



Aortopathic effect of androgenic anabolic steroids

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Abstract

Background Anabolic androgens have been reported to be associated with cardiovascular complications. One study revealed that increase in vascular stiffness in bodybuilders is associated with anabolic androgens and improvement in vascular function may occur following anabolic androgens discontinuation. The aim of this study was to investigate any possible relation between aortic elastic properties and anabolic androgens.

Methods Study population was divided into 3 groups: Group-1 [$n=35$] consisted of bodybuilders who denied any current or previous use of anabolic androgens. Group-2 [$n=18$] was bodybuilders with regular using of anabolic androgens for at least 2 year prior to the start of our study. Group-3 was 13 healthy age-matched sedentary men as a control group. Cardiac echocardiography was performed in the bodybuilders and controls and indexes of aortic function were calculated.

Results Aortic stiffness was approximately twofold higher in anabolic androgens user bodybuilders compared with drug-free bodybuilders [$P<0.001$].

Conclusion The present study demonstrates that chronic anabolic androgens use clearly produces significant decrease in the elastic properties of aorta.

Keywords Anabolic androgens · Aortic stiffness · Bodybuilding

Background

Anabolic androgenic steroids [AAS] have been demonstrated to be associated with cardiovascular problems including myocardial infarction, cerebrovascular events, pulmonary embolism, cardiomyopathy, malignant arrhythmias, sudden cardiac death, and left ventricular hypertrophy [1, 2, 3, 4, 5, 6, 7, 8, 9, 10]. Previous reports described an increase in vascular stiffness in bodybuilders which was independent of AAS use [which may result from smooth muscle hypertrophy] but one study revealed that vascular stiffening is related to AAS and vascular function improvement occurs following

AAS discontinuation [11]. In an animal study, treatment with AAS has resulted in impairment of both endothelium-dependent and endothelium-independent dilatation of aortic rings [12]. The aim of this study was to investigate any possible relation between aortic elastic properties and AAS.

Methods

Study population

Fifty-three consecutive professional bodybuilders referred to the sport centers were enrolled in this study. Individuals were excluded from the study if they were Marfan syndrome, smokers or known to suffer from ischemic heart disease, diabetes mellitus, or hypertension. Study population was divided into three groups: Group-1 [$n=35$] consisted of bodybuilders who denied any current or previous use of AAS. Group-2 [$n=18$] was bodybuilders with regular using of AAS [on a cycle of Oxymetholone 25 mg/day] for at least 2 years prior to the start of our study. Group-3 was 13 healthy age-matched sedentary men as a control group.

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All subjects completed a medical questionnaire and provided written informed consent before enrolment to the study. Pulse pressure was obtained by non-invasive cuff sphygmomanometry of the left brachial artery as systolic blood pressure minus diastolic blood pressure.

Echocardiographic measurement

Cardiac echocardiography was performed in the bodybuilders and controls. Measurements of left ventricular (LV) dimensions were obtained from both M-mode and two-dimensional echocardiography. The LV measurements were performed at end-diastole and end-systole according to the recommendations of the American Society of Echocardiography [13]. Only frames with optimal visualization of interventricular septum, posterior wall, and LV internal diameter throughout the entire cardiac cycle were used for measurements. The LV mass was calculated using the Devereux formula [14].

Thoracic aortic diameter (mm/m²) was measured 3 cm above the aortic valve by two-dimensional guided M-mode transthoracic echocardiography of the aortic root at left parasternal long-axis view by the leading-edge technique. Aortic systolic diameter (AoS) was measured at the time of full opening of the aortic valve (mid-systole), and diastolic diameter (AoD) at the peak of the QRS complex at the simultaneous electrocardiogram recording. Diameter measurements were perpendicular to the long-axis of the aorta. The following indexes of aortic function were calculated [15, 16, 17, 18].

→ Aortic strain = (AoS – AoD)/AoD,

→ Aortic root distensibility = $2 \times (\text{AoS} - \text{AoD}) / (\text{AoD} \times \text{PP})$,

→ Aortic stiffness index = $\ln(\text{systolic BP} / \text{diastolic BP}) / [(\text{AoS} - \text{AoD}) / \text{AoD}]$.

