Adverse effects from different anabolic androgenic steroids

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Project thesis

University of Oslo

2022

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Abstract

Introduction: The use of anabolic androgenic steroids (AAS) are associated with a long list of harmful adverse effects, including cardiovascular, psychiatric, and physical side effects. Polypharmacy is common among AAS users, both on regards to different types of performance enhancing drugs and other drugs of abuse. This makes it difficult to study the side effects of specific AAS.

Aim: The present study aimed to examine whether the use of oral AAS, trenbolone and growth hormones are associated with more self-reported side effects and objective adverse health measures, than other AAS users.

Method: Our sample consisted of 91 male AAS users, with at least 1 year of cumulative exposure to AAS, recruited through social media, posters in gyms and other platforms targeting individuals engaging in resistance training. Cross-sectional data were collected using an online questionnaire and clinical examination including echocardiography. The questionnaires assessed relevant background and health information, characteristics of training history, and sport achievements. They were asked about the extent of current previous AAS use, doses applied, symptoms of dependence and extent of subjectively experienced side effects.

Results: Individuals using more compounds, overall experienced more psychiatric side effects than those using fewer. The use of trenbolone were associated with more self-reported psychiatric and physical side effects, as well as more symptoms of dependence, compared to other AAS users. Users of oral AAS reported more cases of hypertension and heart arrythmia than other participants.

Conclusion: Our findings support research indicating trenbolone to have a unique harmful effect on the nervous system. Dependency is a problem for many AAS users, and trenbolone users seem to experience this in a larger degree. Trenbolone also seem to be more associated with adverse psychiatric side effects than other commonly used AAS.

1 Introduction

Anabolic androgenic steroids (AAS) are a large group of compounds, that includes testosterone, and synthetic variants of testosterone. When taken in supraphysiological doses, AAS efficiently improve skeletal muscle strength and volume (1). Misuse of AAS for athletic and aesthetic purposes have turned out to be a bigger public health issue than earlier thought. Previously it was thought that non-medical AAS use only occurred within organized sports, where the cheating was the central issue. Today we know that a large portion of AAS-users, is what we can call recreational lifters and bodybuilders – that is, individuals who do not compete in organized sports (2, 3).

AAS' ability to increase muscle strength and volume was demonstrated in a recent study of weightlifters (4). Users of AAS were stronger on all measurements of strength, and had higher BMI, despite spending less time per week on lifting weights than the non-exposed weightlifters (4). Some side effects of AAS-use have been acknowledged for a long time, like depression, male infertility, hypertension, increased risk of cardiovascular events and masculinization in females (5, 6), but newer studies show that a greater number of negative side effects can be due to AAS use.

1.1 Prevalence

The prevalence of AAS-use varies from different countries and different subcultures. In a Swedish study from 2011, Leifman et al. asked gym members in 36 different training facilities in Stockholm via questionnaires, about their experience with performance enhancing drugs (PEDs) (7). The results showed that 3.9 % of men were either users of or had tried AAS at least once in their life (7). These numbers are several times higher than the estimated lifetime prevalence of Swedish men, which is estimated to around 1 % (7). One study from the United Kingdom may indicate that AAS use is an increasing problem (8). The study shows that the number of AAS users in England and Wales nearly has doubled from 2007 to 2017 (8). Even though numbers since 2017 have decreased slightly (8), this may point towards a trend of increasing usage.

The distribution of AAS users does not seem to be random. Gym members have a higher risk of being offered AAS than the general population (7). The risk also seems to increase with more hours spent in the gym (7). The same goes for individuals who have used other narcotics in the last 12 months, who also have a higher risk of being offered AAS (7). Men is

overrepresented among AAS users, even though usage in females exists as well (5, 9). Prevalence among women is not very well studied, but was estimated to be around 0.1 % in the United States in the 1990s (9). The growing AAS use, together with new research detecting more severe side effects, makes it clear we must look at AAS use as a public health problem.

1.2 Health among users

1.2.1 Contact with the health system

Despite AAS users having more hospital contacts than the general population (10), there is some research indicating that users rarely inform their doctor about their AAS use. In a study from 2015, Hope et al. reported that 43 % of male injectors of PEDs have had contact with a general practitioner (GP) in the last year (11). Of the users who had contacted a GP the last year, only 41 % disclosed their use to their doctors. This tendency seems to be supported by other studies. In a study from 2014, only 56 % of users reported that they had ever told a doctor about their AAS use (6).

1.2.2 Dependence

Dependence is a common phenomenon among AAS users. In a study from 2012, Ip et al. 2012, gathered information from 479 AAS users, via an internet survey (2). In this study 23.4 % of the participants had behavior that corresponded with AAS dependence. This seem to be consistent with other studies which typically estimates around 30 % of users being classified as dependent, which again is higher than for other drugs of abuse (12, 13).

AAS-dependent users have been shown to use a greater number of different substances, larger weekly doses, and shorter off-periods (time which no active drug is being administrated), compared to non-dependent AAS users (2, 14). Dependent users also administrate more non-AAS substances compared to non-dependent users; like caffein, triiodothyronine (T3), human growth hormone (hGH), tadalafil, sildenafil, insulin and insulin-like growth factor 1 (IGF-1) (2). In the last few years significantly psychiatric and neuroanatomical differences between dependent and non-dependent AAS users have been revealed. Dependent users experience more side effects of AAS use, have a larger degree of anxiety and depression symptoms and use more psychiatric medication than non-dependent users (14). Moreover, brain imaging

studies have shown that AAS dependence is associated with thinner cerebral cortex in several regions, particularly pronounced in prefrontal regions, and accelerated brain ageing (14, 15).

