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Adverse health effects of anabolic–androgenic steroids

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ABSTRACT

Anabolic–androgenic steroids (AAS) are synthetic drugs derived from testosterone. Illegally, these drugs are regularly self-administered by body builders and power lifters to enhance their sportive performance. Adverse side effects of AAS include sexual dysfunction, alterations of the cardiovascular system, psyche and behavior, and liver toxicity. However, severe side effects appear only following prolonged use of AAS at high dose and their occurrence is limited. Occasionally, AAS abuse may be linked to certain social and psychological traits of the user, like low self-esteem, low self-confidence, suffered hostility, childhood conduct disorder, and tendency to high-risk behavior. The overwhelming stereotype about AAS is that these compounds cause aggressive behavior in males. However, the underlying personality traits of a specific subgroup of the AAS abusers, who show aggression and hostility, may be relevant, as well. Use of AAS in combination with alcohol largely increases the risk of violence and aggression. The dependence liability of AAS is very low, and withdrawal effects are relatively mild. Based on the scores for acute and chronic adverse health effects, the prevalence of use, social harm and criminality, AAS were ranked among 19 illicit drugs as a group of drugs with a relatively low harm.

1. Introduction

Anabolic steroids (anabolic–androgenic steroids; AAS) are synthetic substances related to the male sex hormones (androgens), which promote growth of skeletal muscle (anabolic effect) and the development of male sexual characteristics (androgenic effects). AAS are used since the 50-ties to improve athletic performance and male physical attractiveness. AAS increase body weight, fat-free mass, muscle size, and strength when combined with strength training in healthy men receiving 600 mg of testosterone weekly for 10 weeks (Bhasin et al., 1996; Forbes, 1985; Young et al., 1993). In the absence of strength training the muscle size is increased by higher doses of AAS (Bhasin et al., 1996; Forbes, 1985; Hartgens and Kuipers, 2004; Herbst and Bhasin, 2004; Sinha-Hikim et al., 2002).

Testosterone is rapidly metabolized in the liver. To resist metabolization and attain high steady state levels, more than 1000 testosterone derivatives have been synthesized which can be categorized in three classes. Synthetic Class A steroids are 17-β-hydroxy testosterone esters with an higher lipid solubility, which require intramuscular dosing. Testosterones belonging to Class B have been alkylated at the 17-α-hydroxy position, which results in compounds that can be given orally. The third group is the Class C compounds which have been alkylated in the A, B, or C rings of the steroid backbone results in orally available AAS that resist hepatic metabolism (Hall and Hall, 2005). Finally, users may take an aromatase inhibitor, like anatrozole, to inhibit the aromatization of anabolic steroids into female estrogen hormones. See the paper of Kicman (2008) for an overview of the different AAS.

The pharmacology of anabolic steroids has been recently reviewed by Kicman (2008). The present paper, reviewing the scientific data about AAS available in the international literature, has been used in a ranking study to assess the relative risk of recreational drugs. The elements of the risk assessment were acute and chronic adverse health effects, the prevalence of AAS use, as well as criminal behavior and disturbance of public order related to AAS use.

2. Use and abuse of AAS

The most common indication for testosterone therapy is hypogonadism in men, such as in delayed puberty, premature termination of the adolescent growth spurt and some types of impotence. In addition, abuse of AAS has become common among athletes and bodybuilders, which coincide with side effects especially in those cases when AAS are used in high dose and over prolonged time. The oral administration of androgenic compounds at 3–5 g per week can achieve blood levels up to 100 times the physiologic range for an adult male (Brower et al., 1990).

AAS's are frequently used in combinations (Hall and Hall, 2005; NIDA, 2000). Abusers may practice "stacking", i.e. they frequently take two or more anabolic steroids together, mixing oral and/or

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intramuscular AAS. Another practice is cyclic dosage regimens called "pyramiding". At the beginning of a cycle low doses of the stacked substances are administered and the dose is gradually increased for 6–12 weeks. In the second half of the cycle, the doses are slowly decreased to zero. Abusers believe that pyramiding allows the body time to adjust to the high doses, and the drug-free cycle allows time for the body's hormonal system to recuperate. Synergism or other benefits of stacking or pyramiding have never been shown.