The recordings were performed twice by two independent observer. Analysis of variance showed that interobserver and intraobserver variability for indexes of aortic function was 5.9–6.3%, respectively.

Statistical analysis

SPSS for Windows, version 16 was used. Values were expressed as means \pm SD. Statistical comparisons between groups were made using one-way ANOVA. Where the F ratio was significant, further comparisons were made using Tukey HSD multiple comparisons. A difference was considered significant when $P < 0.05$.

Results

Baseline characteristics

Baseline group characteristics are demonstrated in Table 1. No differences were observed in age and pulse pressure among sedentary men and drug free and drug using bodybuilders. Bodybuilders had greater body surface area than sedentary men.

Standard echocardiographic findings

The standard echocardiographic data are listed in Table 2. No differences were found in LV morphologic parameters (i.e., LV internal diameter, LV wall thickness, and LV mass) between drug-free bodybuilders and AAS user bodybuilders. In contrast, bodybuilders (drug free and AAS users) exhibited greater LV mass index than normal controls.

Results of aortic elastic properties

Echocardiographic data of aortic elastic properties are listed in Table 3. In the control group, distensibility of the aorta was significantly higher than drug free and AAS user bodybuilders [$P < 0.001$]. Interestingly, aortic stiffness was approximately twofold higher in AAS user bodybuilders compared with drug free bodybuilders [$P < 0.001$].

Table 1 Baseline Characteristics of the 3 Groups

	Group-1 [AAS free bodybuilders] (n = 35)	Group-2 [AAS user bodybuilders] (n = 18)	Group-3 [control] (n = 13)	P value		
				Group 1 versus 2	Group 1 versus 3	Group 2 versus 3
Age (years)	27 \pm 5.7	25 \pm 7.6	26 \pm 3.2	0.76	0.83	0.39
Body surface area (m ²)	1.94 \pm 0.14	1.95 \pm 0.14	1.81 \pm 0.14	0.99	0.019	0.030
Systolic blood pressure (mmHg)	138 \pm 11.8	136 \pm 12.2	129 \pm 13.6	0.11	0.16	0.15
Diastolic blood pressure (mmHg)	82.1 \pm 7.3	84.4 \pm 8.6	82.1 \pm 11.7	0.18	0.22	0.20
Pulse pressure (mmHg)	45 \pm 9.12	46.11 \pm 7.18	43.84 \pm 7.67	0.99	0.99	0.93

Table 2 Echocardiographic data of the 3 groups

	Group-1 [AAS free bodybuilders] (n = 35)	Group-2 [AAS user bodybuilders] (n = 18)	Group-3 [control] (n = 13)	P value		
				Group 1 versus 2	Group 1 versus 3	Group 2 versus 3
Septal wall thickness (mm)	9.3 ± 1.7	9.7 ± 1.2	9.1 ± 1.7	0.952	0.511	0.166
Relative wall thickness (mm)	0.41 ± 0.05	0.42 ± 0.06	0.38 ± 0.03	0.95	0.51	0.16
Ejection fraction (%)	58.68 ± 3.77	57.05 ± 4.03	59.30 ± 3.09	0.72	0.99	0.493
LV end-systolic volume (ml)	43.12 ± 7.62	50.44 ± 10.81	42.69 ± 8.32	0.155	1.00	0.156
LV end-diastolic volume (ml)	104.11 ± 13.70	116.44 ± 23.05	107.46 ± 18.61	0.394	1.00	0.352
LV mass index (g/m ²)	95.68 ± 13.11	98.66 ± 18.19	71.30 ± 10.54	0.982	0.001	< 0.001
Left atrial diameter (mm)	34.3 ± 3.1	34.4 ± 3.6	33.5 ± 4.2	0.27	0.80	0.40