1.2.3 Side effects

Cardiovascular

AAS have been shown to elicit several adverse effects on the cardiovascular system. A prospective study from 1988, by Lenders et al., concluded that both systolic and diastolic blood pressure increased through a cycle of AAS (16). Five months after ended cycle, their systolic blood pressure was still elevated above baseline (16). This effect on blood pressure is confirmed by newer studies. Users of AAS have both higher blood pressure in general (17), and a higher percentage of users display clinical hypertension (HT), with 51 % of current AAS users having HT, compared to 33 % of past AAS users and 17 % of non-users (18, 19). In 2012, Angell et al. 2012 published a study examining 28 AAS users and 19 controls, using echocardiography (20). The users of AAS had higher septal thickness and higher posterior wall thickness compared to non-users (20). Estimating left ventricular (LV) mass using ultrasound, they found that AAS users had higher LV mass compared to their body length (20). Users of AAS also have reduced LV systolic and diastolic function, compared to controls (17). In a study by Rasmussen et al. 2018, it was found that LV ejection fraction (EF) was reduced among current AAS users compared to non-users, in addition to impaired global longitudinal strain (GLS) in both former and current users compared to non-users (18). AAS can cause accelerated coronary atherosclerosis, with higher coronary plaque volume among users (17). Lifetime-dose of AAS seem to be strongly associated with coronary atherosclerotic burden (17). In a study done by Lane et al. 2006, they measured the elasticity of the radial artery and aorta using aortic augmentation index (AIx) (21). After dilatation using glycerol trinitrate, AAS users displayed a smaller reduction in AIx, suggesting current AAS users to have less elastic vessels (21). Aorta distensibility index assessment done by Rasmussen et al. 2018 demonstrated a higher aortic stiffness as well, both in current and former AAS-users (18). AAS use negatively affects serum levels of cholesterol, with high-density lipoprotein (HDL) cholesterol declining, and low-density lipoprotein (LDL) cholesterol increasing throughout a cycle (16). Current and former AAS users displays lower insulin sensitivity, perhaps partially mediated by higher visceral adipose tissue and total body fat percentage (22). Impaired glucose tolerance is most prevalent in former AAS users, but also occurs in current users (22).

Psychological

There is a lot of data pointing towards a higher risk of psychiatric symptoms and disorders among AAS users. Several studies have associated current AAS use with symptoms usually related hypomania/mania, such as irritability, aggressiveness, increased self-confidence, hyper-activity, and carelessness (23, 24). Due to AAS's ability to suppress the normal hypothalamic-pituitary-testicular function (25), users may find themselves hypogonadal after an ended cycle of steroid-use. This may contribute to dependence if the individual finds the symptoms upon discontinuation uncomfortable. Symptoms of depression are common side effects following discontinuation of AAS (23). Current users report a stronger drive for muscle tone and thinness, perfectionism and body dissatisfaction compared to non-users (26). Current AAS use is also associated with higher risk of body image- and eating disorders (26).

Certain AAS seem to have a more serious effect on neurons than others. Trenbolone is a synthetic androgenic steroid, originally used as an animal growth stimulant, most famed in the cattle industry (27). In a qualitative study exploring the health support wanted by 23 males regarding their AAS use, several participants mentioned trenbolone as having many negative side effects, including behavioral changes, loss of empathy and having a negative impact on personal relationships (28).

Physical

Physical adverse effects are among the most acknowledged side effects of AAS. Nearly all users of AAS reports subjective side effects when asked in surveys (3). Among the most common reported side effects are sexual dysfunction, changes in mood, testicular atrophy, and edema (3, 29). Gynecomastia is also frequently reported among AAS users and may be even more common in former users (3, 29).

Other organs

AAS' effect on the liver have been discussed for many years. It has been shown that the use of AAS may affect the liver's function, but this is most prominent with orally administrated (17α-alkylated) AAS (30). However, as Pertusi et al. suggested in an article from 2001, the hepatotoxicity from AAS use may be overestimated due to muscle-damage from intense

workout sessions may cause transaminases to rise (31). AAS use can cause an increase in serum-creatinine due to reduced glomerular filtration rate (GFR) (32).

1.3 Polypharmacy

AAS use is commonly combined with other substances. In addition to combining different types of AAS, many users also administrate other PEDs, such as insulin, hGH, IGF-1 and thyroid-hormones (2, 6). Some also use other drugs of abuse, like opioids and benzodiazepines (6), to perform at a higher level, or to relieve adverse effects from the AAS. Many AAS users self-medicate with antiestrogens, fertilization-agents, and/or medication against erectile dysfunction and androgenic alopecia (2). Individuals competing in drug tested sports, may use masking agents, like epitestosterone, to prevent the detection of AAS (6). These factors can cause user to end up with a cocktail of different substances to optimize their AAS usage.

