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Evolution of serum lipids in two male bodybuilders using anabolic steroids

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We followed weekly the evolution of serum lipid concentrations in two bodybuilders undergoing a cycle of treatment with anabolic steroids. These drugs caused maximum depression of high-density lipoprotein cholesterol concentrations by 69.1% in the fifth week after the beginning of the cycle for subject 1, and by 72.4% in the fourth week for subject 2. Maximum increases in low-density lipoprotein cholesterol concentrations were 144% and 156%, respectively. Total cholesterol and apolipoprotein (apo) B were highly increased with anabolic steroid use. We also saw depression of apo A-I by 84% and 91%, and lipoprotein(a) decreased to undetectable amounts in both cases. These effects were reversed 10 weeks after the end of the steroid cycle in subject 1, but subject 2 still presented abnormal concentrations of serum lipids 13 weeks after drug cessation. The periods until reversibility of anabolic steroid effects on lipids were longer than those reported in previous studies.

INDEXING TERMS: cholesterol • lipoproteins • apolipoproteins • risk factors • testosterone

The first study about the effects of anabolic steroids (AS) on plasma lipid values, done in 1980 *[1]*, showed that oxandrolone reduced high-density lipoprotein cholesterol (HDL-C) concentrations in hyperlipidemic subjects.[1] In 1982, Taggart et al. presented the first study involving normolipidemic subjects *[2]*. The postulated mechanism to explain AS-induced changes in HDL-C concentrations is an increase in hepatic triglyceride lipase activities *[3]*. This enzyme, localized to the luminal surface of hepatic endothelium, catabolizes HDL with its phospholipase activity. 17α-Alkylated AS produce a bigger depression of HDL-C than do 17β-esterified AS or testosterone esters, but it still is not clear whether the route of administration influences this effect *[4]*. Increases of low-density lipoprotein cholesterol (LDL-C) attributable to AS are thought to be caused by increased VLDL catabolism and decreased activity of lecithin–cholesterol acyltransferase *[5]*.

We monitored two nonprofessional bodybuilders to investigate alterations in their serum lipid concentrations during AS use. On the basis of a single HDL-C determination we had made in subject 2 a year before the beginning of this study, we had reason to think that the time until reversibility of AS effects on serum lipids could be longer than previously reported.

Materials and Methods

SUBJECTS

Subject 1, a 25-year-old man, underwent four anabolic cycles in the 2 years preceding this study, the last one ending 9 months earlier. Subject 2, a 29-year-old man, had undergone ~18–20 anabolic cycles in the previous 8 years, the last one ending 5 months before the beginning of this study. Both subjects were nonsmokers and did not consume any alcohol. They presented with normal liver, kidney, and hematologic function. During our study, subjects 1 and 2 followed AS cycles of 7 and 8 weeks, respectively. We informed them of all the risks they were taking by using these drugs. As reported in a written protocol by both subjects, the drugs they used were:

week 1—stanozolol 50 mg on Monday, methenolone enanthate 100 mg on Wednesday, and methandrostenolone (orally) 5 mg daily

week 2—stanozolol 50 mg on Monday; testosterone propionate (30 mg), phenylpropionate (60 mg), isocaprionate (60 mg), and decanoate (100 mg) on Wednesday; methenolone enanthate 100 mg on Friday; and methandrostenolone (orally) 10 mg daily

week 3—same as week 2 but with stanozolol 100 mg on Monday

week 4—stanozolol 100 mg on Monday, nandrolone decanoate 50 mg on Tuesday, testosterone esters (same as in weeks 2 and 3) on Thursday, and methandrostenolone (orally) 10 mg daily

weeks 5, 6, and 7—stanozolol 100 mg on Monday; nandrolone decanoate 50 mg on Tuesday and Thursday; testosterone propionate (60 mg), phenylpropionate (120 mg), isocaproate (120 mg), and decanoate (200 mg) on Wednesday;

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[1] Nonstandard abbreviations: AS, anabolic steroids; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; apo, apolipoprotein; and Lp(a), lipoprotein(a).

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methenolone enanthate 100 mg on Friday; and methandrostenolone (orally) 15 mg daily

week 8 (subject 2 only)—same as week 4.

Serum samples from the subjects were analyzed weekly on Wednesday; the cycles began on Monday. Fasting time before analysis was between 8 and 9 h; longer fasting times were not possible because of the feeding schedules of these bodybuilders. Subjects 1 and 2 were monitored from 1 week before the beginning of the cycle until 10 and 15 weeks, respectively, after its end. Diets, unchanged throughout the study, were high in protein, ~300 g/day, and low in fat, ~60 g/day (~5000 kcal/day for subject 1 and 6500 kcal/day for subject 2). Subject 2 began another steroid cycle on week 14 after the end of his preceding cycle, though he was strongly advised not to do so.

