REVIEW

Anabolic androgenic steroid abuse in young males

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Abstract

This review summarizes 10 years experience with male abusers of anabolic androgenic steroids (AAS). The typical user of AAS is male, aged between 20 and 40 and lifting weights. Illegal AAS are cheap and easily obtained via internet or local suppliers. AAS are mostly used in cycles with a duration between 6 and 18 weeks. Most AAS cycles contain multiple agents, used simultaneously in a dose vastly exceeding a substitution dose. A variety of other performance and image-enhancing drugs are commonly used, including human growth hormone, thyroid hormone, tamoxifen, clomiphene citrate and human chorionic gonadotrophin. Short-term clinical and biochemical side effects are well established. Long-term side effects are uncertain, but may include heart failure, mood-and anxiety disorders, hypogonadism and subfertility. We share our views on the management of common health problems associated with AAS abuse.

Key Words

- anabolic androgenic steroids
- side effects
- hypogonadism
- infertility
- gynaecomastia

Endocrine Connections (2020) **9**, R102–R111

Introduction

Every now and then a clinical endocrinologist will be visited by a patient that uses anabolic androgenic steroids (AAS) or has been using them in the past. The interaction between doctor and patient may be hampered for a number of reasons. First, some doctors may feel reluctant to help a patient who has self-inflicted health issues due to the use of banned substances. They do not understand why someone would jeopardize his health in order to gain muscle mass or strength and simply advise the patient to stop using steroids at once. Secondly, most doctors, including endocrinologists, do not have much experience with AAS abusers and do not have detailed knowledge of the different compounds and the adverse health effects they may inflict. This is partly due to the fact that there is limited scientific evidence about the health effects of AAS and hardly any evidence to guide treatment of side effects. Thirdly, most AAS abusers have low expectations concerning a doctors knowledge of AAS and may be reluctant to disclose details about their AAS abuse (1). They frequently have strong opinions about laboratory results and treatment strategies, based on biased and incomplete knowledge.

These are the reasons why we started our AAS outpatient clinic almost 10 years ago in Haarlem, the Netherlands. Goals were to gain more insight into the characteristics of AAS users, the methods of AAS use and the health risks associated with AAS use. Users of AAS can be referred to us by their general practitioner or medical specialist if they want advice or treatment for health problems associated with current or past use of AAS. In the past years we have seen almost 400 patients. A summary of our findings in these patients can be found elsewhere (2). The population seen in our outpatient clinic is selected on the basis of health problems and may not be representative for all steroid users in the Netherlands. Therefore, we started an observational cohort study in 100 AAS abusers without health problems, the HAARLEM study (acronym for Health risks of Anabolic Androgenic steRoid use by maLE aMateur athletes), of which the design and baseline characteristics have been published recently (3). The results of 12 months follow-up are expected soon. Based on our experience, we discuss the management of steroid

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https://doi.org/10.1530/EC-19-0557

abuse and give treatment recommendations for the clinical endocrinologist.

What are AAS?

AAS comprise a group of compounds that are structurally similar to testosterone and have similar actions when administered in an appropriate dose. The term 'anabolic androgenic steroids' refers to the anabolic (muscle building) and androgenic (virilising) effects of these compounds. The term has been criticized and deemed obsolete since all compounds included in this group bind and activate the androgen receptor, making them basically androgens, which, by definition, have muscle building and virilising effects (4). Injectable testosterone esters are among the AAS most used, but there is a wide variety of synthetic derivatives available. Testosterone, as most other AAS, undergoes extensive metabolism when administered orally. Therefore, some AAS have been alkylated to increase bioavailability after oral administration. However, decades ago, it became evident that 17-alkylated androgens are hepatotoxic and clinical application was largely abandoned (5). Although most AAS abusers are well aware of this, oral AAS, such as methandienone (Dianabol), chlorodehydromethyltestosterone (Turinabol), oxandrolone (Anavar) and stanazolol (Winstrol), are still widely abused. To bypass first pass metabolism in the liver, AAS are injected. Without modification, steroids rapidly enter the blood, resulting in high peak levels and a very short plasma half-life. To improve pharmacokinetics, a fatty acid chain is attached to the steroid. The longer the fatty acid, the slower the release from the injected depot (6).