Users of AAS report that they experience different types and degrees of side effects from different types of AAS (28). Since polypharmacy is normal among users, investigating specific substances' association with specific side effects can be difficult (2, 6). We know from interviews that due to the little data available, some users rely on others' subjective experiences for information. Some individuals expresses a demand for more information about adverse effects and long term side effects from AAS use (28). Few studies have examined the association between different types of AAS, as well as hGH, and different types of side effects in human beings.

1.4 Adverse effects from different anabolic androgenic steroids

With a sample of 91 AAS users, we examine whether the use of selected commonly used PEDs are associated with self-reported side effects of use and objective health measures. Specifically, we aim to identify:

(i) whether users of oral AAS, trenbolone and growth hormones experience more psychological, cognitive, or medical side effects than other AAS users.

(ii) whether the use of these compounds are associated with more pathology on objective study measures including cardiovascular, liver- and kidney function

(iii) whether the use of certain compounds are associated with more symptoms of dependence.

2 Materials and methods

2.1 Data collection

The study sample consisted of 91 male participants, all reported using AAS with at least one year of cumulative exposure (summarizing on-cycle periods). Participants were recruited through social media, posters in gyms and other platforms targeting individuals engaging in resistance training. Cross-sectional data were collected using an online questionnaire. The participants were requested to complete a set of structured questionnaires using av web solution offered by the Services for Sensitive Data (TSD), provided by the University of Oslo. The questionnaires assessed relevant background and health information, characteristics of training history, and sport achievements. They were asked about the nature of their AAS use, the extent of current previous AAS use, doses applied, age of initiation, symptoms of dependence and extent of subjectively experienced side effects. Items regarding symptoms of dependence were formulated from ICD-10-CMs criteria for F1x.2 Dependence syndrome (e.g., Over time the effect of steroids has declined, even though I use same dose). To characterize the commonly used compounds, the participants were requested to list the PEDs used in their last or current cycle, and rank their top five most used AAS. The list included different types of AAS and other well-known substances of abuse typical in strength and hypertrophy training, as listed in Table 1. For 19 participants we did not receive a ranking of their five most used compounds, these were excluded when analyzing statistics of most used compounds.

Table 2 displays drugs which can/must be administrated orally. We assume that participants who reported that they used one or more of these drugs in their current/last cycle, also use more of these types of compounds.

Table 1 Commonly used performance enhancing drugs

Testosterone enanthate
Testosterone propionate
Testosterone undecanoate
Sustanon®/Omnadren®
Trenbolone
Winstrol®
Deca-Durabolin®/Nandrolon Decanoate
Dynabolon®/Nandrolon Undecanoate
Growth hormone
Masteron®
Oral Turinabol®
Dianabol®
IGF-1, GHRP and/or MGF
SARMs
Primobolan®
Anadrol®
Anavar®
Equipoise®
Arimidex®
Halotestin®
Proviron®
Nolvadex® or other anti-estrogens
Methasterone/Superdrol
T3
T4
Clenbuterol
Efedrin
Insulin
Beta blockers
hCG
Testosterone gel

Table 2 Commonly used oral performance enhancing drugs

Oxymetolon (Anadrol®)
Metandostenolon (Dianabol®)
Stanozolol (Winstrol®)
Chlorodehydromethyltestosterone (Turinabol®)
Oxandrolol (Anavar®)
Testosterone undecanoate (Andriol®)
Anastrozol (Arimidex®)
Tamoksifen (Nolvadex®)
Fluoxymesterone (Halotestin®)
Mesterolone (Proviron®)
Methasterone (Superdrol)
T3 (Liothyronin®)
T4 (Levaxin®)
Beta blockers
Clenbuterol (Ventipulmin®)

Self-reported side effects

In the survey the participants were asked in detail about their experiences with different side effects that might be attributed to AAS usage. To investigate if specific substances were associated with more side effects, different data were grouped together creating scores for distinct categories of self-reported side effects; cardiovascular, psychiatric, cognitive, physical, and other organ-related side effects.

Cardiovascular side effects were examined by asking the participants if they have and were aware of the following health problems/disorders; systemic hypertension, abnormal cholesterol-levels, heart arrythmias, myocardial hypertrophy, myocardial infarction, thrombus, chest-pain and stroke. The presence of each side-effect was scored as 1 point in the variable called "self-reported cardiovascular side effects". The maximum score of this variable was eight points.

Psychiatric side effects were examined by asking the participants if they have experienced sleeping problems, tiredness, depression, mood changes, anxiety, paranoia, irritability, short temperedness, aggression, jealousy or reduced empathy, that they might give blame to AAS usage, and to what degree they have experienced these problems. No experience = 0 points, some experience = 1 point, moderate experience = 2 points, substantial experience = 3 points. This variable has a maximum score of thirty-six points.

"Self-reported cognitive side effects" were examined by asking the participants if they have experienced impaired memory and/or concentration since started using AAS. This variable has a maximum score of six points; no experience = 0 points, some experience = 1 point, moderate experience = 2 points, substantial experience = 3 points.

Other physical side effects were explored by asking the participants if they have experienced more of the following effects after using AAS; stretch-marks, acne, sweating, fluid-retention, feeling of physical pressure, hair-growth, loss of hair, reduced appetite, muscle-rupture, tendon-rupture, sore injection-points, abscess, skin-rupture, loss of sex-drive, sexual dysfunction, gynecomastia, altered voice, reduced sperm-function, smaller testicles or acromegaly. In total it was possible to reach the maximum of twenty points in the variable "self-reported physical side effects", if the participant had experienced all the above.

