The effects of supplementation with 19-nor-4-androstene-3,17-dione
and 19-nor-4-androstene-3,17-diol on body composition and athletic
performance in previously weight-trained male athletes

Abstract The purpose of this study was to determine the
effects of 8 weeks of nonsteroid supplementation on
body composition and athletic performance in previous-
ly weight-trained males. Subjects were weight and
percent body fat matched and randomly assigned to
receive either 100 mg of 19-nor-4-androstene-3,17-dione
(N-dione) and 56 mg of 19-nor-4-androstene-3,17-diol
(N-diol; 156 mg total nonsteroid per day), or a placebo
(a multivitamin). Each subject participated in resistance
training 4 days/week for the duration of the study. Body
composition was assessed via dual-energy X-ray ab-
sorptiometry. Circumference measures were taken of a
relaxed and flexed arm (maximum circumference of the
arm), waist (level of umbilicus), and thigh (15 cm
proximal to the patella). Strength was determined with a
one-repetition maximum bench press, while force
and power were determined with a dumbbell bench press
(60% body weight) on a Stratec Galileo force platform.
Profile of mood states scores were evaluated for vigor
and fatigue. There were no significant changes in any of
the parameters measured. In conclusion, low-dose sup-
plementation with N-dione and N-diol does not appear
to alter body composition, exercise performance, or
mood states.

Keywords Steroid · Nonsteroid · Androgen ·
Exercise · Weight-lifting

Introduction

Athletes have been using androgens to enhance athletic
performance and increase skeletal muscle mass since
1954 (Cowart 1987). Since then, the use of androgens
and anabolic substances in competitive sports has be-
come illegal. However, androstenedione and androsten-
diol have been recently introduced to the supplement
market as so-called “legal” over-the-counter
androgens in the United States. In addition, two an-
drogens, 19-norandrostenedione and 19-norandrostene-
diol, are also supposedly available over-the-counter, in
spite of the International Olympic Committee’s (IOC)
medical commission, sports regulation, and state legis-
lation in Europe and elsewhere. It has been speculated
that all of these so-called “legal” androgens and sup-
posedly over-the-counter supplements work in a manner
similar to nortestosterone (NT) and anabolic steroids
(Wilson 1988).

Both androstenedione and androstenediol are pre-
ursors of testosterone (T; Hedge et al. 1987). Athletes
ingest these particular supplements in the belief that
their conversion into T will increase anabolic processes
and help build up skeletal muscle mass. A study by
Earnest et al. (2000) examined the acute effects of oral
treatment with 200 mg of 4-androstene-3,17-dione, 4-
androstene-3 beta,17 beta-diol, and placebo (PL) on
peripheral plasma T concentration. They found that
both androstenedione and androstenediol significantly
increased the T concentration when compared to a
placebo.

However, androstenedione can also convert directly
to estrone, especially in women (Gompel et al. 1986),
whereas T is also converted to estradiol. In a study by
Rasmussen et al. (2000), plasma T concentrations did
not significantly increase, and luteinizing hormone was
not significantly repressed after the ingestion of 100 mg
of androstenedione daily for 5 days. Nonetheless, the
concentrations of estradiol did significantly increase
from 0.12 (0.02) to 0.17 (0.02) mM after oral adminis-
tration of androstenedione when compared to pre-treatment [0.10 (0.01) nmol/l]. Neither estrone nor estradiol have anabolic effects on skeletal muscle.

Since androstenedione and androstenediol have readily been available, few studies have addressed the chronic effects of the supplementation of these steroids on body composition and exercise performance in humans (Antonio and Sanders 1999; King et al. 1999; Van Gammersen et al. 2000; Wallace et al. 1999; Ziegenfuss and Kerrigan 1999). Of these studies, only Ziegenfuss and Kerrigan (1999) showed improvements in body composition and athletic performance.

Norandrostenedione and norandrostenediol are similar to androstenedione and androstenediol, respectively. However, in norandrostenedione and norandrostenediol, the angular 19th carbon of androstenedione and androstenediol is removed, respectively. This modification will supposedly enhance the anabolic properties of norandrostenedione and norandrostenediol without a conversion to T. One might speculate that norandrostenedione and norandrostenediol confer an anabolic effect in skeletal muscle via direct activation of the androgen receptor (AR), since nandrolone and norsteroids are similarly metabolized. Furthermore, it is clear that nandrolone and several of its derivatives bind to the AR (Bergink et al. 1985; Toth and Zakar 1982), and that the superiority of nandrolone to T with regard to myotrophic activity is related to the lack of 5-alpha-reductase activity in skeletal muscle (Toth and Zakar 1982). Therefore, the purpose of this study was to determine whether ingesting a supplement that contains low levels of norandrostenedione and norandrostenediol could affect body composition, athletic performance, and mood states in young, resistance-trained males.

