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ANDROGENIC STEROID EFFECTS ON LIVER AND RED CELLS

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ABSTRACT

Haematological and hepatic effects of testosterone/anabolic steroid self-administration were investigated in five power athletes during 26 weeks of training.

During steroid administration blood haematocrit had increased 9.6% ($p < .05$) in the study group ($n = 5$), but not in the control group ($n = 6$). This erythropoietic phenomenon was supported by increased ($p < .05$) RBC and unchanged MCV. Blood haemoglobin concentration did not change markedly and consequently MCHC level in the study group decreased significantly ($p < .001$). Also the erythrocyte sedimentation rate decreased ($p < .05$) in the study group.

The mean values of serum alanine aminotransferase, alkaline phosphatase and gamma-glutamyltransferase were and remained within normal range in both groups, although those of the study group were higher. The mean values of serum aspartate aminotransferase exceeded the normal range (56 U/l, at highest) but this may be of muscular rather than hepatic origin because of the severe training. It can be concluded that erythropoiesis was stimulated and liver function mildly impaired due to sustained high-dose testosterone/anabolic steroid administration.

Key words: Testosterone, Anabolic steroids, Strength training, Liver function, Red cell count, Doping.

INTRODUCTION

The attempts to document objectively the effects and side-effects of anabolic steroids have produced seemingly conflicting results (see e.g. Ryan, 1981; Lamb, 1984). As regards to haematological and hepatic phenomena, clinical studies have shown an increase in erythropoiesis (Gurney, 1976; Palacios et al, 1983) because of the administration of anabolic steroids, whereas most hepatological studies suggest that changes in serum transaminase, total bilirubin and alkaline phosphatase values during the use of androgens are both minor and infrequent (see e.g. Nishino, 1975). Hepatic lesions (peliosis and tumours) are, however, reported in patients treated with synthetic anabolic steroids (Turani et al, 1983; Overly et al, 1984). For other possible effects of such steroids on adult males the recent extensive review of Wilson and Griffin (1980) should be consulted.

Because it is not legal in Finland to get a physician's prescription for any drug to be used only for improving the performance of a healthy person, testosterone and/or anabolic steroids used as ergogenic aids are obviously obtained mainly from the black market. A recent trend in the use of these compounds seems to be the incorporation of testosterone among the anabolic steroids administered (Hill et al, 1983; Strauss et al, 1983). The simultaneous use of very high doses and several androgenic compounds leads to metabolic (Alén et al, 1985) and endocrine changes (Schürmeyer et al, 1984), and it can also be expected to result in haematological and hepatic changes.

The purpose of the present investigation was to study the

effects of sustained high-dose use of testosterone and anabolic steroids in association with strength training on red blood cell values and liver function indicators.

METHODS

In the pilot study 40 male power athletes answered a questionnaire in which their habits of taking testosterone and anabolic steroids, and their future plans in training and hormone use were enquired. Altogether 15 of these men volunteered as subjects. Written informed consent was obtained from them all for the present study. The Ethical Committee of Kuopio University approved the study protocol.

Four subjects selected for the study were excluded because of profound change in the training programme and/or refusal to participate in all the tests performed.

The control group consisted of 6 athletes (3 powerlifters and 3 bodybuilders), who had decided not to take any steroid drugs during the next nine months of training and follow-up period. Two of them had earlier taken androgenic steroid (methandienone) for a few weeks but not during the 12 weeks preceding this study.

The study group comprised 5 athletes (3 bodybuilders, 1 powerlifter and 1 wrestler). They had not taken androgenic hormones during the 8-12 weeks preceding the study. All men in this group were experienced in the use of androgenic steroids. They had decided to self-administer testosterone and anabolic steroids in a similar way to what they were previously used to during the following six months in combination with heavy resistance strength training. The self-administration of the androgenic steroids was followed by medication diaries and random urine analyses with gas chromatography-mass spectrometry using the Varian MAT 212 instrument. On every occasion in every subject the random urine analyses were positive for the hormones listed in the personal drug diaries. Only one in this group took alcohol in small quantities, the others abstained.