Information about other internal organ functions were obtained by asking the participants if they have any problems with the kidneys or liver, hepatitis, or an otherwise organ-failure. A maximum score of four points is attainable in this variable.

2.2 Echocardiography

Echocardiography was performed using Vivid E95 (GE Vingmed Ultrasound, Horten, Norway). One investigator obtained all the echocardiographic measurements. The measurements were analyzed offline, by another investigator, blinded to AAS status, using the

software EchoPAC v203 (GE, Horten, Norway). Using the formula from Devereaux et al. (33), LV mass was estimated from parasternal views, and adjusted for the body surface area using Du Bois' formula (34). Left ventricular hypertrophy (LVH) was defined by LV mass/BSA > 117 g/m^2 in accordance with recent heart evaluation recommendations from EAPC and EACVI (35). LV mass was not calculated in cases with poor image quality or insufficient alignment. HT was defined as either systolic blood pressure >140 mmHg or diastolic pressure >90 mmHg. Left ventricular ejection fraction (LVEF) was calculated using modified Simpson's biplane method. Abnormal LVEF was defined as <52 %, but participants with LVEF <40 % were also noted. A total score was given to each participant, ranging from 0 to 4 points. One point was given if LVEF was <52 %, and two points if LVEF was <40 %. LVH = 1 point. If the participant has HT at the time of the examination, one more point was given. Not all 91 participants accepted examination using echocardiography and BP measurements, these are not included when analyzing statistical differences.

2.3 Statistical analyses

Group differences in demographic data were evaluated with two-tailed independent sample t-tests and x^2 and Fisher's exact tests for categorical data. Continuous outcome measures were evaluated using linear regression. All statistical calculations and analyses were performed using SPSS Statistics (version 26, IBM, Chicago, IL). Alpha level of .05 were used for all statistical tests.

2.4 Ethics

This study was approved by Regional Committees for Medical and Health Research Ethics South East Norway (REC) (2013/601 and 2018/736). All data were gathered and administered in concordance with the Declaration of Helsinki. Participants received 500 NOK in compensation for contributing to the research. Newly discovered health markers associated with pathology or negative outcomes, were evaluated by a physician, and investigated further when required.

3 Results

3.1 Demographics

The mean age was 38 years (median = 37 years) among the 91 male participants. 28 percent were living as single, 9 percent as divorced, and the remaining as married (24.2 %) or domestic partnership (39.6 %). On average the participants had 15 years (median = 15 years) of education, which in Norway is equivalent to completed high school (13 years) plus 2 years in university/college. The results showed that 77 % of participants were working full-time, 12 percent working part time, and 11 percent not working. About 16 % of the participants were students at the time of answering the questionnaire. The average amount of minutes spent in the gym per week lifting weights were 349 min (median = 300 min). Maybe surprisingly, some participants reported a very low amount of time spent lifting weights, with 8 participants reported spending 90 minutes or less each week. Three participants were excluded from statistics about time spent lifting weights, for not answering the question.

Table 3 Demographics and characteristics of the participants

	Mean	Median	Std. Deviation	Minimum	Maximum
Age	38.4	37.0	10.4	21	73
Years of education	14.9	15.0	2.5	9	14
Minutes spent lifting weights per week	349.0	300.0	213.1	0	1050
Age when first time using AAS	22.7	20.0	7.9	15	55
Number of years using AAS	11.8	10.0	8.5	1	36

		n	%
Marital status			
	Married	22	24.2
	Domestic Partner	36	39.6
	Divorced	8	8.8
	Single	25	27.5
Employment			
	Full-time	70	76.9
	Part-time	11	12.1
	Not working	10	11.0
Studying			
	Yes	15	16.5
	No	76	83.5
Using anxiolytics/antidepressants today			
	Yes	13	14.3
	No	78	85.7
Smoking			
	Yes	8	8.8
	No	83	91.2

3.2 General use

All compounds combined the participants used on average 1078 mg/week (SD = 709.89). Most participants seem to use some form of testosterone as a cornerstone in their drug regime. 59 users (81.9 %) reported testosterone enanthate to be among their top five most used compounds, and 76 users (83.5 %) have used testosterone enanthate in their current/last cycle. The second most used compound is trenbolone, with 41 users (56.9 %) reporting trenbolone to be among their top five most used compounds, and 35 users (38.5 %) using trenbolone in their current/last cycle. The number of participants favoring each compound is listed in table 4. The average amount of years using AAS was 11.8 years (median = 10.0 years).