Testosterone can be converted to oestradiol via the aromatase enzyme and converted to dihydrotestosterone (DHT) via the 5α-reductase enzymes. Administration of supraphysiological doses of testosterone thus results in increased levels of oestradiol and DHT. Elevated oestradiol levels are responsible for a number of side effects: they may stimulate breast glandular tissue and suppress endogenous LH and FSH production. Dihydrotestosterone, primarily produced in the skin, liver and prostate, due to the high local 5α-reductase activity, may lead to male pattern baldness and increased body hair. Although intraprostatic DHT levels are primarily derived from conversion of plasma precursors such as testosterone, local DHT concentrations appear largely unrelated to plasma levels of either DHT or its precursors, when present in physiological concentrations. As a result, there is no evidence that plasma androgen concentrations have any relevance with respect to development of prostate pathology (7). If this also holds true when plasma androgen levels are highly supraphysiological, as can be encountered in AAS abusers, is unknown.

By modifying the testosterone molecule, aromatisation or 5α-reduction can be prevented, attempting to improve the benefit-to-harm ratio of the compound. Although the majority of these steroids have not been extensively studied in humans, users and sellers claim relevant differences and suggest synergism between compounds. There should be no misconception that using anabolic steroids, in combination with an adequate diet and strength training, is very effective. Bhasin *et al*. (8) showed that administration of testosterone increases muscle mass and strength in healthy male volunteers and that the effects of testosterone are dose-dependent. Strength training enhances the effects of steroids significantly.

Who is using anabolic steroids and why are they using it?

The typical user of AAS is male, aged between 20 and 40 and engaged in weight lifting, bodybuilding, strongman competitions or martial arts, primarily kickboxing and mixed martial arts. A minority participates in competitions. Although most body building organizations have a drug free policy, drug tests are mostly not executed. As a result, using anabolic steroids among competitors is widespread and is a necessity to be competitive, especially at the elite levels.

In our clinic, only 1% of AAS abusers was female (2). More than 50% of users reported recent (<3 months) recreational drug use, such as ecstasy, amphetamines, cocaine and cannabis (3).

It is not surprising that gaining muscle mass and strength are the most important motives to start AAS.

Since the majority of AAS abusers is non-competitive, their AAS abuse appears to be internally motivated, such as the ambition to achieve a more ideal body, to reach a new level of performance or to improve self-esteem. Only 3% of our HAARLEM cohort reported that becoming more attractive was a reason to start using AAS. Although the internet is filled with drug-build physiques, only 5% of users admitted that this inspired them to use AAS (3).

One-third of users have friends or relatives who are also using AAS. This indicates that potential users

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frequently seek the company and advice of other users. Thirty-two percent of subjects took the initiative to start using AAS entirely by themselves and usually had carried out extensive research beforehand. Almost half of AAS users consider themselves to be addicted to AAS, mainly due to the perceived positive effects on mind and body. Almost all users report positive effects when using AAS – more muscle mass, more strength, less fat mass, more energy and enhanced concentration. Although almost all users also report negative effects, these are mostly expected, mild and transient and do not outweigh the beneficial effects (3).

What are the origin and quality of anabolic steroids?

In the Netherlands, as in most other European countries, anabolic steroids, such as testosterone, can only be obtained via a pharmacy with a doctor's prescription. Since most doctors are not willing to prescribe steroids for performance and image-enhancing purposes, most steroid abusers are dependent on illegal suppliers. It appears to be easy to obtain illegal anabolic steroids. On the internet, many websites market anabolic steroids and offer shipment all over the world. In our experience, most users of AAS use the internet as a source of information, but retrieve products via local dealers. Mostly, products are obtained via personal contacts in the gym. With some experience, abusers of anabolic steroids are easily spotted based on physical appearance. A short conversation with such a person in the gym usually suffices to retrieve information about the local supplier. Although selling and buying of AAS is prohibited in most countries, the chances of being caught are negligible.