The characteristics of the subjects studied are given in Table 1, and Figure 1 summarises the time schedule of the study.

During the first 26 weeks of training (Phase I) the study group self-administered anabolic steroids and testosterone (Fig. 2, Fig. 3 a-e). Methandienone (17 α -methyl-17 β -hydroxy-1, 4-androstadien-3-one) was taken daily with slightly increasing doses. The intramuscularly self-injected nandrolone (17 β -hydroxy-4-estren-3-one phenylpropionate) and stanozolol (17 α -methyl-5 α -androstano[3, 2-c]-pyrazol-17 β -ol) were

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TABLE I

Age, training background and anthropometric characteristics of the groups studied before and after 26 weeks of training. The values indicate mean $\pm$ SEM. The intergroup values for significance levels are also given.

Variable	Study group (n = 5)	Control group (n = 6)	t-test
Age (yr)	27.0 $\pm$ 2.5	25.7 $\pm$ 2.1	N.S.
Strength training (yr)	7.4 $\pm$ 2.6	5.1 $\pm$ 0.8	N.S.
Height (cm)	177.8 $\pm$ 1.5	173.1 $\pm$ 1.9	N.S.
Weight (kg)			
Before	86.8 $\pm$ 5.1	82.8 $\pm$ 2.5	N.S.
After	92.0 $\pm$ 4.1	82.2 $\pm$ 2.5	p < 0.05
Fat free weight (kg)			
Before	72.8 $\pm$ 3.4	70.2 $\pm$ 2.2	N.S.
After	80.6 $\pm$ 3.3	69.8 $\pm$ 2.2	p < 0.05
Body fat (%)			
Before	15.6 $\pm$ 2.9	15.3 $\pm$ 2.2	N.S.
After	12.1 $\pm$ 2.1	14.4 $\pm$ 2.2	N.S.

Fig. 1: Design of the investigation.

used usually weekly but the frequency of injections increased progressively, whereas the doses injected (both 50 mg per injection) remained the same. Testosterone (17 β -hydroxy-4-androsten-3-one) was self-administered (250 mg/injection, consisting of testosterone-propionate (30 mg) -phenyl-propionate (60 mg), -isocaproate (60 mg) and -undecanoate (100 mg)) initially twice a month but at the end of the study 4 times/month.

The study and the control groups had an intensive strength training programme during the investigation. Personal training diaries were filled in daily after each training session for subsequent control. Both groups trained for special purposes in their power event, and it included heavy resistance strength training, but no aerobic training for an average of six times per week. Because the subjects were highly motivated power athletes at top national level and had trained for competitive purposes for an average of 6.2 years, the exercises were only supervised randomly.

Random one week diet recalls, filled in daily, were completed three times by the subjects for the calculation of caloric intake and composition of the diet. The mean daily caloric intake in the study group was reported to be 15,400 kJ (3,700 Kcal) and in the control group 14,700 kJ (3,500 Kcal) and protein intake 2.3 and 2.6 g $\times$ kg⁻¹, respectively. This appears rather low for those athletes in heavy events involving strength training, but not for bodybuilders who avoided an increase in body fat.

After one day reduced training and overnight fast the subjects entered the laboratory at 8.00 a.m. for medical examinations and blood sampling. The height, weight, subscapular, triceps, biceps and crista iliaca skinfold thicknesses of the subjects were measured. The amount of body fat was estimated (see Table I) according to Durnin and Rahaman (1967). The blood pressure was measured after ten minutes rest in the sitting position from the right upper arm with the sphygmomanometer.

