Anabolic steroid use in male bodybuilders - implications upon cardio-metabolic health.

By Dr Ian G. Davies
Overview

• Cardiometabolic/Cardiovascular disease
• Lipids and lipoproteins
• The effect of anabolic androgenic steroids (AAS) on lipoproteins
• Putative mechanism of AAS
• The old and the new: enter lipoprotein-omics
• Aims and objectives of proposed study
• Methods
• Expected results
• Summary
Distribution of computed tomography coronary angiography measures in anabolic-androgenic long-term steroid users and nonusers.

N = 86 users, 54 non-users

Associated with long-term use

Cardiometabolic Health/Disease

Risk factors:
Age, gender, smoking, LDL-cholesterol, blood pressure

Metabolic syndrome:
Hyperglycaemia, hyperinsulinaemia, atherogenic dyslipidaemia, T2d

Drugs e.g. AAS

Cardiometabolic Disease

ASCVD


Show more

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Lipid markers of cardiometabolic health

<table>
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<tr>
<th>Traditional lipid profile</th>
<th>Athergoenic dyslipidaemia</th>
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<tr>
<td>Elevated total cholesterol</td>
<td>Elevated triglycerides</td>
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<tr>
<td>Elevated low density lipoprotein cholesterol (LDL-C)</td>
<td>Low high density lipoprotein cholesterol (HDL-C)</td>
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<tr>
<td>Low high density lipoprotein cholesterol (HDL-C)</td>
<td>Elevated <strong>small, dense LDL</strong></td>
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<tr>
<td>Elevated triglycerides</td>
<td><strong>LDL particle number</strong></td>
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Lipoproteins and AAS

- LDL-cholesterol 20%
- HDL-cholesterol 20-70%

3 – 6 fold increase in CVD risk

Achar et al., 2010; Gårevik et al., 2011
The role of LDL and HDL in atherosclerosis

- LDL oxidation & inflammation in atherogenesis
- The role of LDL and HDL in atherosclerosis

- HDL inhibits LDL oxidation
- HDL inhibits cytokine expression
- HDL promotes cholesterol efflux
- HDL inhibits adhesion molecule expression

- Monocyte
- Adhesion molecules
- Cytokines
- Macrophage
- LDL
- Oxidised LDL
- Foam cell
- Vessel lumen
- Endothelium
- Intima
Lipoprotein structure and main function

VLDL
- Transports triglycerides to adipose/muscle

LDL
- Transports cholesterol to peripheral tissue and lesions

HDL
- Transports cholesterol away from lesions to liver

Key:
- Apo A-1
- ApoB 100
Hepatic lipase: a putative mechanism

Baldo-Enzi et al, 1990
LDL, not one size fits all.
Small, dense LDL – small but deadly!

LDL particle decreasing in size, increasing in density, atherogenicity and number while losing cholesterol.

But does this not lower LDL-C?
LDL particle number can increase

Individual with LDL-C of 2.6 mmol/L

Individual with LDL-C of 2.6 mmol/L
Evidence from in vitro studies suggests that large, buoyant LDL particles are more resistant to oxidative stress and small, dense LDL particles more susceptible to oxidation.
Atherogenic dyslipidaemia

- Abdominal obesity
- Insulin resistance
- Elevated plasma triglyceride
- Low HDL-C
- Small, dense LDL
- Mild hypertension
- Increased risk of CHD

Insulin sensitivity in relation to fat distribution and plasma adipocytokines among abusers of anabolic androgenic steroids.

Rasmussen T1,2, Schou M2,4, Selmer C1, Johansen NC1,2, Gustafsson F2,4, Frydendal K6,8, Dela FX1,2, Faber J1,2, Kistorp C1,2.

Abstract

OBJECTIVE: Abuse of anabolic androgenic steroids (AAS) is prevalent among young men, but information regarding effects on insulin sensitivity and fat distribution is limited. The objective was to investigate insulin sensitivity in relation to fat distribution and adipocytokines among current and former AAS abusers compared with controls.

DESIGN: Cross-sectional study among men involved in recreational strength training. Current and former AAS abusers (n=37 and n=33) and controls (n=30) volunteered from the community.

METHODS: We assessed insulin sensitivity by Matsuda Index (oral glucose tolerance test). Using overnight fasting blood samples, adiponectin and leptin were measured. Body composition and fat distribution, including visceral adipose tissue (VAT), were assessed by dual energy X-ray absorptiometry.

RESULTS: Current and former AAS abusers displayed lower Matsuda index than controls (%-difference (95%CI) from controls, -26% (--45, -1) and -39% (--55, -18)). Testosterone was markedly higher among current AAS abusers and subnormal among former AAS abusers compared with controls. Current AAS abusers displayed higher mean VAT than controls (388 (17) vs 293 (12) cm², P < 0.01) whereas body fat %, adiponectin and leptin concentrations were lower. In contrast, former AAS abusers showed highest leptin concentrations and body fat %.

Multivariate linear regressions identified VAT as independent predictor of lower Matsuda index among current AAS abusers compared with controls; while body fat % independently predicted lower Matsuda index among former AAS abusers.

CONCLUSIONS: Both current and former AAS abusers displayed lower insulin sensitivity which could be mediated by higher VAT and total body fat %, respectively.

Keywords: adipocytokines; androgens; glucose intolerance; insulin resistance; inter-abdominal fat

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Does AAS increase sdLDL?
Lipoprotein-omics: small molecules, big questions!

Traditional approach

- Phospholipid monolayer
- ApoB-100
- Triacylglycerols
- Free (unesterified) cholesterol
- Cholesteryl esters

Contemporary approach

- Phospholipid monolayer
- ApoB-100
- Triacylglycerols
- Cholesteryl esters
- Free (unesterified) cholesterol

Small, polar molecules – largely unknown
Research questions number 2 & 3

What are these small molecules?

Are they different in AAS?
Aims and objectives

Aims: To use a ‘lipoprotein-omic’ approach to investigate small polar molecules associated with LDL subclasses in AAS use.

Hypothesis: AAS use will induce small, dense LDL and alter the small molecules covalently attached.

We will test these hypotheses by performing a proof of concept study consisting of the following objectives:-

• 1. Prepare LDL subclasses from AAS & non-AAS Bodybuilders
• 2. Detect small polar molecule species contained in LDL subclasses
Sample

10 AAS-users (in cycle)

Vs. 10 non-users
Methods: Lipoprotein fractionation

Blood → Plasma

2000g
20 min

LDL I
CE
TG

LDL II
CE
TG

LDL III
CE
TG

Davies et al., 2003
Methods

- Anthropometric (body composition) measurements
- 24 hour dietary recall survey
- Food frequency questionnaire
- Physical activity training log
- Steroid use interview (validated)
Expected results?

- Identification of small, polar molecules
- Involved in various biochemical pathways
- Enhance our knowledge of CM risk in AAS use
Summary

• Increased LDL-C and decreased HDL-C commonly observed in AAS use
• No evidence on LDL size
• No evidence on small, surface molecules
• Reveal new biomarkers associated with CM risk mechanisms
• Provide evidence for larger study
• Influence future interventions
• Provide HCP with information for patient care
References


