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Antiandrogens in Hormonal Contraception Limit Muscle Strength Gain in Strength Training: Comparison Study

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Aim. To determine antiandrogen effects on muscle strength gain and fat-free mass increase during exercise in women using hormonal contraception with antiandrogen content.

Methods. The study included 50 women (age range, 18-30 years; mean ± SD, 26 ± 3) using hormonal contraception for at least 12 months before the beginning of the study. They were divided into two groups: "antiandrogen" group (n = 26) and "estrogen-progestogen" group (n = 24) groups. The subjects participated in strength training sessions 3 times a week during 16 weeks. Initially, there were no differences between the groups in fat-free mass, muscle strength, or maximum oxygen uptake. The parameters were measured before, during, and after the training period.

Results. After the training period, the mean increase of fat-free mass was significantly greater in the estrogen-progestogen group ($p < 0.001$). The mean gain in the muscle strength (in Newtons) was also more evident in estrogen-progestogen group (1289.0 17.1 N vs 101.9 18.5 N; $p < 0.001$). There were no differences in the maximum oxygen consumption (VO_2max).

Conclusion. Antiandrogens had a negative effect on muscle strength, minimizing the effects of strength training in women. Hormonal contraception containing antiandrogens should be avoided in young exercising women.

Key words: *androgen antagonists; body composition; contraception; exercise; physical fitness; skinfold thickness; women*

Androgens exert their anabolic effects through protein synthesis, and increase muscle mass in men (1-4). Experimentally induced androgen deficiency is associated with a loss of fat-free mass. In contrast, physiological testosterone replacement in healthy, androgen-deficient men increases the fat-free mass and muscle protein synthesis (5).

Data on the effect of the androgens on women are scarce (6). An acute bout of exercise can stimulate the endocrine system and increase testosterone and dehydroepiandrosterone levels in premenopausal women (7). The study of Douchi et al (8) confirmed that increased testosterone concentration influenced regional bone mineral density through increased regional muscle mass in women with polycystic ovary syndrome. The free testosterone concentration is related to leg lean mass (9).

Common indication for the use of antiandrogens in women is hirsutisam, the condition caused by the increased level of testosterone in women (10,11). The main symptoms of hirsutism (excess hair, acne, and greasy skin and hair) could be significantly minimized and treated by antiandrogens. Antiandrogen cyproterone-acetate is usually combined with estrogens in a pill, to increase its effectiveness and serve as a contraceptive (12).

According to the pilot survey we conducted in Croatia before the beginning of this study, 20% of women aged 18-30 years and using hormonal contraception used antiandrogen-containing pill. The main reason for such a widespread use of antiandrogen pill, sometimes without the prior consultation with a gynecologist, is the concern about excess hairiness, greasiness of the skin, and acne.

Strength training increases the serum concentration of androgens and protein synthesis (13), presumably affecting the gain in the muscle mass. Thus, the parallel use of antiandrogens could inhibit the gain in muscle mass. According to Hakkinen et al (14,15), the lack of androgen increase after the strength training session in older women could result in limited strength increase. Similarly, the suppression of increase in androgen concentration caused by antiandrogens in younger women could also limit the benefits of strength training. Therefore, the use of antiandrogens during strength training process could elicit desirable effects of training in competing athletes. The aim of the study was to determine the possible in-

fluence of antiandrogens on muscle strength gain and changes in fat-free mass during the strength training sessions.