3. Characteristics of AAS users

Anabolic steroids were first used by athletes in the mid 1950s and by the 1960s their use was widespread to build muscles and boost their athletic performance; the anabolic steroid abuse among athletes ranges between 1% and 6%. Increasingly, others (adolescents) also have been taking these synthetic substances. The aim of recreational users (sports men, adolescents) is to increase their sportive performance or to receive the admiration that Western societies give to a 'perfectly toned' body (Rashid et al., 2007). The obsession that he or she is not looking muscular enough i.e. a pathological preoccupation with muscularity, may even lead to muscle dysmorphia, which may lead to AAS abuse (Pope et al., 1997). According to American sources, the typical AAS abuser is a male poly-substance abuser who has a poor self-esteem, poor school performance, used other illicit drugs before AAS use, displayed high levels of childhood conduct disorder, noted higher levels of antisocial behavior (such as school truancy), higher rates of self-reported violence and aggression, poor body image before AAS use, and a cluster B personality disorder or traits (Bahrke et al., 2000; DuRant et al., 1995; Kanayama et al., 2003; Perry et al., 2003). Males abuse 2–3 times more than females (Bahrke et al., 2000; DuRant et al., 1995), and the majority (60–70%) of AAS abusers actively participate in organized sports (Bahrke et al., 2000).

AAS abuse is positively associated with experienced physical or sexual abuse. As an example, in a NIDA research report (NIDA, 2006) female weightlifters who had been raped were found to be twice as likely to report use of anabolic steroids or another purported muscle building drug, compared with those who had not been raped. They believed that being bigger and stronger would discourage further attacks. In addition, adolescents may abuse steroids as part of their high-risk behavior.

A study from 2007 (Cohen et al., 2007) shows, however, quite another profile of the typical AAS user. The cohort studied consisted of 1955 North American male AAS users, recruited via various AAS-related internet websites. The typical user was a Caucasian, highly-educated, gainfully employed professional approximately 30 years of age, who was earning an above-average income, was not active in organized sports, and whose use was motivated by increases in skeletal muscle mass, strength, and physical attractiveness. Of the users 50% was not married, and 64% had no kids. The majority of respondents did not initiate AAS use during adolescence and their steroid use was not motivated by athletics. Various explanations can be put forward for the different results obtained about the typical AAS user. The validity of an internet survey is probably lower than directly addressed questionnaires. On the other hand, responses given via internet are more anonymous and allow a more honest answers to the questions posed which are sensitive and may even be embarrassing. Finally, in contrast to the internet survey of Cohen et al. (2007), the other studies cited refer to a relatively low number of subjects or investigated the general population.

4. Prevalence

American surveys from the 90-ties report a prevalence of use of 4–11% and 2.5% by male and female high-school students, respectively (Bahrke et al., 2000; Buckley et al., 1988; DuRant et al., 1995; Yesalis et al., 1997). Two-thirds of AAS abusers started their abuse by age 16 years (Buckley et al., 1988). The 'Monitoring the Future Study', an annual survey of drug abuse among middle and high-school students across the country, showed in the late 1990s a significant increase in AAS abuse among middle scholars. In 2008, of the 8th and 10th-graders 0.95% reported having taken AAS at least once in the last 12 months, whereas of the 12th-graders this figure was 1.5% (Johnson et al., 2008). These figures represent dramatic increases of approximately 38–50% since 1991. Steroid use by males in the USA has been, as measured by four national surveys, generally stable since 1991 (McCabe et al., 2007). Using self-administered mail surveys from randomly selected US college students, it appeared that the prevalence of lifetime, past-year and past-month non-medical use of AAS was 1% or less (McCabe et al., 2007). There was also a sharp drop in 2005 in the perceived availability of these drugs, very likely due to the Anabolic Control Act of 2004, which placed 32 additional steroids into Schedule III and expanded the Drug Enforcement Agency's regulatory and enforcement authority regarding their sale and possession.