PROCEDURES

Serum aliquots (1 mL) from each subject were processed as indicated by Bachorik *[6]*. For sequential ultracentrifugation of lipoprotein *[7, 8]* to separate lipoproteins VLDL, LDL, and HDL, we used a Beckman 50.3 Ti fixed-angle rotor (Beckman Instruments, Palo Alto, CA). Cholesterol, apolipoprotein (apo) A-I, apo B, and triglycerides in every fraction and in total serum were analyzed with a Hitachi 747 and Boehringer Mannheim reagents (all from Boehringer Mannheim, Mannheim, Germany).

Lipoprotein(a) [Lp(a)] was measured in duplicate with an ELISA, TintElize® (Biopool, Umea, Sweden). Phospholipids were analyzed with the kit Phospholipides enzymatiques PAP 150 (bioMèrieux, Marcy L'Etoile, France).

This study was approved by the Ethical Committee of our Hospital.

Results

Figure 1 shows the evolution of total cholesterol, HDL-C, and LDL-C concentrations in subjects 1 and 2. In both cases, maximum concentrations of total cholesterol [7.31 mmol/L (2825 mg/L) and 6.81 mmol/L (2631 mg/L), respectively] and LDL-C [6.30 mmol/L (2436 mg/L) and 6.03 mmol/L (2330 mg/L)] were reached in week 5. In subject 1, the minimum HDL-C concentration [0.36 mmol/L (140 mg/L)] was reached in week 4, but was similar to that of week 5 [0.37 mmol/L (143 mg/L)]. The concentration of apo A in the HDL fraction, however, was lowest in week 5: 65 mg/L, compared with 110 mg/L in week 4 and 117 mg/L in week 6. In subject 2, the lowest HDL-C concentration was seen in week 5, 0.34 mmol/L (134 mg/L), along with the lowest value of apo A-I in the HDL fraction (81 mg/L).

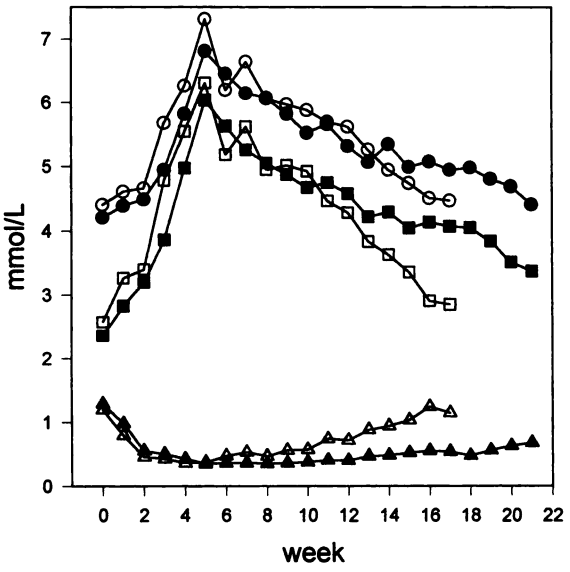

Fig. 1. Evolution of total cholesterol (*circles*), LDL-C (*squares*), and HDL-C (*triangles*) in subject 1 (*open symbols*) and subject 2 (*solid symbols*).

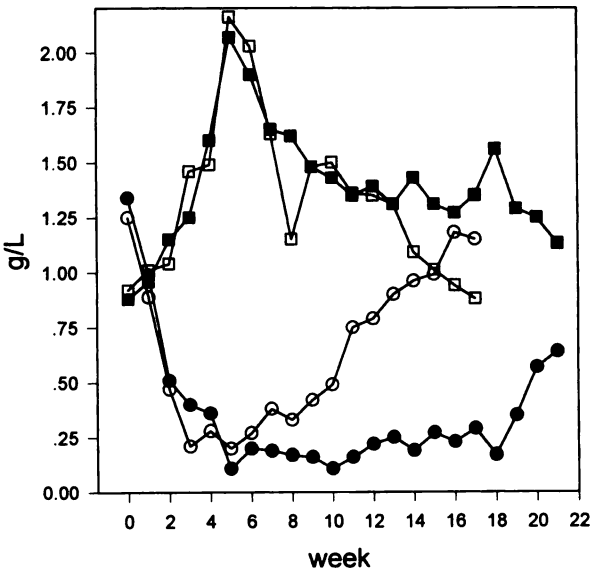

Fig. 2. Evolution of apo B (*squares*) and apo A-I (*circles*) in subject 1 (*open symbols*) and subject 2 (*solid symbols*).