Subjects and Methods

The sample was composed of 60 young women, mostly students or young employees, aged 18-30 years (mean ± SD age, 26 3 years), who were using hormonal contraception for at least 12 months before the beginning of the study. The women were recruited from the new members of a fitness center. Those who consented to participate in the study were asked to fill out a short questionnaire on their current health status and the contraception methods they used. The survey was carried out by a physician. The women using the two types of hormonal contraception were asked to participate in the study and offered free membership during the study as a reward for participation. All of the selected subjects gave their informed consent. The subjects had not been included in any kind of organized sports-recreational activity for at least 2 years before the study. The sample was divided into two groups. The "antiandrogen" group (n = 29) used contraceptive pills containing antiandrogens and estrogens (2 mg of cyproterone acetate and 0.035 mg of estradiol; Diane 35, Schering AG, Berlin, Germany, 1999). The control, or "estrogen-progestogen", group (n = 31) used standard estrogens-progestogen pill (Stedirilm, KRKA Pharmaceuticals, Novo Mesto, Slovenia, 1999). The progestogen in a standard pill was levonogestrel (0.15 mg). According to the pre-study questionnaire, none of the antiandrogen subjects were ever diagnosed with hirsutism or policystic ovary syndrome. The main reason for antiandrogen use in those subjects was their subjective perception of excessive hairiness and greasiness of the skin. There were no significant differences between the antiandrogen and the estrogen-progestogen group in mean age (26 3 vs 26 4 years, respectively; t = -0.122; p = 0.908) or initial muscle strength (240.4 27.9 vs 239.3 36.5 Newton, respectively; t = 1.314; p = 0.821) before the beginning of the study.

The subjects participated in strength training 3 times a week over a 16-week period. The strength training sessions were designed by a physical educator specialized in physical training of athletes. Strength training sessions consisted of 5 obligatory exercises for leg muscles and the rest of the training was composed of optional exercises according to the subject's preferences (leg exercise excluded). The aerobic component of the training included a warm-up phase on cycle ergometer (15 min. at 65% of maximum heart rate). Strength training sessions were of high intensity because the expected acute response of testosterone during the high-intensity protocol is greater than during the moderate-intensity protocol (16). The measurements were made before the training period, after 8 weeks, and after the training period (16 weeks).

Measurements

Muscle strength of the quadriceps muscles was measured by isometric dynamometry according to Štuka and Heimer's protocol (17). Fat-free mass was determined by bioimpedance method (Biodynamics Body Analyzer, 1998, Biodynamics Corporation, Seattle, USA) and controlled by skinfold thickness method. The Biodynamics Body Analyzer calculated the percentage of body water, which was a good indicator of adequate hydration. Adequate hydration of the body is a precondition for bioimpedance method application (18). The measurements were performed always at 6 p.m.

Cardiopulmonary fitness was determined by Astrand test on a cycle-ergometer, to evaluate maximum oxygen uptake (VO_2 max), representing the aerobic abilities of the subjects.

Statistics

Data obtained by repeated measurements were performed by ANOVA. Significance of differences in muscle strength between the antiandrogen and the estrogen-progestogen group at each time point was determined by t-test for independent samples. The differences were calculated as delta values, i.e. the mean increase in muscle strength.

Results

Only the subjects who completed at least 36 sessions were analyzed, which left 26 subjects in the antiandrogen group and 24 subjects in the estrogen-progestogen group (Fig. 1). The mean increase in fat-free mass was 1.4 0.2 kg in the antiandrogen group and 1.6 0.3 kg in the estrogen-progestogen group ($p < 0.001$). The muscle strength increased significantly ($p < 0.001$) during the training period in both groups (Table 1).

The estrogen-progestogen group showed greater increase in muscle strength than the antiandrogen group after the completed strength training period

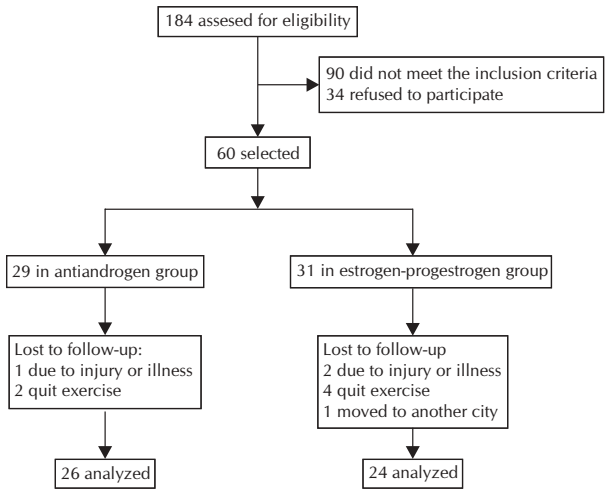

Figure 1. Flow chart of the study.

