occurs in patients with advanced wasting diseases, but it has also been associated with prolonged use of anabolic steroids for aplastic anemia and hypogonadism treatment as well as for enhancing performance and muscles in body building.

Case reports usually show mortality from internal hemorrhage or hepatic failure secondary to blood-filled cysts. Peliosis associated with anabolic steroids may or may not fully revert by stopping these drugs. The mechanism by which peliosis affects steroids users is not known yet since it has been observed either on 17aa steroids or testosterone (which is not 17-alpha-alkylated) users.

Hepatic Tumors

Human liver expresses estrogen and androgen receptors and experimentally both androgens and estrogens have been implicated in stimulating hepatocyte proliferation, probably causing liver tumor. Patients treated with anabolic androgenic steroids are all at risk of developing liver tumors.

The most serious complication of anabolic steroid use is the development of hepatic adenoma (benign liver neoplasm) or hepatocellular carcinoma (HCC) (first reported in the 1950s). Adenomas rarely turn into malignant tumors, but present risks of sudden rupture and bleeding, leading to hemoperitoneum, a life-threatening complication. Usually, a spontaneous regression of this tumor may occur, when the anabolic steroids are stopped or after early detection.

The hepatic tumors arise in patients on long-term androgenic steroids therapy, usually for 2 to 4 years or over, and occasionally in athletes or body builders illicitly abusing anabolic steroids. For patients with pre-existing pathologies (e.g., hepatitis B or C, Fanconi’s anemia) the liver tumor appearance can be shorter. Both parenteral and oral androgens may induce hepatic neoplasms. The type of neoplasm can be associated with the type of androgen. Among the oral 17 alpha-alkylated steroids associated to liver tumors in patients (n=36) treated for Fanconí’s anemia (FA), there are oxymetholone, methyltestosterone, norethandrolone, methandienone, oxandrolone; among the oral 1-methyl type there is methenolone; and among the parenteral 17-beta-ester type there are nandrolone decanoate, testosterone cypionate, enanthate, and propionate. HCC in FA patients were 58%, and adenomas were 36%. Among the patients (n = 97) with liver tumors, who received androgens for other pathologies (non-FA aplastic anemia and non-aplastic anemia disorders), there are the following 17 alpha-alkylated steroids: oxymetholone, methyltestosterone, danazol, methandrostenolone, norethandrolone, fluoxymesterone, stanozolol, ethylestrenol, methandienone, oxandrolone; among the oral 1-methyl type there are methenolone and mesterolone; among the parenteral 17-beta-ester type there are nandrolone decanoate, nandrolone phenpropionate, testosterone enanthate, propionate, and not-specified.

In non-FA aplastic anemia group HCC were 60% and adenomas 30%; in non-aplastic anemia group, HCC were 44% and adenomas were 42%. Oxymetholone was the most used in FA and non-FA groups; methyltestosterone and danazol were common in non-FA individuals.

Case Reports of AAS Hepatotoxicity

As regards to the use of anabolic steroids in sports, especially in male bodybuilders, and subsequent development of hepatocellular carcinoma or adenomas, several case reports have been recently reported (Table I).

A 35-year-old bodybuilder, completely asymptomatic, after taking high doses of AAS (oral stanozolol and oxymetholone; parenteral nandrolone decanoate, testosterone enanthate, and methenolone enanthate) for more than 15 years, developed hepatic adenomas secondary to AAS abuse. Withdrawal of anabolic steroids, after 4 years, promoted the slight reduction of the size of the tumors and liver function improvement. Nevertheless, the individual has been included in a liver transplantation program because of the severe hepatomegaly and of the risk of lesions in the liver to turn into malignant.

Another case involved a bodybuilder, 23 years old, who self-administered high doses of oral stanozolol and oxymetholone, parenteral nandrolone decanoate, testosterone phenylpropionate and boldenone. After 6 months upon AAS and 1 month of diuretics and restrictive diet, the patient started to show symptoms such as asthenia and...
anorexia; analysis reported hypernatraemia, renal failure and muscular damage. A mild hepatomegaly was detected as well as adenomas without any malignancy that after 1 year showed a decrease in the size and analytical values close to normal upon AAS cessation.

A giant hepatic adenoma was detected in a bodybuilder, 28 years old, who reported the consumption of oral androstenedione and intramuscular nandrolone over 6 years. The risk for large adenoma is malignant transformation, hemorrhage and sometimes death. After surgical treatment and stopping the intake of AAS, 6 months later there were no signs of further focal lesions.

Chronic intake of AAS and development of HCC was observed on a 37 years old bodybuilder who reported a huge consumption of AAS for 5 years: testosterone propionate, phenylpropionate, isocaproate and decanoate, trenbolone acetate, 5-alpha-androstanediol, boldenone and methandriol dipropionate, 17alpha-methyl-5alpha-androstano[3,2-c]pyrazole-17beta-ol.
17beta-ol, 17beta-hydroxy-17alpha-methyl-2-oxa-5alpha-androstane-3-one and oxymetholone. Furthermore, he used spironolactone, mesterolone, fluoxymesterone, and torasemide (diuretics) eighteen hours before competition. A daily intake of other substances such as amino acid, vitamins, and mineral tablets, thyroxine, and growth hormones was also reported. It has to be noticed that this case regards a polydrug use pattern and the precise mechanisms of HCC development remain unclear.

Another case of HCC secondary to AAS was observed in 2004 on a young bodybuilder 24 years old that started testosterone abuse (200 mg/week) since age 17. At that time a hepatic adenomatosis was revealed. The individual persisted in AAS consumption in 2013 developed chronic kidney disease, coronary artery disease and was diagnosed with HCC.