A cycle of anabolic steroids is not expensive. In our HAARLEM cohort, the mean cost per week was €30, adding up to €400 per cycle (3). This means that cost is rarely a barrier to start using AAS. Due to their illegal nature, it is hard to find exact figures about the origin and quality of illegal steroids. Moreover, these figures may be different between countries, dependent on local legislation, infrastructure and activity of regional suppliers. Nowadays, steroid production and trafficking is a multimillion-euro international business, mostly in the hands of organized crime. Due to the unregulated production, the quality of the illegal products may be poor. Therefore, users are at risk of overdosing and being exposed to other drugs than anticipated. Although exact figures are lacking, one may question the microbial safety of injectable products produced in illegal 'underground' labs.

For the HAARLEM study, we made a qualitative inventory of the products obtained by our 100 study participants (Table 1). Only about one half of analyzed AAS samples contained the AAS type as indicated on the label and more often than not the samples contained AAS types not indicated on the label. In a minority of products, no active ingredient was found (3). We suspected that roughly 40% originated from Eastern Europe and Asia, whereas 60% appeared to be produced locally in illegal, so called underground laboratories. Underground labs are improvised labs hidden in cellars or warehouses where raw materials, mostly originating from Asia, are processed into tablets and injectable depots.

How are anabolic steroids used?

Although there is hardly any scientific evidence supporting the common practice of AAS abuse, most users have strong opinions about which type, dose and combination of AAS best suits their purpose. AAS cycles are rarely identical, not even for a single individual. Abusers tend to experiment, frequently escalating AAS dose and duration of use during their career. However, some common principles can be deduced when examining AAS cycles and questioning users.

Anabolic steroids are mostly used in cycles with a duration between 6 and 18 weeks. The unproven rationale behind this strategy is to gain muscle mass and strength during a cycle, allowing the body to

Table 1 Percentage of participants of the HAARLEM study that used one of the below mentioned androgens during one cycle of anabolic steroids (based on label information).

	%
Testosterone	96
Trenbolone	52
Drostanolon	39
Boldenone	38
Nandrolone	33
Stanazolol	29
Methandienone	25
Oxandrolone	23
Mesterolone	19
Methenolone	17
Oxymetholone	15
Dehydrochlorotestosterone	2

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recover between cycles. The contents, dose and duration of the cycles are mostly directed by advice from self-proclaimed experts and are based on unproven beliefs and personal experience. Since muscle mass and strength decline after discontinuation of AAS, multiple cycles or continuous use are deemed necessary to maintain or further increase gained muscle mass. In our cohort study, the mean weekly estimated androgen dose was almost 1000 mg, ranging between 250 and 3300 mg (3). This estimate does not accurately reflect the actual androgen exposure, due to the fact that it is based on the declared and not the actual concentration of the abused products. Moreover, it combines oral and injectable products and different types of androgens. However, it gives an indication that the weekly dose varies enormously between users and that the mean dose is highly supraphysiologic. For comparison, a normal substitution dose of an injectable testosterone-ester to treat male hypogonadism should not exceed 100 mg per week (6).

Most AAS cycles contain multiple agents, used simultaneously, referred to as 'the stack'. A stack usually contains an injectable testosterone ester, mostly combined with nandrolone, trenbolone, drostanolone and/or boldenone esters. In first users or prudent individuals, cycles sometimes comprise only oral anabolic steroids, mostly a single agent, in a low to moderate daily dose (20–50 mg). More frequent, oral anabolic steroids are added to injectable ones, for instance, in the first few weeks of the cycle, referred to as a 'kick start'. Some have adopted the so-called 'blast and cruise' strategy, in which cycles with multiple high dose AAS are alternated with a lower maintenance dose, to prevent muscle loss in between cycles.

