PROJECT REVIEW

"Exogenous DHEA administration and performance: Possible mechanisms of action and metabolic signature"

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It is generally accepted in the sporting world that dehydroepiandrosterone (DHEA) use enhances physical performance, and DHEA therefore figures on the World Anti-Doping Agency (WADA) list of prohibited substances in sports, both in and out of competition. DHEA is a weak androgen that needs conversion to more potent testosterone, and the assumption is that athletes expect a significant increase in circulating testosterone through exogenous DHEA administration, with a subsequent improvement in performance. The literature on the ergogenic effects of DHEA intake is nevertheless very scant, and to our knowledge none of the studies has presented evidence that DHEA use improves athletic performance. However, this does not mean that an effect should be ruled out as these studies were focused on young male athletes, and no study has yet investigated DHEA effects in female athletes. Most of the time, the urine concentrations of endogenous DHEA are lower than 100 ng/mL in athletes, but in some cases concentrations may reach 200 ng/mL. It was recently demonstrated that exogenous DHEA administration impacted not only DHEA itself, but also the two metabolites, 5g-androstane- $3a, 17\beta$ -diol and 5β -and rost ane $-3a, 17\beta$ -diol, both of which are included in the steroidal module of the Athlete Biological Passport. However, there are no studies on how DHEA affects the other steroids included in this steroidal module.

We therefore propose to more fully investigate DHEA action during exercise, with a particular focus on:

1) the ergogenic impact of this drug in men and women during supramaximal and maximal exercise, using validated laboratory and field tests;

2) the metabolic and endocrine responses after DHEA administration;

3) the concentrations of urine steroids after physical exercise, in order to determine the metabolic signature of DHEA use as part of the steroidal module of the Athlete Biological Passport.

Results and Conclusions:

We investigated the ergogenic, metabolic and endocrine effects of short-term DHEA administration in young healthy women. In parallel, we determined the impact of DHEA on food intake, body composition and cytokines as well as on urine steroid concentrations in order to find the metabolic signature of

exogenous DHEA as part of the Athlete Biological Passport. First, we showed that short-term DHEA intake (100 mg per day for 28 days) markedly increased blood DHEA, DHEA-S, androstenedione, testosterone, DHT and estrone in recreationally-trained women. No changes were found in the other parameters investigated, i.e., cortisol, IGF1, SHBG, free, blood glucose, liver transaminases and lipid status. Curiously, the marked increase in blood testosterone (10 fold) and DHT (5 fold) induced by DHEA administration did not induce a significant improvement in supramaximal or maximal performance. Moreover, there was no significant difference in body composition, food intake, cytokines and mood. Regarding the urine analyses for the potential metabolic signature of DHEA, it appears that short-term DHEA administration in women significantly impacted up to 24 hours after the last administration urine concentrations of etiocholanolone, 7 keto DHEA, 7β-OH DHEA, 3α -5cyclo DHEA, 5α -Aane, 5β - Aane. In parallel, we found after DHEA treatment a transient classical increase in testosterone, coupled to an increase in epitestosterone, never previously reported. Last, we noted high significant correlations between urine and saliva concentrations for both DHEA and testosterone up to 24 hours after the last DHEA administration. In conclusion, these data indicate that our short-term DHEA administration did not improve performance or have an anabolic effect in young female recreationally trained athletes, despite the striking increase in androgenic hormones. Further studies are specifically needed to determine whether a higher daily dosage administered in small doses over the course of the day and/or longer DHEA treatment would generate an ergogenic effect in young female athletes during such anaerobic exercise.