Methods

Subjects

Sixteen healthy men with at least 1 year of resistance-training experience (self-reported) were recruited from the university population via posted advertisements. In order to participate in the study, subjects had to meet the following criteria: (1) 19–35 years of age, (2) not currently taking any type of androgens (legal or illegal), and (3) already performing resistance training at least 3 day/week for the last year. Informed consent was obtained from each subject, and the university’s Institutional Review Board approved the experimental procedures. In appreciation of completing the study, subjects were compensated with dietary supplements (whey protein powder) worth approximately 100 U.S. dollars.

Experimental procedure

Subjects were matched for body mass and percent body fat. They were then randomly assigned to a so-called legal norsteroid [19-nor-4-androstene-3,17-dione [N-dione] and 19-nor-4-androstene-3,17-diol [N-diol]] or placebo (multivitamin manufactured by Schiff group. The placebo contained all of the fat- and water-soluble vitamins (the total dose was equal to the recommended dietary allowance in the USA). Each subject was instructed to swallow two capsules of the above-mentioned norsteroids daily for 8 weeks. The consumption of these pills was verified by the investigators through personal interview with the subjects. The concentrations of N-dione and N-diol were examined by an independent laboratory (San Rafael Chemical Services, Salt Lake City, Utah, USA) using high-pressure liquid chromatography. Specifically, for N-dione and N-diol, a weighed portion of the contents of a composite capsule was dissolved/extracted in 1:1:1 acetonitrile:methanol:water. The extracts were filtered and then analyzed under the following instrument conditions. High-pressure liquid chromatograph (Hewlett Packard Model 1090 II/L); column 1: Luna 15 × 0.46 cm × 3 μm C8 detector: photodiode array, scanning from 190 to 600 nm, quantitation at 210 nm for N-diol, and 245 nm for N-dione. Data from this independent laboratory showed that there was 28 mg and 50 mg of 19-norandrostenedione and 19-norandrostenediol per capsule, respectively. Thus, in the present study, the total dose consumed daily was 156 mg (i.e., 100 mg of N-dione and 56 mg of N-diol).

All subjects were instructed not to change their dietary habits. Twenty-four-hour dietary recalls were obtained from all subjects before and after intervention. Energy, protein, carbohydrate, and fat intake were determined via computer analysis (Nutribase ’98, Phoenix, Ariz., USA). All subjects were also instructed to continue their current resistance-training program for the duration of the study. Subjects provided a training log of a typical week of training. Therefore, the only change that was imposed on each subject was the regular ingestion of the norsteroids or placebo. Neither group was provided with any other dietary supplements during the treatment period.

Testing

After approximately three warm-up sets, subjects were instructed to perform a one-repetition maximum (1-RM) on the supine free-weight bench press. Measures of peak force and power were also obtained by having the subjects perform a supine dumbbell bench press with 60% of their pre-test body weight at a maximum velocity on a Stratec Galileo force platform. The force platform is a plate with transducers that are capable of measuring force and power. The force platform is interfaced with a computer that gives readouts of peak force and peak power. The subjects were given three attempts, and the mean of the three attempts was recorded. During both the 1-RM and force/power tests, subjects had their feet planted on the floor, and hips and scapula on the bench at all times; a slight lumbar lordosis was allowed.

Body composition was assessed via whole-body, dual-energy X-ray absorptiometry (DEXA; Lunar DPX-IQ, Madison, Wisc., USA) using the adult, medium-resolution mode (software 4.6b). The subjects lay on the DEXA machine in a supine position with the palms of their hands on the lateral aspect of their thighs. The subject’s lower extremities were placed in a comfortable position within the parameters of the DEXA machine. Each scan lasted approximately 25 min. A single pre-test and post-test scan was performed with the subjects in a fasted state, prior to performance testing. The use of DEXA as a method for estimating body composition has been validated previously (Haaibo et al. 1991; Pirtle et al. 1991).

In addition, the coefficient of variation for fat mass and lean body mass (LBM) has been estimated to be in the range of 1.8–6.4% and 0.6–3.1%, respectively (Chilibock et al. 1994; Prior et al. 1991; Pritchard et al. 1993). Unpublished data from our laboratory has shown DEXA measures to have a coefficient of variation of 1.49% and 1.00% for fat mass and bone-free LBM, respectively. To ensure quality control, the DEXA unit was calibrated daily using a bone reference and standard provided by the manufacturer. In addition, relaxed and flexed-arm circumferences were taken at the maximum girth of the arm. A waist circumference was taken horizontally at the level of the umbilicus, and a relaxed thigh circumference was taken 15 cm proximal to the superior border of the patella.

Finally, subjects completed a profile of mood states (POMS) questionnaire for vigor and fatigue before and after supplementa-