Among users, cycles can be characterized as 'bulking' or 'cutting' cycles. Bulking refers to the period in which an individual maintains a caloric surplus in combination with heavy weight training in order to maximize muscle growth. Testosterone, boldenone, nandrolone and methandienone are typically, but not exclusively, seen as bulk agents. Bulking invariably results in an increase of s.c. fat tissue, whereas for body builders, a very low body fat percentage is required to obtain a lean or 'shredded' look. A cutting phase aims to minimize body fat and maintain muscle mass as much as possible. Therefore, a relatively low caloric diet combined with weight and cardio training mostly follows the bulking phase. To prevent loss of muscle, the cutting phase is accompanied by a cutting cycle of anabolic steroids. Since estrogens are assumed to promote s.c. fat apposition, androgens in the cutting cycle should not be prone to aromatization. Therefore, trenbolone, stanozolole and drostanolone are typically regarded as cutting agents.

What is post cycle therapy?

Post cycle therapy, or PCT, is an unproven strategy that aims to restore endogenous testosterone production as soon as possible after a cycle of AAS. An inevitable side effect of AAS abuse is suppression of gonadotropin production, mostly to undetectable levels, and subsequent shutdown of testicular testosterone production. This will become clinically evident once exogenous androgen levels start to decay after the last pill or injection of the cycle. In the recovery phase, there may be a variable period of low plasma androgen levels. This may result in clinical signs of hypogonadism such as fatigue, loss of libido, erectile dysfunction and depressed mood. This period is particularly feared because it may result in loss of strength and muscle mass due to a lower anabolic state and less frequent and intense training.

The speed of recovery of endogenous testosterone production depends primarily on the type and dose of the anabolic steroids used in the last phase of the cycle. As stated before, anabolic steroids are mostly injected as an i.m. depot. Depending on the type of fatty acid chain attached to the steroid, the plasma half-life after injection may be weeks or months (6). Taking into consideration that the administered doses are many times the natural endogenous production, it may take many weeks before exogenous androgen levels are low enough to allow endogenous testosterone production to ignite (9). Oestrogens, although present in much smaller concentrations compared to androgens, have strong suppressive effects on gonadotrophin production (10). Anti-oestrogens, such as tamoxifen and clomiphene citrate, have been shown to stimulate gonadotrophin and testosterone production moderately in eugonadal men (11). Consequently, these substances are frequently used as PCT, based on the unproven assumption that they will speed up recovery of the male hypothalamic-pituitary-gonadal axis.

Human chorionic gonadotropin (hCG) is frequently used to start or maintain spermatogenesis and endogenous testosterone production. Although it is effective to stimulate gonadal function, it does not stimulate gonadotrophin production. It may

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actually delay recovery of gonadotrophin production by artificially increasing plasma testosterone levels and thereby prolonging the underlying hypothalamic suppression of reproductive function.

What else do they use?

Although anabolic steroids are by far the most abused drugs, a variety of other performance and image-enhancing drugs are commonly used (2, 3). These can be categorized as muscle builders, fat burners, pre-workout agents and agents to prevent or treat side effects. Depending on the nature and dose of these agents, additional adverse health effects can be expected. Similar to AAS, most of these products are illegally obtained and their quality should be questioned. Moreover, scientific evidence supporting the claimed effects is mostly absent.

Human growth hormone is typically used as a muscle builder in addition to anabolic steroids. Insulin is used during a bulking phase to facilitate weight gain. Selective Androgen Receptor Modulators (SARMs) are viewed by illicit sellers and users as 'boutique' agents, claiming a better ratio of muscle growth vs side effects. Although this claim is far from being supported by clinical trials, SARMs are promoted as a safer, albeit more expensive, alternative to steroidal androgens. Thyroid hormone, clenbuterol and dinitrophenol (DNP) may be used in the cutting phase to reduce s.c. fat. DNP raises the basal metabolic rate and may result in life threatening hyperthermia (12). Pre-workout agents are basically stimulants such as caffeine, clenbuterol and ephedrine to improve training intensity. As stated previously, tamoxifen, clomiphene and hCG are frequently used to speed up recovery of gonadal function after a cycle of anabolic steroids. Tamoxifen or aromatase inhibitors may also be used to prevent or treat gynaecomastia. Isotretinoine is sometimes used to treat acne. Sildenafil or other phosphodiesterase inhibitors are used to improve erectile function. Diuretics are typically used by competitive bodybuilders days before a contest to reduce body water and improve muscle definition.