Among 687 British college students, 4.4% of males and 1.0% of females currently or previously used AAS. Of them 56% had first used anabolic steroids at the age of 15 or younger (Williamson, 1993). Over the past decade the use of anabolic steroids has increased in the UK. This was highlighted in a report from 2002 (BMA, 2002) which stated that as many as half of the members of dedicated bodybuilding gyms admitted to taking anabolic agents, and that steroid use ran as high as 13% even in some high-street fitness centers. In addition, a third of all general practitioners were treating patients who took steroids. An investigation among 6000 Swedish adolescents revealed a prevalence of 3.2% in males, whereas steroids were not used by females (Nilsson, 1995; Nilsson et al., 2001). As expected, much higher estimates of AAS use have been obtained in groups such as visitors of fitness centers, bodybuilders, weightlifters and prison populations (Thiblin and Petersson, 2005). Between 1993 and 2006 the Swedish Anti-Doping hot-line got 40,000 calls with questions about AAS; callers connected with gyms were the largest group (30%) (Sjoqvist et al., 2008). Some studies may give over-estimated prevalence's of steroid use, because the questionnaires ask for 'steroid use' without specifying that steroids are used to increase muscle strength (i.e. corticosteroids and some food supplements are also steroids) (Kanayama et al., 2007).

In The Netherlands the illegal trade of doping drugs amounted in 1998 70–90 million euro (Koert and van Kleij, 1988); more recent figures are not available. In 2002, the last-year prevalence of AAS use, assessed among 700 sportsmen and women in six branches of popular sports (including football, athletics and strength sports) was between 0% and 3% (van den Heuvel et al., 2002) with a lifetime prevalence between 0% and 6%. Among the strength sportsmen the prevalence is twofold higher. A more recent survey among visitors of sport schools shows a prevalence (ever use) of 30% (Detmar et al., 2003). The authors regarded this high figure as largely over-estimated, because the questionnaire was announced on drug related websites and therefore not representative for the general population. Some 100,000 Dutch subjects have ever used doping to improve their sport performance; half of them being active user (Abraham et al., 2001). About 4–6% of clients of Dutch sport and fitness clubs use doping (Stubbe et al., 2009; Vogel, 2002); most prevalent were AAS, growth hormone and insulin. The same figure of 6% is mentioned as estimate of doping use for most European countries (Surmann et al., 2002), where the use refers predominantly to AAS, but includes also other drugs like growth hormone and ephedra-containing drugs. Finally, in Porto Alegre (Brasil), 288 subjects draw from a sample of 13 gyms were interviewed. The prevalence of current and past use of AAS

was about 11.1% (32/288), and other hormones 5.2% (16/288); the most used AAS were nandrolone and stanozolol (Silva et al., 2007).

In summary, interviews of high-school students and recreational sporters in several European countries and the USA reveal that 1–6% have ever used AAS. These estimates roughly equate to 1% of the population. Figures about the prevalence of chronic AAS use are not available.

5. Adverse effects

Steroid abuse disrupts the normal production of hormones in the body, causing both reversible and irreversible changes. Side effects of AAS, however, develop virtually only during long-term use (Thiblin and Petersson, 2005). The most common side effects are cosmetic in nature, which are reversible with cessation. Class B AAS cause hepatic toxicity (Welder et al., 1995) leading to jaundice which develops generally after 2–5 months. Hepatotoxicity has never been described with the parenteral use of testosterone esters. Severe side effects on the liver and lipoproteins mainly result from alkylated AAS at high dose (Ishak and Zimmerman, 1987), whereas parenteral AAS appear to damage heart muscles which may become clinically prominent after several years. Fortunately most of the serious life-threatening effects appear relatively infrequent.

5.1. Acute adverse effects

Minor acute side effects of steroid use are: headaches, fluid retention (especially in the extremities), gastrointestinal irritation, diarrhea, stomach pains, and an oily skin. Acute effects with some more clinical impact are jaundice, menstrual abnormalities, and hypertension. Infections can develop at the injection site, causing pain and abscess. In both sexes acne develops at puberty (i.e. not in adults) during treatment with androgens which due to the growth of sebaceous glands and the secretion of the natural oil sebum (Király et al., 1987).

Aromatization is the process by which steroid hormones are interconverted. Testosterone and other aromatisable anabolic steroids are metabolized in part to estradiol and other estrogen agonists. As such, males using high doses of AAS can have the circulating estrogen levels typical of women during a normal menstrual cycle (Wilson, 1988). This can lead to breast pain in men and, the often irreversible, gynecomastia. Observational studies suggest that a majority (88–96%) of anabolic steroid users experience at least one objective side effect, including acne (40–54%), testicular atrophy (40–51%), gynecomastia (10–34%), cutaneous striae (34%) and injection-site pain (36%) (Evans, 2004). Table 1 summarizes the reported side effects by AAS abusers ($N = 4339$) on a telephone hot-line in 1996–2000 (one could report more than one side effect) (Eklof et al., 2003).