Venous blood samples were drawn from the antecubital vein. Blood haemoglobin concentration (Hb) (analysed by the cyanomethaemoglobin method), haematocrit (PVC) (determined by microcentrifugation) and erythrocyte sedimentation rate (ESR) were analysed from EDTA blood, and calculation of mean corpuscular haemoglobin concentration (MCHC) was also performed. The activities of serum aspartate amino-

Fig. 2: Meal daily doses ($\pm$ SEM) of self-administered testosterone and anabolic steroids (mg) in the study group.

transferase (ASAT), alanine aminotransferase (ALAT), gamma-glutamyl-transferase (γ -GT), alkaline phosphatase (AFOS) and total bilirubin concentration (TBIL) were analysed from serum samples stored at -80°C . The reagents of Boehringer Mannheim GmbH were used. These procedures were performed at 0, 8, 14, 20, 26, 32, 38 and 42 weeks of training.

The following blood values were measured only before and after Phase I: Red blood cell (RBC), platelet and leucocyte counting were carried out by Coulter Counter autoanalyser. Also the mean corpuscular volume (MCV) was calculated.

Statistical methods. Means and standard errors were calculated. Differences between the mean values of the subject groups and between intragroup values were tested for significance by the two-tailed Student's t-test.

RESULTS

The mean values of Hb, PCV, MCHC and ESR are shown in Figure 4 a-d and those of ASAT, ALAT, AFOS and γ -GT in Figure 5 a-d. Significant differences were not noticed between the study and control groups at the beginning of the investigation.

In blood Hb concentrations in the study group there was an initial decrease at 8 and 14 weeks (Fig. 4a), which then returned to pretreatment levels at 20 and 26 weeks. In general Hb values tend to be higher in the study group than in the control group.

PCV values had an increasing tendency in the study group throughout the period of testosterone/anabolic steroid administration (Fig. 4b) and the volume reached at 26 weeks (51%) was significantly ($p < .05$) higher than at the beginning of the investigation (46%). Drug withdrawal led to a slow decrease in PCV and reached the pretreatment level at 38 weeks. Blood PCV was very stable in the control group.

MCHC values decreased significantly ($p < .001$) in the study group during the first 14 weeks of steroid administration (Fig. 4c). Following

Fig. 3: Individual daily doses of testosterone and anabolic steroids (mg/kg). The values indicate means for the periods between the blood tests.

drug withdrawal MCHC returned relatively slowly to the onset level. There were some fluctuations in MCHC values in the control group but no clear-cut trends.

The values of blood ESR had a decreasing tendency in the study group during the androgenic steroid administration (Fig. 4d) and returned to the pretreatment level at 38 weeks. No systematic changes were observed in blood ESR in the control group.

The mean values of RBC, MCV, platelet and leucocyte count are given in Table II. Significant differences between the groups were not noticed before Phase I.

The mean value of RBC during Phase I increased significantly ($p < 0.05$) in the study group, but did not change in the control group. Consequently the difference between the groups in RBC mean values was significant ($p < 0.001$) at 26 weeks.

No marked changes were noticed in MCV values in both group during Phase I.

An increase in mean platelet count was observed in the study group but not in the control group. The difference between the groups was significant ($p < 0.05$) at 26 weeks.

Also the mean value of leucocyte count increased ($p < 0.05$) in the study group by 26 weeks, while no change was observable in the control group.

MCH mean values also presented in Table II demonstrate difference ($p < 0.05$) between the groups at the end of Phase I.

The pattern of serum ASAT activities increased significantly ($p < .05$) during the first 14 weeks of drug administration and remained at this higher level at 20 and 26 weeks (Fig. 5a). After drug withdrawal the values returned to the onset level in 12 weeks.

The activities of serum ALAT and AFOS were at higher level in the study group than in the control group. However, their mean values remained within the normal range in both groups during the investigation (Figs. 5b and 5c).

Fig. 4: The values of (a) blood haemoglobin (Hb), (b) hematocrit (PCV), (c) mean corpuscular haemoglobin concentration (MCHC), and (d) erythrocyte sedimentation rate (ESR) in the study group (closed circles, lines) and in the control group (open circles, broken lines). Mean values, standard errors of means and statistical significance of the intra- and intergroup differences are given (* $p < .05$, ** $p < .01$, *** $p < .001$). The study group self-administered testosterone and anabolic steroids during the time indicated (weeks 0-26).