What are side effects of AAS and when should I suspect AAS abuse?

All users of anabolic steroids, assuming a significant exposure, have side effects, although the majority of these side effects is mild and transient and some go unnoticed by the abuser. Some of these effects are sensitive indicators of androgen abuse and can be used to confront the patient if he is unwilling to disclose.

Suppression of gonadotrophins is a very sensitive finding, even with relatively low doses and short exposure. Plasma testosterone and oestradiol levels may be high or low, depending on the type of androgen abused. Spermatogenesis is usually reduced following suppression of gonadotrophins and may take months to recover. Testicular volume decreases during abuse. Sex Hormone Binding Globulin and High Density Lipoprotein-cholesterol are liver derived-markers of androgen use and both are markedly suppressed during and weeks after exposure. Erythropoiesis is stimulated by androgens resulting in a mild rise in haematocrit, which may be exaggerated by smoking, sleep apnoea or the use of diuretics. Androgens stimulate sebum production and therefore androgen abuse is frequently associated with oily skin and acne. Androgens affect mood and fluctuating androgen levels may result in mood swings and agitation, particularly in vulnerable individuals. Due to disruption of the oestrogen-androgen balance, breast tenderness or gynaecomastia is frequently reported. The use of oral anabolic steroids is associated with liver toxicity; however, the mild elevation of ALT and AST frequently encountered in steroid abusers mostly reflects muscle damage that results from intensive weight training. Improper injection hygiene or contaminated steroids may give rise to local inflammation or infection. The increased muscle mass and strength that results from AAS abuse may result in injuries such as tendon rupture, lumbar hernia and overloaded joints (13).

The long-term side effects are less well defined. Randomized controlled trials are ethically unrealizable, large prospective studies are unavailable and case-control studies and case series have methodological shortcomings. Several reports indicate that anabolic steroid abuse is associated with cardiac disease, ranging from diastolic dysfunction, overt heart failure to sudden cardiac death (14). Also, AAS abuse is associated with mood and anxiety disorders (15). In a retrospective study, men who tested positive for AAS in fitness centers had a higher mortality risk compared to matched controls (16). It is unclear whether this can be causally attributed to anabolic steroids abuse. It has been shown that users of anabolic steroids are more prone to a hazardous lifestyle. For instance, in a Swedish study approximately 40% of deaths among those who had tested positive for AAS were homicide or suicide, compared with 14% among those who tested negative (14).

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Some studies indicate that AAS abuse may have detrimental effects that persist long after AAS abuse has ended or may even be permanent. A case-control study, comparing past abusers with healthy controls, showed significantly lower testosterone and gonadotrophin levels in past users up to 3.7 years after stopping AAS (17). We and others (2, 18) have reported on individuals with persistently symptomatic low testosterone levels more than 6 months after stopping anabolic steroids. We observed that individuals that had used a high cumulative dose of anabolic steroids in the past appeared to be more prone to post-exposure hypogonadism; however, such an association was not found in the aforementioned case-control study. Unfortunately, pre-AAS testosterone levels in these individuals are mostly unavailable, therefore a causal relationship between steroid abuse and persistent gonadal dysfunction cannot be established in most cases. A recent case-control study suggested complete restoration of gonadal function in all 31 past users, albeit this may take years after stopping anabolic steroids (19). To date, it cannot be excluded that irreversible damage to gonadal function can be a result of AAS abuse. Additional, larger, prospective studies are necessary to clarify this topic.

What to do?

Treating (past) steroid abusers can be complicated for several reasons. As outlined previously, there is a lack of knowledge about adverse health effects of anabolic steroid abuse, especially concerning the long-term effects. There is uncertainty about the actual contents of the abused products and there is large variability in dose, duration and type of abused substances.

