

A LOCAL STUDY ON THE ADVERSE EFFECTS OF ANABOLIC ANDROGENIC STEROID ABUSE ON LIBYAN MALE ATHLETES

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Abstract

Anabolic androgenic steroids (AAS) are man-made derivatives of the male sex hormone testosterone, originally designed for therapeutic uses to provide higher anabolic potency with lower androgenic effects. Increasing numbers of young athletes are using these agents illicitly to enhance physical fitness, appearance, and performance despite their numerous side effects and worldwide banning. Today, their use remains one of the main health problems in sports because of their availability and low price. The present study focused on investigating the adverse effects of anabolic androgenic steroid abuse on serum sex hormones, liver and renal function tests, fasting glucose levels, and lipid metabolism in Libyan male recreational bodybuilders. We have recruited fifteen (15) male bodybuilders (age 19-32 years) and an equal number of healthy non-obese, non-AAS-using sedentary controls. Serum sex hormones {luteinizing hormone (LH), follicle-stimulating hormone (FSH), total testosterone, and prolactin (PRL)}, liver function indices {serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total and direct bilirubin}, renal function parameters (serum creatinine and urea), lipid profile {total cholesterol (TC), triglyceride (TG), low density lipoprotein-cholesterol (LDL-C), very low density lipoprotein-cholesterol (VLDL-C), and high density lipoprotein-cholesterol (HDL-C)}, and serum glucose levels were measured. Abuse of AAS was associated with significant decreases ($p < 0.005$) in serum levels of LH (66.9%), FSH (49.8%), and total

testosterone (63.7%) together with significant increases ($p < 0.05$) in PRL concentrations (49.8%) in AAS-using bodybuilders compared to sedentary controls. AAS-using athletes had significantly higher ($p < 0.05$) circulating levels of total bilirubin (116.3%), direct bilirubin (127.6%), aspartate (1752.9%) and alanine (263.1%) transaminases than those of sedentary control subjects. Serum ALP levels were not significantly different ($p > 0.05$) between the two groups. Concerning renal functions, AAS-using athletes had significantly higher serum concentrations of creatinine (28.6%) and urea (21.3%) than sedentary controls. Meanwhile, AAS abuse was accompanied by atherogenic lipid profile. AAS-using athletes had significantly higher ($p < 0.05$) serum levels of TG (45.6%), LDL-C (26.0%), and VLDL-C (45.6%) together with significantly lower serum concentrations of HDL-C (31.3%) than sedentary controls. Serum TC and fasting glucose concentrations were not significantly different ($p > 0.05$) between the two groups. The results presented in the study confirm that abuse of AAS induces unfavorable body functions and undesirable side effects. Therefore, efforts should be sought against use of these compounds outside the therapeutic frame.

Keyword: anabolic androgenic steroids (AAS), abuse, adverse effects, athletes, bodybuilding, exercise.

1. INTRODUCTION

Self-administration of large doses of anabolic androgenic steroids by athletes to obtain a well-shaped body and to increase muscular strength has been

increasingly noticeable since the 1950s^{1,2}. AAS are widely used by professional and recreational athletes as well as nonathletes³. Abuse of AAS is not limited to male adults but also reported in female adults as well as adolescents of both sexes¹. Every tissue in the body, including the brain, has androgen receptors; therefore, AAS exert systemic as well as psychological effects⁴. AAS have been linked with a wide range of unwanted adverse effects. These effects may range from physically unattractive, such as acne and gynecomastia in males, to serious and life threatening, such as cardiovascular diseases and hepatic carcinoma. Most effects are reversible upon withdrawal^{2,5}. Because of their widespread use, many side effects may turn out to be significant risk factors when considering public health. Increased risk of violent death was reported among AAS abusers from impulsive, aggressive behavior, or depressive symptoms⁶. AAS have been taken in cycles. Traditionally, AAS users combine two or more different drugs, mixing oral and injectable AAS. They begin a cycle with a low dose of AAS and slowly increase the dose and then the dose is tapered to zero³. Doses taken by abusers can be 10-100 times higher than those used for medical purposes. The aim of the present study was to evaluate the changes in serum sex hormones, liver and renal function indices, glucose level and lipid metabolism in Libyan male AAS abusers.