TABLE II

Platelet, leucocyte and erythrocyte (RBC) counts and mean corpuscular volume (MCV) in the groups studied before and after Phase I. The values indicate mean $\pm$ SEM. The intergroup values for significance levels are also given.

Variable	Study group (n = 5)	Control group (n = 6)	t-test
Platelets ($\times 10^9/l$)			
Before	316 $\pm$ 33	281 $\pm$ 23	N.S.
After	357 $\pm$ 39	244 $\pm$ 17	$p < 0.05$
Leucocytes ($\times 10^9/l$)			
Before	6.3 $\pm$ 0.3	6.4 $\pm$ 0.7	N.S.
After	7.4 $\pm$ 0.4	6.1 $\pm$ 0.5	$p < 0.05$
RBC ($\times 10^{12}/l$)			
Before	5.3 $\pm$ 0.2	5.1 $\pm$ 0.2	N.S.
After	5.8 $\pm$ 0.3	5.2 $\pm$ 0.1	$p < 0.001$
MCV (fl)			
Before	88.8 $\pm$ 2.2	89.6 $\pm$ 0.6	N.S.
After	84.7 $\pm$ 2.5	89.8 $\pm$ 0.7	N.S.
MCH (pg)			
Before	30.5 $\pm$ 0.9	30.6 $\pm$ 0.3	N.S.
After	28.1 $\pm$ 1.0	30.5 $\pm$ 0.3	$p < 0.05$

In serum γ -GT activities in the study group there was an initial significant ($p < .05$) decrease at 14 weeks, which also remained at this lower level during the use of steroids. The return to pretreatment level took 12 weeks (Fig. 5d).

The activities of serum ASAT, ALAT, AFOS and γ -GT in the control group were relatively stable during the investigation.

There were no systematic changes from the initial concentrations of serum total bilirubin in the study and control groups (10.7 and 10.5 $\mu\text{mol/l}$, respectively).

The values of blood pressure were initially at normal level ($\times 125/85$ mmHg) and no systematic changes were observed in any of the subjects studied.

DISCUSSION

The mean daily doses and the duration of administration of testosterone and anabolic steroids taken by athletes exceeded substantially those recommended for medical purposes and those administered in experimental conditions (Wilson and Griffin, 1980; Wright, 1980). Furthermore, a tendency to increase mean daily doses of exogenous androgens was observed and this was obviously due to decreased secretion of endogenous androgens (see e.g. Caminos-Torres et al, 1977; Schürmeyer et al, 1984). However, subject No. 5, who was less experienced in the use of testosterone and/or anabolic steroids took 25 mg/day without any progression in doses or self-administration frequency. His dose was only 38% of the total mean doses (65 ± 20 mg/day) used by the four other athletes. Because of the main competition (of that year) subject No. 1 took androgens in progressive doses only until 14 weeks.

a

b

c

d

Fig. 5: Activities of serum (a) aspartate aminotransferase (ASAT), (b) alanine aminotransferase (ALAT), (c) alkaline phosphatase (AFOS), and (d) gamma-glutamyltransferase (γ -GT) in the study group (closed circles) and in the control group (open circles). For other details see Fig. 4.

As expected this sustained high-dose use of testosterone and several anabolic steroids led to effects on haematological system and liver. There was a gradual increase in blood PCV in the study group to values not seen due to "pure" strength training. The mean of increase (in percentage) of PCV during Phase I was significantly higher in the study group as compared to that in the control group (9.6 ± 1.6 vs. 1.1 ± 1.7 ; $p < .01$). When the results of subject No. 5 were excluded from the analyses the difference between the groups in PCV mean values came out even more clearly. This erythropoietic phenomenon was supported by increased RBC and unchanged MCV values at the 26 week measurement. That was expected, since androgens and especially their 5β -metabolites stimulate erythropoiesis (see e.g. Necheles and Rai, 1969; Palacios et al, 1983).