It is the policy of our clinic not to offer routine health and blood checks to active users *without* health problems. Although these checks may be part of a harm-reduction strategy, we have concerns that it may invite potential users to start using AAS and convince current users to keep on using or even start experimenting as long as the health checks indicate no (serious) harm. For similar reasons, we do not prescribe anabolic steroids for performance or image enhancing purposes.

Managing health problems in active users asks for a strategy of harm reduction. The problem is that the harms for the individual patient are hard to predict and there are no evidence-based harm-reduction strategies. Doctors may experience moral, ethical, legal or practical barriers, making them feel uncomfortable to check and treat patients who are continuously jeopardising their health for a cause they cannot relate to. Whenever healthcare is provided to active AAS abusers, we advise to contemplate on these issues and to devise an individually tailored protocol, describing very clearly the type and extent of the care we are willing to offer.

Treating health problems in *past* users is less complicated. In our clinic, the reasons to visit were mostly related to symptoms indicating disrupted gonadal function, such as loss of libido, erectile dysfunction, low energy, depressed mood, subfertility and gynaecomastia. As long as the patient refrains from anabolic steroids, we treat him according to applicable guidelines.

The advice we will give subsequently is based on our experience with AAS abusers over the past 10 years who presented with health problems. Please note that it is expert-based and hardly evidence-based.

A careful history should be taken addressing prior use of AAS, including number of cycles, cycle length and weekly AAS dose. We also advise to routinely check for clinical signs that may indicate pre-AAS gonadal (dys) function, such as cryptorchidism, gynaecomastia and infertility. We also check for recent use of recreational drugs, smoking and alcohol intake. Abuse of other drugs may contribute to health problems but may also indicate an addictive personality. We inquire about training frequency, type of training and diet. If these are suboptimal, potential users of anabolic steroids should be encouraged to consult a certified trainer or sports nutritionist before considering further use of anabolic steroids.

We also ask for side effects during or after previous cycles of anabolic steroids. We believe it is important to address the patients goals and the motives for anabolic steroid abuse. As stated previously, only a minority of users take part in competitions and thus their goals are self-constructed and their motives largely internal. In our experience, a lot of AAS users do not have clear goals for their use, apart from being 'as big as possible'.

A considerable number of (former) AAS abusers seeking help have mental problems. Havnes *et al*. showed that mental problems such as depression, anxiety, behavioural change and AAS dependence are reported even more frequently than physical problems (20). By the patient, these symptoms are mostly attributed to hormonal disturbances such as testosterone deficiency, but this may not always be the case. It may be quite revealing to ask why a muscular physique is so important for the patient and why he is even willing to use drugs for it. It may be of help to explore whether there is a low self-esteem or a distorted self-image that needs to be addressed. Lastly, we

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ask the patient if they have ever reflected on the possible health consequences of their abuse, now and in the future.

Based on this information, we try to discriminate between high-risk and lowrisk abusers. Characteristics of high-risk or problematic abuse are escalating steroid use (longer cycles, experimenting with different steroids and higher doses over time), continuous use ('blast and cruise'), addictive behaviour, impulsive behaviour (e.g. starting a cycle without proper consideration), unrealistic, ill-defined or absent goals, being overly concerned with body appearance (body dysmorphic traits) and having the tendency to treat AAS associated health problems with drugs instead of stopping the causative agent. On the basis of this assessment, we reflect with the patient on the potential risks of his current behaviour and try to find out if and to what extent the patient is willing to change. If the patient is cooperative, we make a diagnostic and treatment plan. Mostly, blood or semen analysis is indicated and a psychologist or addiction specialist is consulted.

The wish to stop using anabolic steroids

If an AAS user wants to stop using steroids permanently, it may be helpful to withdraw from the 'steroid environment', such as the hard-core gym or the steroid using training partners.