Table 4 Frequencies of most used performance enhancing drugs

	Number of participants	
	Using compound in current/last cycle (n=91)	Ranking compound among top five most used (n=72)
Testosterone enanthate	76	59
Testosterone propionate	17	18
Testosterone undecanoate	5	2
Sustanon®/Omnadren®	15	21
Trenbolone	35	41
Winstrol®	10	23
Deca-Durabolin®/Nandrolon Decanoate	14	34
Dynabolon®/Nandrolon Undecanoate	0	3
Growth hormone	8	17
Masteron®	14	15
Oral Turinabol®	6	7
Dianabol®	13	26
IGF-1, GHRP and/or MGF	2	0
SARMs	0	0
Primobolan®	2	10
Anadrol®	1	9
Anavar®	6	5
Equipoise®	9	14
Arimidex®	6	2
Halotestin®	1	8
Proviron®	6	5
Nolvadex® or other anti-estrogen	13	8
Methasterone/Superdrol	0	-
T3	2	-
T4	6	-
Clenbuterol	9	-
Efedrin	4	-
Insulin	3	-
Beta blockers	0	-
hCG	3	-
Testosterone gel	5	-

3.3 Polypharmacy

When asking the participants how many different types of compounds they typically use in combination, they on average use 2.6 different agents (mean = 2.59, SD = 1.01), in contrast to when asking how many compounds used in their current/last cycle, on average using 3.2 (mean = 3.24, SD = 2.52), t(89) = -2.575, p = .012. This represents a significant dissociation

between stated typical use and stated use in current/last cycle. One can hypothesize that the number of different AAS will affect the typical total dosage of all compounds used. Our test shows that AAS users taking more compounds on average take larger total dosages than those taking fewer compounds. But this association is not significant, $F(1, 89) = 1.687$, $p = .197$.

The number of years using AAS do not affect how many compounds the participants use in a typical cycle. In this study only 2.8 % of the variance in the number of different compounds in last/current cycle can be explained by the number of years using AAS, $F(1, 89) = 3.569$, $p = .062$. The correlation is not significant.

There is a positive correlation between self-reported psychiatric side effects and number of compounds used in combination. 5.7 % of the variance of self-reported psychiatric side effects can be explained by the number compounds taken, $F(1, 89) = 5.375$, $p = .023$.

3.4 Oral AAS

Users of orally administrated drugs had significantly more self-reported cardiovascular side-effects (mean = 1.61, SD = 1.39) compared to those who only used injectable PEDs (mean = 1.00, SD = 0.97), $t(80.84) = -2.421$, $p = .018$. When investigating this further it appears this difference mainly is due to a significant difference in the portion of participants having high blood-pressure (57% vs. 33%) and heart arrythmia (24% vs. 7%). These and other cardiovascular side effects are listed in table 6. No other side effects were significantly associated with oral AAS use in the current/last cycle, as seen in table 5.

Table 5 Oral AAS used in current/last cycle

	Oral AAS users (n=46)	Non-oral users (n=45)		
	Mean (SD)	Mean (SD)	t	p-value
Self-reported cardiovascular side effects	1.61 (1.39)	1.00 (0.97)	-2.421	**.018***
Objective cardiovascular side effects	1.53 (1.08)	1.45 (0.99)	-0.374	.710
Psychiatric side effects	9.83 (9.33)	8.16 (7.66)	-0.932	.354
Physical side effects	8.02 (3.62)	8.24 (3.71)	0.290	.773
Cognitive side effects	1.22 (1.74)	1.13 (1.67)	-0.235	.815
Other organ related side effects	0.15 (0.52)	0.18 (0.54)	0.233	.817
Symptoms of dependence	3.35 (2.33)	2.98 (2.32)	-0.759	.450

Data are presented as means (standard deviation). *Significant difference between the groups ($p < .05$). SD = standard deviation. 3 oral users and 5 non-oral users missing in objective cardiovascular side effects.

Table 6 Reported cardiovascular side effects in oral and non-oral AAS users

	Oral AAS users (n=46)		Non-oral users (n=45)			
	n	%	n	%	x^2	p-value
High blood pressure	26	56.5	15	33.3	4.941	**.035***
Abnormal cholesterol levels	11	23.9	12	26.7	0.091	.813
Arrythmia	11	23.9	3	6.7	5.197	**.022***
Cardiomegaly	12	26.1	7	15.6	1.527	.303
Heart attack	1	2.2	1	2.2	-	-
Thromboembolism	2	4.3	1	2.2	-	-
Chest pain	11	23.9	6	13.3	1.676	.283
Stroke	0	0	0	0	-	-

3.5 Trenbolone

Users of trenbolone seem to display more symptoms of dependence than AAS users not taking trenbolone. Both users taking trenbolone in their current/last cycle and users ranking trenbolone among top five most used compounds, reported a higher dependence score than other AAS users. Users ranking trenbolone among top five compounds reported significantly more symptoms of dependence (mean = 3.5, SD = 2.3) than other participants (mean = 2.6, SD = 2.0), t(70) = -2.289, p = .025, but no differences in dependence scores were seen when comparing participants using or not using trenbolone in their last cycle. AAS users taking trenbolone in their last/current cycle had a significantly higher number of self-reported psychiatric side effects (mean = 11.7, SD = 10.9) than those not using trenbolone (mean = 7.3, SD = 6.2), t(47) = -2.133, p = .038. Participants ranking trenbolone among top five most used compounds had significantly higher levels of self-reported physical side effects (mean = 9.2, SD= 3.7) than did those not ranking trenbolone among top five most used (mean = 7.3, SD 3.3), t(70) = -2.256, p = .027. No other side effects were associated with the use of trenbolone, as displayed in table 7 and 8.