2. MATERIALS AND METHODS

2.1. Participants

Fifteen (15) non-obese male bodybuilders aged 19-32 years (mean 23.27 ± 3.73) were recruited at local gyms in El-beida city from February 2019 to July 2019. Bodybuilders were interviewed concerning their health (current diseases and family diseases), consumption of high protein diet, regular exercise, lifetime steroid abuse, pattern of use, and whether other supplements and drugs being used. Exclusion criteria included smoking, presence of chronic medical conditions (diabetes mellitus, liver or kidney disorders), and the use of growth hormone. Anabolic steroid abusers were selected if they were currently using AAS. Table 1 summarizes AAS used with their doses and duration of use prior to sample withdrawal. All of the participants took androgens in cycles and none was taking AAS in a continuous pattern. Cycles were 4-8 weeks in duration

separated by suspension periods of 4-12 weeks. A control group of healthy sedentary males ($n=15$) with a mean age of 22.1 ± 3.65 years were recruited from the community and historically had not ever used anabolic steroids. Unfortunately, absence of bodybuilding controls was evident because, as was found, persons who continue to exercise regularly use AAS routinely. The two groups of volunteers were comparable with respect to their age and height. However, the study group taking AAS had significantly greater mean weight and body mass index (BMI).

2.2. Sample collection

Subjects' weights and heights were measured using a balance beam and a vertical ruler. Participants were asked to fast for 12 hours and avoid heavy physical exercise before attending for sample collection. One blood sample was collected from each volunteer by venipuncture between 08:00-10:00 AM. A total of 15 ml blood was obtained and placed in EDTA-free tubes to be centrifuged for 5-10 minutes at 3000 rpm. Serum was then divided into several 1.5 ml Eppendorf tubes and stored at (-20°C) until time for the assay.

2.3. Laboratory measurements

Serum concentrations of LH, FSH, PRL, and total testosterone were determined by immunofluorometric assays on a mini VIDAS analyzer^{7,8}. Liver and renal function indices were measured by colorimetric methods using the commercially available kits^{9,10,11,12,13,14,15}. Serum TC, TG, HDL-C, and fasting glucose concentrations were determined by routine autoanalyzer methods^{16,17,18,19}. Serum LDL-C and VLDL-C concentrations were determined through the Friedwald formula².

2.4. Statistical analysis

Data were expressed as mean \pm SD (standard deviation). Unpaired t-test was employed to examine the difference in means of the AAS-using group and sedentary controls. Pearson correlation (r) was used to analyze the relationships between total dose of AAS used prior to sample withdrawal and the hormonal and biochemical changes. A level of p value < 0.05 was considered statistically significant difference.

Table 1: Doses and duration of AAS use for fifteen (15) bodybuilders.

Subject no.	AAS used	Route of administration	Dose (mg/kg)	Duration of prior sampling (wk)	Total dose received (mg)
1	Methandrostenolone	O	175	6	1350
	Nandrolone decanoate	P	50		
2	Methandrostenolone	O	140	4	660
	Nandrolone decanoate	P	25		
3	Methandrostenolone	O	140	4	760
	Nandrolone decanoate	P	50		
4	Methandrostenolone	O	245	4	980
5	Methandrostenolone	O	210	4	840
6	Testodderone proponate	P	50	3	450
	Nandrolone decanoate	P	100		
7	Methenolone	O	20	3	660
	Oxymetholone	O	150		
	Nandrolone decanoate	P	50		
8	Methandrostenolone	O	175	6	1350
	Nandrolone decanoate	P	50		
9	Methandrostenolone	O	140	4	760
	Nandrolone decanoate	P	50		
10	Methandrostenolone	O	175	6	1650
	Nandrolone decanoate	P	100		
11	Methandrostenolone	O	245	4	2780
	Sustanon	P	250		
	Nandrolone decanoate	P	200		
12	Methandrostenolone	O	175	4	1800
	Nandrolone decanoate	P	25		
	Sustanon	P	250		
13	Methandrostenolone	O	175	4	1100
	Nandrolone decanoate	P	100		
14	Methandrostenolone	O	245	6	2670
	Nandrolone decanoate	P	200		
15	Methandrostenolone	O	245	6	2670
	Nandrolone decanoate	P	200		

3.RESULTS

3.1. Serum hormone levels

Serum LH, FSH, and total testosterone levels in AAS-using bodybuilders were significantly lower ($p < 0.005$) than those in the sedentary controls (66.9%, 49.8%, and 63.7% respectively). However, AAS-using bodybuilders had significantly higher ($p < 0.05$) PRL concentrations (49.8%) than sedentary controls (table 2).