A 29 years old male professional bodybuilder presented severe hepatomegaly with signs of HCC after 6 years of AAS abuse including nandrolone decanoate, 4 ester based testosterone (testosterone propionate, testosterone phenylpropionate, testosterone isocaproate, testosterone decanoate), methandienone, stanozolol. Other substances assumed by the sportsman were human growth hormone, insulin, tamoxifen and diuretics (aldosterone and thiazide). The case required liver transplantation.

Hepatotoxicity due to dietary supplements ingestion containing AAS was detected in 2 males, 25 and 45 years old respectively. The dietary supplement contained the AAS 2alpha-17alpha-dimethyl-etiocholan-3-one, 17beta-ol. It is possible that the AAS could have inhibited expression of the biliary transporter proteins ATP8B1/ABCB11 and therefore induced cholestatic hepatitis. Adolescents with pre-existing liver disease, such as non-alcoholic fatty liver disease (NAFLD), are more easily at risk of hepatotoxicity due to AAS intake. This was showed by a case report concerning a young man 18 years old who developed cholestatic hepatitis, with hepatocellular and intracanalicular cholestasis, following to AAS 2 alpha, 17alpha-dimethyl-17beta-hydroxy-5 alpha-androstan-3-one consumption for 2 weeks preceding the onset of symptoms.

AAS Misuses Potentially Responsible for Hepatotoxicity

The following modalities of consumption are probably or consistently related to hepatotoxicity since the way in which AAS are used, misused or abused can compromise liver function.

Polydrug Use

Athletes (usually body builders and weightlifters) are inclined to polydrug use for reducing side effects and boosting AAS effects. The polydrug or polypathy behavior, such as the concomitant consumption of different licit and illicit substances may contribute to the toxicity of AAS, making hard to ascertain a causal relationship between a specific substance and its consequent adverse effects.

AAS Dependence

AAS use is often related to misuse of prescription drugs (such as sedatives or analgesics) and current or past dependence on illicit substances like cocaine, heroin, and opioids. Individuals using high doses of anabolic steroids for a long time may develop depressive symptoms, anhedonia, fatigue, impaired concentration, and even suicidality due to steroid withdrawal. It has been noted that these withdrawal effects may contribute to a syndrome of dependence. A role of reinforcement of compulsive exercise in AAS dependence has also been suggested.

AAS Pattern of Use

Doses of AAS that exceed 10 to 100 times the physiological limits or doses usually prescribed for pathologies and used with high frequency may cause a variety of clinical effects, which often are not taken into the right consideration, even if they can seriously endanger life. To hypothetically minimize side effects or maximize the drug effects, AAS abusers follow different patterns of use: pyramiding (gradually increasing the doses and then a tapering phase), cycling (cycles of several weeks and periods of abstinence), stacking (users combine different injectable and oral AAS), blast and cruise or bridging (never stop AAS but alternate periods of high doses and lower doses) and blitz-cycles (quick change of AAS to prevent tolerance and androgen receptor down-regulation). It is not scientifically proven that these patterns of use are helpful to avoid severe adverse effects of these substances.

AAS as Image Performance Enhancing Drugs

AAS are reported in the literature also for being included as a subset of the numerous group of substances, licit or illicit, such as GH.
(Growth Hormone), insulin, erythropoiesis-stimulating agents, stimulants, cutting drugs (synthetic thyroid hormones), ancillary agents (sildenafil, tamoxifen, human chorionic gonadotropin etc.) supplements (e.g. creatine, protein powder, L-carnitine), diuretics, recreational drugs and analgesics. All these substances are variously reported under similar names considering either the scopes of boosting muscles and performance or the cosmetic finalities: PED (Performance Enhancing Drugs), PEA (Performance-Enhancing Agents) or PES (Performance Enhancing Substances), IPED (Image and Performance-Enhancing Drugs), APED (Appearance and Performance Enhancing Drug), or PAED, Body Image Drugs. Most of AAS and IPED are easily available on thousands of web sites where are marketed without any warning about the eventual harmful effects but, on the contrary, favorably supporting them. Legal IPED such as dietary supplements are frequently contaminated by AAS. In particular, it has been reported that dietary supplements are daily used by 33% of the adults and are contaminated with anabolic steroids in the 12.5% of the samples. This poses severe health risks to the unaware consumer.

Further Complications of AAS


Conclusions

AAS and polydrug abuse can be harmful to health, causing a variety of side effects including mainly liver injuries, which in some cases can be life threatening. Nowadays also dietary supplements containing designer steroids are a serious health risk for the consumers, who easily buy these products on Internet, without any control. AAS has been detected in vitamin products suggesting that many products may be contaminated with a variety of unlabeled ingredients. World Anti-Doping Agency (WADA) established in 1999 as an international independent agency composed and funded equally by the sport movement and governments of the world, prohibits any AAS use or related compound. DEA constantly include substances into controlled substances list; nevertheless, new compounds frequently appear in the marketplace. The availability of designer steroids over-the-counter for more than 10 years may have promoted significant exposure in the population. Individuals should be warned about the use of either AAS or dietary supplements potentially containing designer steroids, because of the adverse effects and theoretical effects of exogenous synthetic androgens.

References

Hepatotoxicity associated with illicit use of anabolic androgenic steroids in doping


18) Nieschlag E, Vorrone E. Doping with anabolic an- drogenic steroids (AAS); adverse effects on non-reproductive organs and functions. Rev Endocr Metab Disord 2015; 16: 199-211.