5.2. Chronic adverse effects

5.2.1. Somatic effects

Health consequences associated with anabolic steroid abuse include urogenital problems, acne, and cardiovascular and hepatic disease (Melchert and Welder, 1995; Rogol and Yesalis, 1992; Sullivan et al., 1998). Changes in males that can be reversed include reduced sperm production, impotence, difficulty or pain in urinating and shrinking of the testicles (testicular atrophy). In one study of male bodybuilders, more than half had testicular atrophy and/or either reversible or irreversible breast development (gynecomastia) (Wilson, 1992). In females, elevated AAS levels result in menstrual irregularities and the development of more masculine characteristics such as decreased body fat and breast size, deepening of the voice, excessive growth of body hair, and irreversible loss of scalp hair (baldness), as well as clitoral enlargement. With continued administration of steroids, some of these effects become irreversible (Shifren, 2004; Wilson, 1992). Steroids have been associated with prostate cancer (Creagh et al., 1988). Of particular concern is premature physeal closure in any child/adolescent, which results in a decrease in adult height. In some cases, however, AAS is clinically used to limit the abnormal body length. AAS give an increased risk for fatal liver cysts, other liver changes, and liver cancer (Soe et al., 1992; Stimac et al., 2002). Class B and C AAS are highly hepatotoxic. The alkylated AAS have also been shown to increase hepatic triglyceride lipase activity between 21% and 123% and low-density lipoprotein by as much as 29% (Bagatell and Bremner, 1996; Thompson et al., 1989). On the other hand, AAS-induced hepatic pathology is often reversible upon discontinuation of AAS (Modlinski and Fields, 2006), and the overall prevalence of adverse hepatic effects among long-term AAS users is likely low (Pope and Katz, 1994).

The long-term use of AAS has been reported to be associated with cardiovascular disease (CVD), like hypertension, heart attack and stroke. Steroids contribute to the development of CVD, partly by changing the levels of lipoproteins that carry cholesterol in the blood. Steroids, particularly oral steroids, increase the level of low-density lipoprotein cholesterol (LDL-cholesterol) and decrease the level of high-density lipoprotein cholesterol (HDL-cholesterol). Notably the alkylated and orally used AAS such as stanozolol (6 mg/day p.o. for 6 weeks) lower HDL-cholesterol by 33%, particularly HDL2-cholesterol which is reduced 23–80% (Bagatell and Bremner, 1996; Thompson et al., 1989). The effect of parenteral testosterone enanthate (200 mg/week for 6 weeks) itself is much less dramatic, with only a 9% reduction in HDL-cholesterol

Table 1
Number of side effects reported by AAS abusers ($N = 4339$) on a telephone hot-line in 1996–2000 (Eklof et al., 2003). Only one side effect could be reported per reply.

Psychiatric symptoms		Urogenital problems in males	
Aggressiveness	835	Gynecomastia	637
Depression	829	Potency problems	413
Worries	657	Sexual problems	130
Personality changes	416	Increased virility	162
Sleeping problems	328	Smaller testicles	130
Mood symptoms	302	Decreased virility	73
Anxiety symptoms	282	Ejaculation problems	65
Irritability	263		
Withdrawal symptoms	248	Other physical complaints	
Psychiatric unspecified symptoms	140	Acne	770
“The biggest, the greatest, the best”	58	Skin striae	295
Body obsession	49	Increased hair growth	113
Thinking of suicide and suicide attempt	20	Pain after injection	94
		Abscess after injection	75

(Thompson et al., 1989). In general, serum levels return to baseline level within several weeks to months after drug cessation (Hartgens et al., 2004). Even the administration of high doses of testosterone enanthate (600 mg/week, parenterally for 20 weeks hardly affected HDL (Singh et al., 2002).