Table 2: Effects of AAS on serum sex hormones in AAS-using bodybuilders compared to sedentary controls.

Variable	Sedentary controls, N=15 (mean±SD)	AAS-using BB, N=15 (mean±SD)
LH (mIU/mL)	3.18 ± 0.94	1.04 ± 1.09**
FSH (mIU/mL)	2.97 ± 1.30	1.47 ± 0.87**

Total testosterone (ng/mL)	7.45 ± 1.95	2.74 ± 1.75**
PRL (ng/mL)	14.43 ± 6.19	21.63 ± 8.88*

The P-values refer to the differences from the control group.

*: P<0.05 significant difference between the two groups.

** : P<0.005 highly significant difference between the two groups.

N= no. of subjects.

3.2. Liver function parameters

AAS-using bodybuilders had significantly higher ($p<0.05$) circulating levels of total and direct bilirubin (116.3% and 127.6% respectively) than sedentary controls. AAS-using bodybuilders had significantly higher serum AST (1752.9%, $p<0.005$) and ALT (263.1%, $p<0.05$) activities than sedentary controls (table 3). Serum ALP levels were not significantly different ($p>0.05$) between the two studied groups.

Table 3: Effects of AAS on liver function tests in AAS-using bodybuilders compared to sedentary controls.

Variable	Sedentary controls, N=15 (mean±SD)	AAS-using BB N=15, (mean±SD)
Total bilirubin (mg/dL)	0.49 ± 0.63	1.06 ± 0.74*
Direct bilirubin (mg/dL)	0.29 ± 0.41	0.66 ± 0.47*
ALP (U/L)	80.20 ± 20.26	93.20 ± 37.19 ^{ns}
AST (U/L)	1.21 ± 4.69	22.42 ± 27.02**
ALT (U/L)	4.69 ± 6.52	17.03 ± 17.02*

ns: non-significant ($P>0.05$) difference between the two groups.

3.3. Renal function tests

Table 4 demonstrates that AAS-using bodybuilders had significantly higher circulating levels of creatinine (28.6%) and urea (21.3%) ($p<0.005$ and $p<0.05$, respectively) than sedentary control group.

Table 4: Effects of AAS on renal function tests in AAS-using bodybuilders compared to sedentary controls.

Variable	Sedentary controls, N=15 (mean ± SD)	AAS-using BB, N=15 (mean ± SD)
Serum creatinine (mg/dL)	0.84 ± 0.19	1.08 ± 0.21**
Urea (mg/dL)	38.07 ± 8.58	46.18 ± 14.37*

3.4. Lipid profile and fasting serum glucose

Circulating levels of HDL-C were significantly lower ($p<0.005$) (31.3%) in AAS-abusing bodybuilders than sedentary controls. Table 5 indicates that AAS-using bodybuilders had significantly higher ($p<0.05$) serum levels of TG (45.6%), LDL-C (26.0%), and VLDL-C (45.6%) than sedentary controls. Serum TC and fasting serum glucose (FSG) concentrations were not significantly different ($p>0.05$) between AAS-using bodybuilders and sedentary control subjects.

Table 5: Effects of AAS on lipid profile and serum glucose in AAS-using bodybuilders compared to sedentary controls.

Variable	Sedentary controls, N=15 (mean ± SD)	AAS-using BB N=15 (mean ± SD)
TC (mg/dL)	153.80 ± 21.62	171.20 ± 37.19 ^{ns}
TG (mg/dL)	74.93 ± 42.84	109.13 ± 57.50*
HDL-C (mg/dL)	44.60 ± 7.15	30.67 ± 7.64**
LDL-C (mg/dL)	94.21 ± 21.13	118.71 ± 34.76*
VLDL-C (mg/dL)	14.99 ± 8.57	21.83 ± 11.50*

FSG (mg/dL)	83.20 ± 17.63	89.93 ± 9.16 ^{ns}
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3.5. Adverse effects

Participants were asked questions about unusual adverse effects that would be felt during an AAS cycle and the most common reported side effects were aggression, changes in libido, acne formation, headaches, and premature hair loss as summarized in table 6.