The evolution of apo A-I and apo B concentrations is shown in Fig. 2. In both subjects, the greatest concentrations of apo B (2.16 and 2.07 g/L) and the least concentrations of apo A-I (0.2 and 0.11 g/L) were reached in week 5. Total triglycerides and phospholipids increased with steroid use, but did not correlate well with the other analytes measured (not shown).

Concentrations of Lp(a) before the anabolic cycle were 40 mg/L for subject 1 and 61 mg/L for subject 2. In subject 1, the Lp(a) evolution was: 32 mg/L in week 1, 5 mg/L in week 2, and 8 mg/L in week 3; in week 4, Lp(a) concentrations became undetectable, not increasing to 6 mg/L until week 13 (6 weeks after the end of AS use) and eventually reaching 82 mg/L in week 17. In subject 2, the Lp(a) evolution was: 46 mg/L in week 1, 21 mg/L in week 2, undetectable between weeks 3 and 16, 7 mg/L in week 17 (9 weeks after the end of the AS cycle), 16 mg/L in week 18, 12 mg/L in week 19, 15 mg/L in week 20, and 12 mg/L in week 21.

Discussion

These drugs, AS, are the ones that cause the most severe alterations in lipid profiles *[9]*. Decreases of HDL-C because of AS use ranged from 39% to 70% in 15 studies *[3]*—which, as Glazer points out, is a narrow range, taking into consideration the variations in drug schedules and variability in lipid measure-

ments. Our two subjects, who showed maximum decreases of 69% and 72%, are in the upper part of this range. We did not measure HDL subfractions but, according to the literature *[2, 10–16]*, AS cause mainly HDL_2-C depression. It is not clear whether there is a dose relationship between AS and the decrease of HDL-C *[3]*.

The maximum increases of LDL-C in our two cases, 144% and 156%, are far greater than the ones described previously. Only two studies *[12, 15]* of subjects with high total AS dose regiments presented LDL-C increases close to ours; in one *[12]*, although the mean increase was 61%, one of their figures showed four subjects whose LDL-C values were comparable with those in our study. In four studies with low AS doses, their weighted average increase in LDL-C was 20% (range, 11–29%) *[3]*. These facts suggest that a dose relationship between AS and LDL-C concentrations may be possible, but no study has seriously addressed this question.

In five previous studies, the apo A-I decreased between 33% and 41% *[3]*, whereas our two cases showed maximum decreases of 84% and 91%. The difference in HDL-C decrease between these studies and ours was similar but smaller. Only two studies have reported changes in apo B, one noting a 35% increase *[10]* and the other a 24% decrease *[17]*. In the former, although the mean increase is very far from our maximum increases (134% and 156%), the SD for the apo B measurements is considerable, and probably the results for some of their cases are closer to ours.

Lp(a) decreases associated with stanozolol *[17]* and danazol *[5]* have been previously described. The mechanism for this decrease is unknown. Carlson et al. *[18]* reported that nicotinic acid produces a decrease in Lp(a) that is strongly correlated with a reduction in LDL-C. Obviously, this parallel course does not happen with AS, which suggests the action of different mechanisms in the metabolic control of these lipoproteins.

The main goal of our work was to investigate the time to normalization of HDL-C concentrations after an AS cycle. Data in previous studies reported that HDL-C concentrations fell near the minimum value in the first week after the beginning of AS use and returned to pretreatment values 3 to 5 weeks after stopping the drug use *[3]*. Our two cases suggest, at least for subjects taking high AS doses, a much longer time for reversibility of AS effects on serum lipids. Glazer and Suchman also suggested this in a recent study but showed no data *[4]*. Although subject 1 returned to pretreatment concentrations of lipids 10 weeks after the end of AS use, subject 2 was very far from his pretreatment values 13 weeks after the end of drug cessation; however, subject 2 had been an AS user for 6 years more than subject 1. It would be interesting to investigate whether prolonged AS use has any residual effect on the capacity to reverse the lipid alterations induced by these drugs. After the end of the AS cycle, subject 2 needed 3 more weeks than subject 1 to recover measurable Lp(a) concentrations; we do not know whether this slower regaining is associated with a slower recovery of HDL-C in other persons using AS.

One point that remains unclear is why the HDL-C decrease and LDL-C increase were greatest in our cases at about week 5 of the cycle, when the highest AS doses are just beginning.

Evaluating the contribution of AS use to coronary heart disease risk is very complicated *[3]* but must be considered very seriously. Most AS users, unfortunately, are not aware of this potential risk. If the time to recover pretreatment concentrations of serum lipids is longer than previously thought, this might imply a greater AS-associated risk of coronary heart disease.

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