We indicate that successful stopping is only possible if the user can accept a loss in muscle mass and strength. Furthermore, the user should be able to endure a period of weeks or several months with symptoms of testosterone deficiency. If the patient has not experienced severe withdrawal symptoms after discontinuation of AAS in the past and does not appear to have social, psychological or somatic issues that impede the patients capacity to cope with symptoms of withdrawal, we advise to stop steroids abruptly. Abusers mostly use injectable depots of anabolic steroids with a half-life up to 2 weeks in highly supraphysiological doses which will cause a gradual decay of the plasma testosterone concentration to subnormal levels. In other cases gradual tapering of steroids may be warranted. In committed individuals, we consider prescribing testosterone, aiming to maintain plasma testosterone levels in the high-normal range for a limited amount of time – needed to address issues that interfere with steroid tapering, such as substance abuse, mood disorders or signs of body dysmorphic disorder. Before prescribing testosterone, we make detailed agreements about testosterone dose, goals of therapy and adherence to the treatment plan. We stop testosterone prescription if the patient violates these agreements or starts using steroids again. Further tapering of testosterone dose should be individualized based on evaluation of treatment goals.

Symptoms of testosterone deficiency after stopping anabolic steroids

If the last administration of AAS has been within 3 months of presentation, provided that the symptoms are well tolerated, we advise to wait for spontaneous restoration of gonadal function. Checking blood is mostly not very helpful at this stage, knowing that levels are probably disturbed by the recent use of AAS. As explained previously, it may take weeks or months until exogenous androgen levels have decayed low enough for the Hypothalamo-Pituitary Gonad (HPG) axis to restart. Oral anabolic steroids have a much shorter half-life and recovery of the HPG axis is expected much faster.

If the patient plans a steroid cycle in the near future, checking blood may not be useful since the levels will be disrupted shortly afterwards.

If symptoms persist for more than 3 months after the last injection, testing for plasma testosterone and gonadotrophins is warranted. Typically, the recovery phase after recent AAS use is characterized by low gonadotrophins, low testosterone and low SHBG levels. Three months after the last injection, at least partial recovery of the HPG axis is expected. If levels are still very low, the patient should be questioned about undisclosed steroid use in the weeks prior to blood testing. If this is denied, other, steroid unrelated causes of hypogonadotropic hypogonadism should be explored. In the unlikely event of finding elevated gonadotropins and low testosterone levels, the patient should be questioned about current use of aromatase inhibitors or selective oestrogen receptor modulators. If this is denied, other, steroid unrelated causes of gonadal dysfunction should be explored.

If testosterone levels are not very low and symptoms are well tolerated, waiting for spontaneous recovery of the HPG axis is advised. If symptoms are not well tolerated, endogenous testosterone production may be stimulated by prescribing tamoxifen 20 mg once daily or clomiphene 50 mg once daily for several weeks. Both drugs mildly stimulate gonadotropin and testosterone production and do not suppress spermatogenesis. Testosterone substitution should be withheld as long as possible, since it interferes with HPG axis recovery, and prescribed only if no further recovery of the HPG is expected.

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Although selective oestrogen receptor modulators (SERMs), such as tamoxifen and clomiphene, have a potential advantage over testosterone substitution, some caveats need to be considered. SERMs act as an oestrogen or an anti-oestrogen, depending on the exposed tissue. The effects of SERMs have not been studied extensively in men and long-term effects are unknown. In men, aromatisation of testosterone to oestradiol is vital to reach and maintain bone mass, and the long-term effects of SERM administration on bone health in hypo- or eugonadal men have not been established. Also, there is evidence that sexual function in men depends on the combined effects of androgens and oestrogens (21). Although detrimental effects of SERMs on sexual function in men have not been reported in small and short-term studies (22), these effects cannot be excluded.

Finally, in postmenopausal women, SERMs have been shown to be mildly thrombogenic and similar, albeit, milder effects on coagulation parameters have been reported in men (23).

Eventually, if other causes of hypogonadism have been explored, testosterone levels remain unequivocally low and there is no desire to have children, testosterone substitution can be started under the same agreements as stated previously.

If necessary, we prefer testosterone gel in the lowest effective dose. Testosterone gel results in fairly stable testosterone levels (24), does not suppress gonadotropin levels as much as most injectables, is unpopular for misuse among steroid users and can be easily tapered in weeks or months.