Table 6: Adverse effects reported by AAS-using bodybuilders.

Adverse effects	No. of subjects, N=15	%
Unusual aggression	6	40
Changes in libido	4	26.66
Acne	2	13.33
Headaches	1	6.66
Hair loss	2	13.33

4. DISCUSSION

Subjects of this study used independently AAS mainly to enhance external physique. Besides being an unethical practice, abuse of AAS has been associated with several health risks and various adverse effects which affect almost all organs and systems of the human body. AAS-using bodybuilders had significantly lower ($p < 0.005$) serum levels of LH, FSH, and total testosterone than sedentary controls (table 2). The results were consistent with those reported by Holma et al²¹ who observed reduced serum levels of LH, FSH, and total testosterone in athletics during a course of oral intake of methandrostenolone (15 mg/day).

Exogenously administered AAS exert a negative feedback on the secretion of gonadotrophins, mostly attributed to a direct effect on the hypothalamus to decrease secretion of GnRH. This in turn causes a corresponding decrease in secretion of both LH and FSH and eventually biosynthesis and release of testosterone from the testes²². In addition, AAS may produce local suppressive effects on the testes and on adrenal androgen production²³. Serum PRL levels in AAS-using bodybuilders were significantly higher than those in

sedentary controls ($p < 0.05$) (table 2). Data reported by Stoffel-Wagner et al²⁴ and Leibenluft et al²⁵ were consistent with the interpretation that testosterone and/or its metabolites facilitate the secretion of prolactin. Estrogen is known to stimulate prolactin release from the anterior pituitary²⁶. Non-aromatizable AAS (stanozolol and methandrostenolone) were reported to activate estrogen receptors through interaction of either the parent compound or its metabolites indicating a possible mechanism for increased prolactin secretion²⁷. The available data in the corresponding literature on the influence of exogenously administered androgens on prolactin serum level were found controversial. Serum total and direct bilirubin levels in AAS-using bodybuilders were significantly higher ($p < 0.05$) than those in sedentary controls (table 3). Androgens can selectively interfere with bile excretion by the liver. Canalicular bile plugs were observed after treatment with methyltestosterone, oxymetholone, mestranol, and norethandrolone²⁸. Cases of cholestatic jaundice have been recorded in patients therapeutically using or athletes abusing AAS (especially 17 alpha alkylated agents)^{29,30}. Serum AST and ALT levels in AAS-using bodybuilders were significantly higher ($p < 0.005$ and $p < 0.05$, respectively) than those in sedentary controls (table 3). Canalicular cholestasis is characterized by mild hepatocellular injury and release of transaminases leading to mild elevations in serum levels of these enzymes²⁹. However, since sustained weightlifting alone can result in mild elevations in serum transaminase activities^{31,32}, the increase in serum transaminases may be attributed to mild hepatocellular damage, muscle injury, or both. Urhausen et al³³ reported that serum transaminase levels were significantly higher ($p < 0.001$) in AAS-abusing athletes than bodybuilders who stopped using anabolic steroids for at least a year. A non-significant difference in serum ALP levels was found between the two studied groups ($p > 0.05$) (table 3). These results are consistent with those reported by O'Sullivan et al³⁴ who observed no significant difference in ALP activities between anabolic steroid users and potential or past users. AAS steroids can induce cholestasis without elevating ALP levels. ALP activity is usually less than threefold elevated and often is normal³⁵. AAS-using athletes had significantly higher serum creatinine ($p < 0.005$) and urea ($p < 0.05$) levels than sedentary controls (table 4). Studies in rat models provide evidence