As a consequence of elevated PCV and relatively stable Hb value the MCHC values decreased during the drug administration. The mean decrease (in percentage) of MCHC was also steeper ($p < .01$) in the study group (8.8 ± 1.8) than in the control group (1.4 ± 0.8). In association with the increase in PCV ESR mean values decreased in the study group.

As regards the liver it seems that 8 weeks was too short a time for recovery after drug withdrawal because serum ALAT was already in the beginning of the investigation at a higher level in the study group than in the control group. This higher

level of serum ALAT remained relatively stable during the use of drugs but decreased statistically significantly ($p < .05$) within 12-16 weeks to the level of those controls after drug withdrawal. However, it is remarkable that the mean values in the study group were also within normal range although subject No. 5 was excluded. The function of the liver was obviously only slightly impaired because the activities of γ -GT in serum also remain within the normal range without any tendency to elevate. This finding was supported by the normal values of serum AFOS and TBIL.

The increase in serum ASAT levels in the study group may be of muscular rather than hepatic origin, since the athletes underwent severe and intensive strength training during the self-treatment (Tiidus and Ianuzzo, 1983).

The stable level of serum ASAT in the control group is difficult to explain. Strength training was severe and intensive, since significant increases of 12.9% ($p < .01$) in the control group and 18.2% ($p < .001$) in the study group took place in the maximal squat lift (Alén et al, 1984). It is suggested that training under the influence of exogenous androgens exposes the athletes to leaking of aspartate aminotransferase from muscles to serum.

There also were some changes in the other blood and serum parameters measured in the control athletes. Because no clear-

cut trend in those changes was observed they might have been random fluctuations within the normal range.

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BOOK REVIEW

Title: AN ATLAS OF THE KNEE
Authors: M. Jacob and P. Segal (Translated from French)
Publisher: Wolfe Medical Publications, London, 1984
Price: £15

I am not certain if this book has suffered from translation, or whether the original French version was equally complicated in its text layout. There is no index, but in its place, a list of abbreviations used throughout the book and their meanings. Every structure is given a leading letter abbreviation on first encounter and thereafter the abbreviation is used as the terminology, which at times leaves one swimming with a head full of letters and the inability to put the anatomy to them. The illustrations are simple and excellent, but again are ruined by the way in which structures are identified with abbreviations.

This is not the book for the uninitiated wishing to know more about knees, but it should have a place on the library of every knee surgeon as it does represent one school of thought in French literature. The book was designed by a team of doctors at the Rheims University Hospital Centre, with the main editors being Philippe Segal who studied with Albert Trillat at Lyon, and Marcel Jacob who is Physician to the French Soccer Federation.

The sections on rotary instability, both acute and chronic, are well worth going through carefully. If I have one further criticism it relates to the attitude taken in the book towards arthroscopy which seems to be far way behind the thinking in the rest of the world and is written off in a quarter of a page of text, less than that taken up by reference to the use of CAT scans in acute knee trauma.

J. Robertson

BOOK REVIEW

Title: 1984 YEAR BOOK OF RADIOLOGY
Editors: Bragg, Keats, Keffer et al
Publishers: Year Book Publications per Blackwells, Oxford
Price: £37.00

The Year Book of Radiology is an excellent digest of papers with reference to Radiology, taken from many journals. It is divided into sections; neuro-radiology, cardiac and interventional, thoracic, abdominal, paediatric radiology and radiation physics.

Only a small section of the book is of interest to those in sports medicine and orthopaedics. For instance, in this addition stress related fractures in the forearm are described in athletes and weight-lifters. There is a series describing stress fractures in the tarsal navicular which confirms the fact that we must look carefully at patients complaining of pain and also emphasises the use of radioisotopic bone scan as a screening procedure. There is a useful review of osteo-chondromatosis in athletes.

Although other papers are of use to radiologists and other clinicians, they are of little interest to readers of this journal. This is a book that belongs on the library shelves in which everyone should be prepared to read the parts related to their own interests and speciality.

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