LV left ventricular, LV mass index LV mass/body surface area

Table 3 Echocardiographic Data of Aortic Elastic Properties of the 3 Groups

	Group-1 [AAS free bodybuilders] (n = 35)	Group-2 [AAS user bodybuilders] (n = 18)	Group-3 [control] (n = 13)	P value		
				Group 1 versus 2	Group 1 versus 3	Group 2 versus 3
Systolic aortic diameter (cm)	2.82 ± 0.16	2.79 ± 0.19	2.79 ± 0.31	0.99	0.99	1.00
Diastolic aortic diameter (cm)	2.59 ± 0.16	2.64 ± 0.21	2.43 ± 0.29	0.98	0.457	0.193
Aortic strain (%)	9.06 ± 2.26	5.50 ± 2.09	15.15 ± 2.91	0.007	< 0.001	< 0.001
Aortic distensibility (cm ² × dyn ⁻¹ × 10 ⁻⁶)	3.36 ± 1.00	2.01 ± 1.04	5.80 ± 1.81	0.040	< 0.001	< 0.001
Aortic stiffness	18.24 ± 4.12	35.43 ± 11.86	11.37 ± 2.59	< 0.001	0.095	< 0.001

Discussion

Androgenic anabolic steroids and cardiovascular system

Previous reports demonstrated premature cardiovascular complications associated with AAS [1, 2, 3, 4, 5, 6, 7, 8, 9, 10]. Thrombo-embolic disease, cerebrovascular events, myocardial infarction, pulmonary embolism, cardiomyopathy, malignant ventricular arrhythmias, and ventricular hypertrophy have been demonstrated in AAS abusers [1, 2, 3, 4, 5, 6, 7, 8, 9, 10]. AAS have been reported to lower HDL levels significantly and pro-atherogenic effect of AAS may be related to decrease in levels of HDL [19, 20].

Effects of androgenic anabolic steroids on vasoreactivity

Androgens showed various effects on arterial reactivity. Supra-physiologic androgen use by genetic females was associated with impaired vascular reactivity [21]. Also, androgen deprivation was associated with increased vascular reactivity in patients with cancer of prostate [22]. On the other hand, acute administration of androgen resulted in vascular dilatation through ATP-sensitive potassium channels [23, 24, 25]. One study reported an improvement in microvascular function after AAS withdrawal in one of seven AAS users [26].

Aortopathic effect of androgenic anabolic steroids

The present study demonstrates that AAS abuse produces significant increase in aortic stiffness. Four possible mechanisms may contribute to aortic stiffness in chronic AAS users:

1. AAS decreases elastic and increases fibrous proteins in arterial vascular tissue [20].
2. In an experimental animal model, treatment of rabbits with anabolic steroid has resulted in impairment of endothelium-dependent and endothelium-independent dilation in aortic rings [12].
3. In human studies, high dose androgen use was associated with impaired vascular reactivity.
4. AAS reduce nitric oxide mediated vasorelaxation in thoracic aorta by inhibition of guanylate cyclase [12].

Aortic elastic properties are an important component of left ventricular afterload and aortic stiffening with AAS use burdens the left ventricular performance. Thus, it is conceivable that in AAS abusers, left ventricle is forced to perform under conditions of increased stress with a resultant increase in oxygen demand.

We postulate that chronic use of AAS causes increased aortic stiffness in the beginning. If AAS abuse continues for a prolonged duration, it may lead to increase in LV size and LV hypertrophy because of increased force against LV ejection. In our study, AAS abusers had more aortic stiffness, but in comparison between two groups echocardiographic parameters of LV were similar. We believe that if AAS is used for an extended period, it might cause in more LV thickening compared to athletes not using AAS, as previous animal studies showed that prolong exposure to aortic stiffness is needed to modify cardiac structures [27].

Study limitation

In the present study, arterial blood pressure was obtained by non-invasive cuff sphygmomanometry as a non-invasive method of estimating central pressure. Central arterial pressure, measured close to the heart, may be of more patho-physiological importance than conventional non-invasive cuff blood pressure. Unfortunately, catheter measurement of central pressure is a highly invasive procedure and is not applicable in our study population.

Conclusion

The present study revealed that chronic AAS use produces significant decrease in the elastic properties of aorta.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interest.

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