Table 7 Trenbolone used in current/last cycle

	Trenbolone users (n=35)	Non-trenbolone users (n=56)		
	Mean (SD)	Mean (SD)	t	p-value
Self-reported cardiovascular side effects	1.46 (1.46)	1.21 (1.07)	-0.850	.399
Objective cardiovascular side effects	1.61 (0.93)	1.42 (1.09)	-0.805	.423
Psychiatric side effects	11.66 (10.94)	7.34 (6.17)	-2.133	**.038***
Physical side effects	8.63 (3.93)	7.82 (3.46)	-1.028	.307
Cognitive side effects	1.37 (1.74)	1.05 (1.68)	-0.868	.388
Other organ related side effects	0.31 (0.72)	0.07 (0.32)	-1.885	.066
Symptoms of dependence	3.49 (2.57)	2.96 (2.15)	-1.043	.300

Data are presented as means (standard deviation). *Significant difference between the groups (p < .05). SD = standard deviation. 3 trenbolone-users and 6 non-trenbolone users missing in objective cardiovascular side effects.

Table 8 Ranking trenbolone among top five most used compounds

	Trenbolone users (n=41)	Non-trenbolone users (n=31)		
	Mean (SD)	Mean (SD)	t	p-value
Self-reported cardiovascular side effects	1.32 (1.06)	1.13 (1.15)	-0.720	.474
Objective cardiovascular side effects	1.55 (0.92)	1.37 (1.10)	-0.759	.450
Psychiatric side effects	9.32 (8.30)	7.23 (6.93)	-1.135	.260
Physical side effects	9.22 (3.67)	7.32 (3.34)	-2.256	**.027***
Cognitive side effects	1.07 (1.71)	1.16 (1.75)	0.214	.831
Other organ related side effects	0.17 (0.54)	0.03 (0.18)	-1.526	.133
Symptoms of dependence	3.51 (2.30)	2.35 (2.00)	-2.289	**.025***

Data are presented as means (standard deviation). *Significant difference between the groups (p < .05). SD = standard deviation. 2 trenbolone-users and 1 non-trenbolone user missing in objective cardiovascular side effects.

3.6 hGH

Users taking hGH in their last/current cycle had a higher number of total substances used in their last/current cycle (mean = 6.1, SD = 3.3) than did those not using hGH (mean = 2.9, SD = 2.2), t(8.786) = -2.810, p = .021. When comparing AAS-dosages in hGH-users versus non-

hGH users, there was no differences between the groups in weekly doses applied; hGH users (mean = 1093, SD = 560) compared to those not using hGH (mean = 1077, SD = 727), t(86) = -0.064, p = .949.

Users of hGH tend to have less symptoms of dependence than others, with participants using hGH in their current/last cycle reporting significantly fewer symptoms (mean = 1.9, SD = 1.5) than non-users (mean = 3.3, SD = 2.4), t(12.6) = 2.456, p = .029.

AAS-users taking hGH in their current/last cycle had fewer self-reported psychiatric side effects (mean = 4.78, SD = 3.153) than did those not using hGH (mean = 9.46, SD = 8.822), t(25.8) = 3.269, p = .003. There was no significant difference in self-reported organ-problems, cognitive, cardiovascular or physical side-effects, or objective cardiovascular measurements between groups using and not using hGH.

Table 9 hGH used in current/last cycle

	hGH users (n=9)	Non-hGH users (n=82)		
	Mean (SD)	Mean (SD)	t	p-value
Self-reported cardiovascular side effects	0.89 (1.05)	1.35 (1.25)	1.072	.287
Objective cardiovascular side effects	1.89 (0.93)	1.45 (1.04)	-1.224	.225
Psychiatric side effects	4.78 (3.15)	9.46 (8.82)	3.269	**.003***
Physical side effects	7.56 (2.40)	8.20 (3.76)	0.497	.62
Cognitive side effects	1.00 (1.00)	1.20 (1.76)	0.506	.621
Other organ related side effects	0.00 (0.00)	0.18 (0.55)	3.027	**.003***
Symptoms of dependence	1.89 (1.54)	3.30 (2.36)	2.465	**.029***

Data are presented as means (standard deviation). *Significant difference between the groups ($p < .05$). SD = standard deviation. 8 non-hGH users missing in objective cardiovascular side effects.

Table 10 Ranking hGH among top five most used compounds

	hGH users (n=17)	Non-hGH users (n=55)		
	Mean (SD)	Mean (SD)	t	p-value
Self-reported cardiovascular side effects	1.24 (1.03)	1.24 (1.12)	0.003	.997
Objective cardiovascular side effects	1.50 (1.10)	1.46 (1.00)	-0.134	.894
Psychiatric side effects	6.53 (5.33)	9.00 (8.32)	1.151	.254
Physical side effects	7.94 (3.29)	8.55 (3.75)	0.597	.553
Cognitive side effects	1.00 (1.28)	1.15 (1.84)	0.303	.762
Other organ related side effects	0.35 (0.79)	0.04 (0.19)	-1.646	.119
Symptoms of dependence	2.41 (2.43)	3.22 (2.16)	1.308	.195

Data are presented as means (standard deviation). *Significant difference between the groups ($p < .05$). SD = standard deviation. 1 hGH user and 3 non-hGH users missing in objective cardiovascular side effects.