High LDL- and low HDL-cholesterol levels increase the risk of atherosclerosis. Indeed, power lifters have a greater risk of atherosclerosis secondary to increased concentrations of LDL-cholesterol and decreased concentration of HDL-cholesterol (Hurley et al., 1984). In addition, steroids induce blood clotting due to increased platelet count and aggregation (Ferenchick et al., 1992; Togna et al., 2003). Steroids can also cause myocardial hypertrophy, which also increases the likelihood of arrhythmias, sudden death, systolic and diastolic hypertension, and myocardial infarct (Frankle et al., 1988; Karila et al., 2003). Some of the cardiovascular effects of AAS, such as hypertension, dyslipidemia, and coagulation abnormalities, remit after AAS use was discontinued, but effects such as atherosclerosis and cardiomyopathy appear to be irreversible (Hartgens and Kuipers, 2004; Sullivan et al., 1998). Bodybuilders, examined a mean of several years after last AAS exposure, still exhibited impaired myocardial function (D'Andrea et al., 2007) which was associated with the duration and dose of previous AAS use. These results were confirmed in two small cohorts (Krieg et al., 2007; Nottin et al., 2006) where AAS had significantly impaired myocardial function. Recently, two cases of sudden cardiac death were reported in healthy bodybuilders who chronically used AAS (Fineschi et al., 2007), and several case reports document myocardial infarction and stroke in AAS abusers which were partially fatal (Frankle et al., 1988; Kennedy and Lawrence, 1993; McNutt et al., 1988). In a 12 years follow-up study (Parssinen et al., 2000), the mortality in 62 Finnish power lifters, strongly suspected of having used mega doses of AAS over several years, was 12.9% (mean age at death 43 year) compared with 3.1% in the control group of 1094 subjects (mean age not documented). Suicide and acute myocardial infarction accounted for six out of eight deaths. In general, the number of case reports on ischemic stroke related to anabolic steroid abuse is limited. Since there are so few empirical studies, it is difficult to estimate the prevalence or severity of cardiovascular pathology in older AAS users. There is, however, no epidemiological evidence for cardiovascular disease due to AAS use, so that this causality remains to be established. It should finally be noted that the risk of cardiovascular complications may also be due to the use of other doping drugs, like growth hormone or EPO (erythropoietin).

5.2.2. Neuropsychiatric effects

The abuse of AAS is associated with behavioral and psychiatric effects, which vary from still social acceptable mild irritation and body training drive to uncontrolled aggression, hostility and even depression and mania. The frequency of these effects is generally low and largely depends on the dose used. Moreover, it is often difficult to judge whether the behavioral and psychiatric effects are attributable to the use of AAS per se, as opposed to underlying personality traits of the AAS abuser, or psychosocial factors surrounding AAS use. In this respect it should be mentioned that chronic AAS users frequently have antisocial, narcissism, and histrionic traits. Nevertheless various studies have suggested that supraphysiologic doses of AAS can directly cause hypomanic or manic symptoms, sometimes associated with aggression and violence. However, not all studies have documented such mood changes, indicating a large variability of symptom presentation because of differences in the dose consumed, the compound used, duration of use, personality type of the abuser, and current or previous use of other recreational drugs (Basaria et al., 2001; Hall et al., 1979), with some exhibiting prominent symptoms and others none.

AAS produce clear psychiatric effects in individuals using excessive doses (more than 1000 mg/week). The most prominent psychiatric features were manic-like presentations defined by irritability, aggression, euphoria, grandiose beliefs, hyperactivity, and reckless or dangerous behavior (Clark and Henderson, 2003; Pope et al., 2000b). For example, many users report feeling good about themselves while on anabolic steroids, but extreme mood swings can also occur, including manic-like symptoms that could lead to violence (Pope and Katz, 1988). AAS users may suffer from paranoid jealousy, extreme irritability, delusions, and impaired judgment stemming from feelings of invincibility. Other presentations: acute psychosis, exacerbations of tics, and the development of acute confusional states (Hartgens and Kuipers, 2004; Perry et al., 1990). Case reports and studies of groups using AAS (e.g. bodybuilders) have described hypomania or manic episodes (Freinhar and Alvarez, 1985; Pope and Katz, 1994), depression or suicide (Parssinen et al., 2000; Pope and Katz, 1994; Thiblin et al., 2000), and psychotic episodes (Freinhar and Alvarez, 1985).

Considering the uncontrolled aggression and mania observed among AAS abusers, it is highly important to realize that 23% of subjects using high dose (>1000 mg/week) met DSM-III-R criteria for major mood syndrome (mania, hypomania, and major depression), and that 3–12% developed psychotic symptoms (Pope and Katz, 1994; Pope et al., 2000b).