Fertility

Anabolic steroid abuse inherently results in suppression of spermatogenesis. In our experience, normalisation of sperm count lags behind normalisation of plasma testosterone concentrations. Therefore, a wait-and-see policy is justified as a first step, that is, semen analysis should not be done within the first 6 months after stopping anabolic steroids. If the sperm count is severely compromised 6 months after the last injection and the patient denies AAS use in the last months, blood needs to be tested to check gonadotrophin and testosterone levels. As stated previously, the recovery phase after recent AAS use is characterized by low gonadotrophins, low testosterone and low SHBG levels. If gonadotrophin levels are elevated, especially if FSH is disproportionally elevated compared to LH, primary gonadal dysfunction, unrelated to steroid abuse, should be suspected. If gonadotrophins, testosterone levels and testicular volume are normal, obstructive azoo- or oligospermia should be suspected. If gonadotrophins and testosterone levels are low, and other causes of hypogonadotrophic hypogonadism are explored and rejected, the wait-and-see policy should be continued for 6 more months. If hypogonadotrophic hypogonadism and oligospermia persist, spermatogenesis and endogenous testosterone production can be stimulated by administration of hCG 1500 IU two to three times weekly. Assuming that spermatogenesis has been normal in the pre-AAS period, hCG is effective in restoring spermatogenesis and endogenous testosterone levels to normal levels (25).

Gynaecomastia

Gynaecomastia or breast tenderness is a common side effect of AAS abuse. It results from distortion of the androgen-estrogen balance during or after administration of AAS. Several AAS, including testosterone, can be aromatized to estrogens. As a result, finding supraphysiological oestradiol levels in AAS abusers is not unusual. Aromatase inhibitors and anti-estrogens such as tamoxifen and clomiphene are frequently used by AAS abusers, either as PCT or to treat or prevent gynaecomastia. Although symptoms are frequently transient, gynaecomastia may persist after stopping anabolic steroids. After ruling out other causes, persistent breast tenderness and gynaecomastia can effectively be treated with a trial of tamoxifen 20 mg once daily for several weeks (25). In our experience there is a high chance of recurrence after stopping tamoxifen, especially if a new cycle of anabolic steroids is started. For recurrent or persistent gynaecomastia, surgical treatment should be considered.

Concluding remarks

AAS abuse has been called ‘a hidden epidemic’ (26). Over the past 40 years, the use of AAS has spread from use for performance enhancement by a relatively small group of elite athletes to widespread use among young men to obtain a more muscular physique. As described previously, AAS are easily obtained, cheap, of bad quality and used in huge quantities. All users experience side effects, a considerable percentage of users suffer long-term health problems after stopping and some long-term effects may not even be recognized. Among medical professionals

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https://doi.org/10.1530/EC-19-0557

there is a lack of knowledge to recognize and treat the problems associated with AAS abuse.

Due to its history in competitive sports, AAS abuse has been associated with cheating and foul play. Over the years, sport organisations and anti-doping institutions have emphasized, and perhaps exaggerated, the adverse effects of AAS to prevent athletes from taking them. This may explain why AAS abuse is frowned upon by the general public. As a result, most AAS users are reluctant to disclose the misuse of androgens. Knowing the numbers of users and the potential hazards associated with abuse, it is surprising that this topic has been largely neglected by the scientific community.

It is a challenge to manage the patient who uses AAS. More clinical studies are needed to fill the major gaps in knowledge regarding long-term side effects. Also, studies should be undertaken focusing on primary and secondary prevention and effective harm-reduction strategies. The results of these studies should be used to educate doctors on how to prevent and recognize these side effects, to treat patients without prejudice and to convince politicians that adequate measures should be taken to confine androgen abuse.

We believe that the endocrine community has a pivotal role in both research and treatment. Due to the controversial nature of AAS abuse and its medical management, it is the responsibility of national and international endocrine societies to give some guidance. Therefore, we strongly recommend management guidelines to support the individual endocrinologist.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this review.

Funding

This work was supported by a grant of the Spaarne Gasthuis Academy (grant 2015).

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Received in final form 17 March 2020
Accepted 30 March 2020
Accepted Manuscript published online 31 March 2020