3.7 Other

3.7.1 Winstrol

Winstrol users have significantly more self-reported cardiovascular side effects (mean = 2.90, SD = 1.73), than non-users $t(9.8) = -3.205$, $p = .010$, as well as more cognitive side effects (mean = 3.00, SD = 1.63 vs. M = 0.95, SD = 1.57), $t(89) = -3.873$, $p < .001$.

Table 11 Used Winstrol in current/last cycle

	Winstrol users (n=10)	Non-Winstrol users (n=81)		
	Mean (SD)	Mean (SD)	t	p-value
Self-reported cardiovascular side effects	2.90 (1.73)	1.11 (1.01)	-3.205	**.010***
Objective cardiovascular side effects	2.00 (1.25)	1.42 (0.98)	-1.677	.097
Psychiatric side effects	17.00 (11.60)	8.01 (7.61)	-2.388	.038*
Physical side effects	9.60 (4.14)	7.95 (3.57)	-1.356	.179
Cognitive side effects	3.00 (1.63)	0.95 (1.57)	-3.873	**< .001***
Other organ related side effects	0.40 (0.84)	0.14 (0.47)	-0.972	.354
Symptoms of dependence	4.40 (2.80)	3.01 (2.23)	-1.807	.074

Data are presented as means (standard deviation). *Significant difference between the groups ($p < .05$). SD = standard deviation. 9 non-Winstrol users missing in objective cardiovascular side effects.

Table 12 Ranking Winstrol among top five most used compounds

	Winstrol users (n=23)	Non-Winstrol users (n=49)		
	Mean (SD)	Mean (SD)	t	p-value
Self-reported cardiovascular side effects	1.13 (1.14)	1.29 (1.08)	0.559	.578
Objective cardiovascular side effects	1.50 (0.86)	1.46 (1.07)	-0.167	.868
Psychiatric side effects	9.26 (8.47)	8.02 (7.45)	-0.630	.531
Physical side effects	8.39 (3.94)	8.41 (3.52)	0.018	.986
Cognitive side effects	1.70 (2.10)	0.84 (1.45)	-1.775	.085
Other organ related side effects	0.04 (0.21)	0.14 (0.50)	0.914	.364
Symptoms of dependence	3.00 (2.20)	3.04 (2.27)	0.072	.943

Data are presented as means (standard deviation). *Significant difference between the groups ($p < .05$). SD = standard deviation. 1 Winstrol-user and 3 non-Winstrol users missing in objective cardiovascular side effects.

3.7.2 Dianabol

Users ranking Dianabol among top five most used compounds have significantly more objective cardiovascular side effects (mean = 1.79, SD = 1.02), compared to non-Dianabol users (mean = 1.30 SD = 0.90), $t(66) = -2.000$, $p = .050$.

Table 13 Used Dianabol in current/last cycle

	Dianabol users (n=13)	Non-Dianabol users (n=78)		
	Mean (SD)	Mean (SD)	t	p-value
Self-reported cardiovascular side effects	1.38 (1.39)	1.29 (1.22)	-0.241	.810
Objective cardiovascular side effects	1.38 (0.96)	1.51 (1.05)	0.415	.679
Psychiatric side effects	6.92 (9.21)	9.35 (8.44)	0.947	.346
Physical side effects	7.69 (2.66)	8.21 (3.80)	0.467	.641
Cognitive side effects	1.08 (1.44)	1.19 (1.74)	0.226	.822
Other organ related side effects	0.15 (0.56)	0.17 (0.52)	0.078	.939
Symptoms of dependence	2.85 (1.68)	3.22 (2.42)	0.533	.596

Data are presented as means (standard deviation). *Significant difference between the groups ($p < .05$). SD = standard deviation. 8 non-Dianabol users missing in objective cardiovascular side effects.

Table 14 Ranking Dianabol among top five most used compounds

	Dianabol users (n=26)	Non-Dianabol users (n=59)		
	Mean (SD)	Mean (SD)	t	p-value
Self-reported cardiovascular side effects	1.27 (1.12)	1.22 (1.09)	-0.192	.848
Objective cardiovascular side effects	1.79 (1.02)	1.30 (0.95)	-2.000	**.050***
Psychiatric side effects	9.50 (8.92)	7.80 (7.05)	-0.890	.377
Physical side effects	9.19 (3.11)	7.96 (3.86)	-1.395	.167
Cognitive side effects	1.38 (1.98)	0.96 (1.55)	-1.017	.313
Other organ related side effects	0.12 (0.43)	0.11 (0.43)	-0.063	.950
Symptoms of dependence	3.38 (2.33)	2.83 (2.17)	-1.020	.311

Data are presented as means (standard deviation). *Significant difference between the groups ($p < .05$). SD = standard deviation. 2 Dianabol-users and 2 non-Dianabol users missing in objective cardiovascular side effects.

4 Discussion

The main findings in the present study were the differences in side effects in trenbolone users and oral AAS users compared to other AAS users. Users of trenbolone experienced more psychiatric and physical side effects, as well as more symptoms of dependence, while oral AAS users reported more arrythmia and HT.

In general, there seems to be a discrepancy between self-reported and objective measures of cardiovascular side effects, like in the case of users of oral AAS. This may be due to participants using BP-medication drugs, masking HT in our clinical examinations. It can also represent an actual difference between the two categories. Our clinical test examines LV mass, LVEF and BP, while the self-reported side effects also included arrythmia, which more oral AAS users reported experiencing.