that, compared with females, aging males exhibit decreased glomerular filtration rate and develop glomerular injury, glomerulosclerosis, and proteinuria³⁶. In addition, cases of acute renal failure had been reported in clinical patients or bodybuilders administering anabolic steroids^{29,37}. However, in the present study, we cannot ignore other factors that may have participated in deteriorating renal function parameters in AAS-using athletes e.g. consumption of high protein diet. Serum concentrations of TG, VLDL-C, and LDL-C were significantly higher in AAS-users ($p < 0.05$) than those in controls (table 5). The rise in serum levels was positively correlated with the intake of AAS. Anabolic androgenic steroids can elevate serum levels of TG by 40-50% in bodybuilders and other power-training athletes³⁸. Kiraly³⁹ in 1988 reported similar results while studying the effects of large doses of testosterone and other anabolic androgenic steroids on serum lipids during a 12-week strength-training period. Elevated serum TG ($p < 0.05$) levels were found with decreased serum HDL-C ($p < 0.005$). Serum LDL-C levels were significantly higher ($p < 0.05$) during steroid intake in studies reported by Fröhlich et al⁴⁰ and Palatini et al⁴¹. AAS-users had elevated levels of apolipoprotein B, a component of both LDL and VLDL^{42,43}. Conversely, circulating levels of LDL-C and VLDL-C were not significantly different while using AAS in studies reported by Sader et al⁴⁴ and Singh et al⁴⁵, respectively. A non-significant difference in serum TC levels was found between the two studied groups ($p > 0.05$) (table 5). Our results confirm those reported by many studies^{40,42}. AAS effects on plasma lipids have been reported to be unpredictable and depend on the dose, route of administration, and type of AAS (aromatizable or not)⁴⁶.

Low dosages have been associated with hypolipemic response, while high doses have had opposite effects^{47,48}. Serum HDL-C levels in AAS-using bodybuilders were significantly lower than those in sedentary controls ($p < 0.005$) (table 4). The postulated mechanism to explain anabolic steroid-induced alteration in serum HDL-C levels is an increase in hepatic triglyceride lipase activity, an enzyme responsible for catabolizing HDL with its phospholipase activity.⁴⁹ In addition, apolipoprotein A-1, a major component of HDL particle, was reported to be decreased by AAS^{42,45}. The results obtained in the present study showed absolute consistency with the available data. A

non-significant difference in serum glucose levels was found between the two studied groups ($p > 0.05$) (table 5). The influence of testosterone and anabolic steroids on glucose metabolism was found controversial. Results of the present study agree with those reported by Friedl et al⁵⁰ who observed no alterations in fasting serum glucose in normal men treated with testosterone enanthate or nandrolone decanoate for 6 weeks. On the other hand, Cohen and Hickman⁵¹ concluded that power lifters taking high dose (mean 200mg/day) of anabolic androgenic steroids had diminished glucose tolerance compared to non-steroid using athletes, obese sedentary men, or non-obese sedentary men. Such controversy in the corresponding literature may be explained to be due to differences in doses used. Higher AAS doses reduce insulin sensitivity and impair glucose tolerance⁴⁶. Although AAS doses used by subjects in the present study were considered to be high; they were much smaller than those used by athletes in Cohen and Hickman⁵¹ study. The most common side effects reported by our subjects were unusual aggression (40%), changes in libido (26.66%), acne formation (13.33%), headaches (6.66%), and premature hair loss (13.33%) (table 6). Perry et al⁵² reported that anabolic steroid using weightlifters were more aggressive than nonusers according to different psychiatric scores. Changes in libido appear to be the most common adverse effect reported in a group of present and past AAS users (approximately 61%)³⁴. Reports do indicate that toward the end of AAS cycle, some males may experience loss of libido⁵³. Acne was also found very common side effect among anabolic steroid users as reported by O'Sullivan et al³⁴. Increases in acne formation is related to stimulation of sebaceous glands resulting in a more oily skin³⁴. Premature hair loss does not appear to be very common. It is likely that androgenic alopecia as a result of AAS use is more prevalent in males who are genetically predisposed to balding⁵⁴.

Headaches are also not very common among AAS abusers. O'Sullivan et al³⁴ reported only 9% of AAS using athletes may develop headaches. However, the exact mechanism is unknown.

5.CONCLUSION

In conclusion, anabolic androgenic steroid abuse lowered serum concentrations of pituitary

gonadotrophins, LH and FSH, and testosterone. Increased levels of PRL were also manifested. Abuse of anabolic steroids probably causes cholestasis, however, with mildly elevated liver enzymes. In addition, effect of AAS on renal function indices was not well established indicating that other factors, such as high protein diet, may have contributed in elevation of blood urea and creatinine levels. Finally, lipid profile was impaired toward evidenced dyslipidemia.

6.CONFLICTS OF INTEREST

We hereby declare that there are no conflicts of interest regarding the publication of this research study.

7.ACKNOWLEDGMENT

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8.ETHICS

All participants provided written permission and consent before collecting data to conduct this research study.

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