Table 1. Changes in muscular strength before training, after 8 weeks, and after the training period (16 weeks) in women taking antiandrogens (n = 26) and estrogen-progestogen (n = 24)

	Muscle strength (Newtons, mean ± SD)			
Contraceptive	before training	8th week	after training	F*
Antiandrogen	240.43 ± 27.91	319.56 ± 29.48	342.29 ± 31.57	2167.46
Estrogen-progestogen	239.33 ± 36.53	325.67 ± 36.51	368.32 ± 39.97	1048.04

*ANOVA analysis, $p < 0.001$.

Table 2. Gain in muscle strength and maximum oxigen uptake (VO_2max) in women taking antiandrogen (n = 26) and estrogen-progestogen (n = 24), before training, after 8 weeks, and after the training period (16 weeks)

	Gain in muscle strength (Newtons, mean ± SD)		Gain in VO_2max in (mL/kg/min, mean ± SD)
Contraceptive	before training	8 weeks	after training
Antiandrogen	77.23 ± 12.24	101.86 ± 18.54	3.13 ± 0.76
Estrogen-progestogen	82.41 ± 14.32*	128.99 ± 17.06*	2.91 ± 0.66

*$p < 0.0073$, t-test for independent samples.

(Table 2). There was no significant difference in maximum oxygen uptake gain between the groups (Table 2).

Discussion

Our study found significant differences in muscle strength gain during and after strength training protocol between women using antiandrogen and those using estrogen-progestagen contraceptives. Muscle strength increased in both groups, which was expected and proved the effectiveness of the designed strength-training protocol. The increase in muscle strength after 16 weeks could be attributed to muscle hypertrophy (19), whereas the increase after 8 weeks period was probably due to the improvement of neuromuscular co-ordination, muscle fiber recruitment, and better muscle fiber activation (20-22). The increase in muscle strength, which occurred in both groups, was high (42.3% in antiandrogen group and 53.9% in estrogen-progestogen group) because of very low initial strength and physical fitness of the subjects. However, those values were not unexpected if we consider a similar study on the elderly where the overall strength gain was 37.6 % (23). In athletes, the changes would not have been so obvious after 16-week period because of a better initial strength.

The significant differences in muscle strength increase between antiandrogen and estrogen-progestogen group suggested better effect of the training protocol on the group using estrogen-progestogen pill. As both groups underwent the same training protocol and were of the same age, it could be presumed that the differences originated from the presence of antiandrogen substances in antiandrogen group pill. The cyproterone-acetate combined with estrogens in contraceptive pills could have an inhibitory influence on strength training benefits by occupying the testosterone receptors, which could have prevented the influence of increased testosterone after the training sessions and decreased the protein synthesis and gain in muscle mass.

No difference in maximum oxygen consumption between the two groups was expected because of the inadequate volume and duration and intensity of aerobic training, because they cannot produce significant increase in cardiopulmonary fitness. The training protocol did not include a more intense aerobic training because higher volume of aerobic training conducted parallel with strength training could limit the gain in muscle strength, which was the major focus of this study. The gain in muscle strength is greater if strength training is applied separately from endurance training (24).

Limitations of the study were small study groups and lack of hormonal concentrations measurements, which could provide an insight into mechanisms of androgen effect. However, it would imply invasive methods and blood sampling, due to which the number of subjects who would voluntarily participate in a study with invasive testing would probably be much lower.

To the best of our knowledge, this is the first investigation of muscle strength gaining and fat-free tissue change in women using hormonal contraceptives. It suggests negative influence of antiandrogens on the muscle strength, especially in female athletes. Of course, the benefits of antiandrogens are not questionable in cases of hirsutism or similar medical conditions. Many women who use the antiandrogen-containing pill as hormonal contraception are neither recreational nor elite athletes and do not really need such a pill. Therefore, it is important that sports medicine specialists are aware of the possible effects of antiandrogen contraceptive preparations on muscle mass. The pill with antiandrogen content should be avoided if possible in young exercising women because of its possible negative influence on muscle strength gain. The use of cyproterone-acetate should be revised, particularly in elite athletes. Administration of cyproterone-acetate in athletes should be limited to the diagnosed cases of hirsutism and should not be prescribed for contraceptive reasons only.

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