Finally, muscle dysmorphia, a pathological preoccupation with muscularity, is prevalent – a student thesis claimed to be about 1.5–6% among Swedish gym visitors) (Ahlson and Ström, 2005) – among AAS users as a result from the obsession that he or she is not looking muscular enough (Pope et al., 1997). Pope et al. suggested that the wide discrepancy between men's actual muscularity and their body ideals may help explain the apparent rise in disorders such as muscle dysmorphia and anabolic steroid abuse (Pope et al., 2000a).

In conclusion, AAS at high dose may elicit neuropsychiatric symptoms, but the prevalence is low. In addition, a subgroup of AAS abusers has psychiatric morbidity which bias the causal relationship between AAS abuse and neuropsychiatric effects.

6. Dependence

In contrast to other drugs of abuse, AAS are not strongly euphorigenic, meaning that they do not trigger rapid increases in dopamine, which are responsible for the "high" that often drives substance abuse behaviors. Still, the effect of well-being of AAS use and the dysphoric effects of withdrawal may contribute to a syndrome of AAS dependence in some individuals (Kashkin and Kleber, 1989; Pope and Katz, 1988). Long-term use of AAS can eventually have an impact on some of the same brain pathways – such as dopamine, serotonin, and opioid systems – that are affected by drugs of abuse.

Steroid abusers may become addicted to the drugs, as evidenced by their continued abuse despite physical problems and negative effects on social relations (Brower, 2002). The positive effects of testosterone on mood are well established, and several studies have found testosterone replacement to substantially reduce negative mood states relating to fatigue, depression, and self-esteem (Anderson et al., 1999; O'Connor et al., 2004; Wang et al., 2000). A two stage model has been proposed for AAS dependence (Brower, 2002). Users initiate steroid use for their anabolic effects, but with continued exposure, dependence on the psychoactive effects of AAS develops. However, the abuse liability of AAS in the classical pharmacological sense is very low, although some recent studies suggested AAS dependence to be fairly common (Brower, 2009; Kanayama et al., 2008, 2009). In our opinion, it may only occur in a minority of AAS users. Moreover, such AAS

dependence may be confounded by factors, like exercise dependence, multi-drug use, sub-optimal family relations.

The low reinforcement of androgens is comparable to that of mild reinforcers, such as caffeine or benzodiazepines. On the hand, individuals using high doses of AAS are at risk to develop dependency to AAS, because they may develop depressive symptoms, anhedonia, fatigue when they stop taking AAS. As a result of such withdrawal symptoms, AAS use may elicit a 'syndrome' of dependence. Finally, a point of concern is the AAS-induced hypogonadism (Tan and Scally, 2009), which may contribute to dependence liability, because users go back on AAS to self-treat their AAS-induced hypogonadism (Scally and Tan, 2009).

In a study of 49 male weightlifters 84% reported withdrawal effects which varied from steroid craving (52%), fatigue (43%), depressed mood (41%), restlessness (29%), loss of appetite (anorexia) (24%), insomnia (20%), reduced sex drive (20%), headache (20%), to muscle and joint pain (Brower et al., 1990, 1991). In this study (Brower et al., 1991) 57% met DSM-III-R criteria for dependence, based on responses to an anonymous self-administered questionnaire. Withdrawal following medical use of AAS have, however, never been reported.

In rodents testosterone induces a conditioned place preference, and is voluntarily consumed through oral, intravenous and intracerebral self-administration in hamsters. Male rats develop a conditioned place preference to testosterone injections into the nucleus accumbens, an effect blocked by dopaminergic antagonists. Nonetheless, androgen reinforcement is not comparable to that of cocaine or heroin. Instead, testosterone resembles other mild reinforcers, such as caffeine or benzodiazepines (Arnedo et al., 2000; Wood, 2004).

7. Social harm

7.1. Aggression

Increased aggressiveness and feelings of hostility are among the adverse effects most frequently associated with AAS abuse. The use of AAS may occasionally trigger violent acts in individuals not previously known to have such tendencies (Choi and Pope, 1994). Others showed that anabolic steroid abuse, particularly in high doses, promotes aggression that can manifest itself as fighting, physical and sexual abuse, armed robbery, and property crimes. Abusers who have committed aggressive acts or property crimes generally report that they engage in these behaviors more often when they take steroids than when they are drug free. It should, however, be emphasized that the mental states of AAS abusers cannot be regarded as typical for the general male population (cf. section Users). Certain internet sources, like http://www.ergogenics.org/345.html, depict long lists of AAS-related violent incidents which involve notably body builders. These reports are merely anecdotal i.e. do not mention crucial details, like personal traits and concomitant alcohol use and are therefore not suitable for scientific evaluation.