Dependence has been a well-known aspect of AAS use, and according to our results, trenbolone is a good representative for this issue. Like other types of addiction, several factors are probably contributing to dependence in AAS use. One of these have been hypothesized to be an association between AAS and opioids. Opioid addiction is more common in AAS users (6), and some research suggest AAS may increase the sensitivity for drugs like opioids and amphetamines (36, 37). Some research also indicates that AAS have an interaction with σ-1 opioid receptors (12, 38).

Studies using cell-cultures have shown that commonly used AAS can induce apoptosis in different cells, including neurons (39, 40). In a current study, using cell-culture, Zelleroth et

al. 2021 suggests that trenbolone inhibits neuronal viability and that trenbolone, nandrolone and testosterone elicit adverse effects on neurite outgrowth and length (41). Trenbolone's negative effects on neurite development is not suppressed by flutamide (a selective androgen receptor antagonist), suggesting it to have unique neuronal toxicity independent from that caused of the androgen receptor pathway (41). Our results point in the direction that trenbolone users might have a higher degree of psychiatric side effects compared to other AAS users. Trenbolone is a compound many individuals use regularly, as seen in this study. Many users are also aware of many of its adverse effects, and still chooses to implement it in their regime (28). Trenbolone therefore represents one of PEDs possibly biggest problems in a community health perspective; having well-known harmful effects, but individuals still choosing to take it.

Our findings suggests that hGH users are taking roughly the same weekly doses of AAS as non-hGH users, and it therefore seems like users of hGH adds this on top of their AAS regime. Users of hGH also take a larger quantity of different compounds. There are some possible reasons behind this. One explanation might simply be that hGH use is often a part of polypharmacy practice. That users who are comfortable with combining more drugs together, are more likely to include hGH in their program. Another explanation can be that these individuals spread their total dosage of AAS over more compounds, as a thought out strategy. This can for instance be part of a precautious behavior, against side effects from each compound.

Somewhat surprisingly, users taking hGH in their current/last cycle seem to experience less symptoms of dependence and fewer psychiatric symptoms compared to non-hGH users. A limitation in our study sample is the low number of participants using hGH, and the differences in side effects might just be an error because of this. When analyzing users ranking hGH among top five most used compounds, a variable having almost double the number of users (17 vs. 9), these findings are no longer statistically significant. The same goes for side effects in users of Winstrol, where the results are no longer significant when the number of users increases in the "among top five"-category. More research is therefore needed to confirm these findings.

When researching side effects from AAS, polypharmacy is problematic. Users of AAS often include different compounds in one cycle to achieve the desired results. A typical approach to using AAS for recreational bodybuilders have been to utilize substances in cycles, using "on" and "off" intervals. Due to side effects like depression, reduced libido and fatigue in the "off"-

phase, some users will also self-medicate to reverse these side effects – which again will lead to even more substance use. Many AAS users have tried additional substances as well, other than what they use today. The administration of multiple compounds makes it difficult to examine if specific drugs cause specific side effects or if it is a combination of several drugs causing an adverse effect. Especially it is difficult to conclude anything about long term side effects from specific AAS, since many users change their drug regime over time. In the study, there is a dissociation between the number of compounds users report as their typical use and what they report to have used in their current/last cycle. This can represent a tendency among the users underestimate what normally use.

Limitations

Although our data comes from a sample size of 91 AAS users, the number of participants using each compound often does not get sufficiently big enough to estimate the effect of each drug. A compound like trenbolone is common enough to conduct statistical analyzes without difficulty. But for others, like Turinabol®, SARMs, Anavar® and Arimidex®, few users implement them regularly, making it challenging to attain reliable data about side effects.
As always in cross sectional studies the obstacle of causality versus association arises. When looking at our results it is tempting to draw the conclusion that trenbolone causes a higher degree of dependence than other commonly used PEDs. However, in reality we don't know if those taking trenbolone are simply more prone to dependency than other users. Since many of the variables are based on the participants memory of events before and after using AAS, we can't eliminate the possibility of users not remembering correctly. To achieve a better understanding of the causation, a prospective study is needed.

5 Conclusion

The results from this study demonstrates that different types of AAS have different degrees and types of adverse effects. The typical AAS user use around three different compounds at once, one of them usually being a testosterone. Individuals using more compounds in combination typically experiences more psychiatric side effects than those using fewer. Users of trenbolone in general reports more symptoms of dependence, as well as psychiatric and physical side effects. Individuals administrating AAS orally tend to have more cardiovascular side effects, due to a higher prevalence of hypertension and heart arrythmia. hGH, even though technically not a steroid, is a popular drug among AAS users. Users of growth hormones tend to report fewer psychiatric side effects and fewer symptoms of dependence, but more research is needed in order to confirm this finding.

Few other studies have looked at differences in side effects between different types of AAS. But we know from qualitative interviews that adverse psychiatric effects is a shared experience among several trenbolone users. One challenge of researching AAS is the user's tendency to combine several compounds. This makes it more difficult to study a single anabolic steroid as an independent variable. AAS being illegal in many countries is another difficult aspect of the research, and this may inadvertently exclude participants from joining the study, out of fear that family, friends, or the government may discover they are using steroids. Prospective studies would be ideal for further research on this topic, but this is difficult to conduct in the real world.

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