AAS use may precipitate violence (Choi and Pope, 1994; Pope and Katz, 1988) with frequent symptoms at high dose (600–1000 mg testosterone per wk) and few symptoms at 300 mg/week or less (Pope and Katz, 1994). Others (Anderson et al., 1992; Bagatell et al., 1994), however, reported that supraphysiologic doses of testosterone enanthate given for several months do not increase aggressive behavior or irritability. A 'roid rage', frenzied violence, which is characterized by indiscriminate and unprovoked aggression, has been reported during high dose cycles of AAS use; the response among the subjects appears, however, to be very variable. For instance, in the placebo-controlled, crossover study in 50 participants treated with a high dose of testosterone cypionate (6 weeks in doses rising to 600 mg/week), eight subjects (16%) showed mild to marked hypomanic responses, whereas the other 42 subjects showed only minimal psychiatric effects (Pope et al., 2000b).

There is, however, no epidemiological evidence for the precipitation of violent behavior by AAS. Furthermore, the association between AAS use and violence is often biased by other risk factors. For instance in one study (Thiblin et al., 1997) 11 out of 14 violent AAS-positive perpetrators were drunk, and eight of the nine subjects had personality disorders. A very important confounder is that in the majority of cases (79%) the use of AAS was associated with concomitant use of psychotropic substances, particularly opiates (Petersson et al., 2006). Animal studies showed that adolescents are more sensitive to the induction of aggression by AAS than adults (Salas-Ramirez et al., 2008), implicating that the widespread use of AAS during adolescence is a significant concern especially if they are used in combination with alcohol or other drugs. Indeed, Thiblin et al. (1997) pointed out that alcohol and AAS seem to be strongly synergistic in precipitating impulsive violent behavior. Available data give no clear, consistent support for the hypothesis that AAS use causes aggression.

7.2. Criminality

Anabolic steroids are legally available only by prescription. Some 75% of Dutch AAS users purchase the drugs via fellow sportsmen or trainers of the sport school (de Hon and van Kleij, 2005). Internet or buying while abroad is an alternative to buy AAS. The middlemen selling the drugs – estimated some 30–40 individuals – are not involved in organized crime who also sell hard drugs. In most cases these middlemen have a legal and sport related job, like personal trainer, owner of the fitness studio or salesman of food supplements. Recently, another type of dealer becomes active, who is exclusively interested in earning money and has no relation with the fitness studio (de Hon and van Kleij, 2005). This type of doping trade is tied up with other criminal activities, notably the trade in XTC (and production of pills), Viagra and hard drugs (Oldersma et al., 2002). This group of middlemen often sells doping of inferior quality. The customers are predominantly young sportsmen.

8. Conclusion

It is concluded, that the abuse of AAS may be associated with adverse somatic, behavioral and psychiatric effects, but their incidence and prevalence seems to be limited. If present, the side effects have resulted from the prolonged use of very high dose of AAS. Though no hard proof is available, the induction of dyslipidemia by AAS use remains a point of concern. The milder and more frequently seen side effects, like acne and testicular atrophy disappear upon discontinuation of use. Users of AAS are normal individuals, who use the drugs to improve their sportive achievements. On the other hand, it has been reported that some AAS users show aberrant social and psychological traits, like low self-esteem, low self-confidence, suffered hostility, previous abuse, childhood conduct disorder, and tendency to high-risk behavior which may explain the presumed association between AAS use and aggressive behavior. Indeed, controlled studies have demonstrated that the frequency and intensity of the aggression induced (only) by supra-maximal doses of AAS is highly variable across individuals. It should, however, be noted that the use of AAS in combination with alcohol consumption largely increases the risk of violence and aggression. The dependence liability of AAS is very low and withdrawal effects are observed but relatively mild.

The results of this review have been used in a recent study to rank the relative harm of anabolic steroids within a selection of 19 illicit drugs, including heroin, cocaine, ecstasy and cannabis.

Based on the scores given by 19 experts with a variety of expertise for acute and chronic adverse health effects, the prevalence, social harm and criminality, AAS were ranked an illicit drug with a relatively low harm. The design of ranking study closely resembles that of Nutt et al. (2007).

Conflict of interest

The authors declare that there are no conflicts of interest.

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