Abnormal Testosterone: Epitestosterone Ratios after Dehydroepiandrosterone Supplementation

The interest in supplementation with testosterone precursors rose to new levels after Mark McGwire disclosed the use of androstenedione (and creatine) during his quest to overtake the 37-year-old home run record of Roger Maris. Banned by the National Collegiate Athletic Association (NCAA), the International Olympic Committee (USOC), and the National Football League, androstenedione, an immediate testosterone precursor, is purported to increase testosterone. Studies performed in East Germany in the 1960s demonstrated transient increases in testosterone up to 300% above normal in women and to a lesser extent in men (1). Increased testosterone was so transient that experts questioned whether any anabolic effects could occur. Indeed, there is no research that shows any performance enhancement in those who have used androstenedione, anecdotal reports notwithstanding.

Similarly, dehydroepiandrosterone (DHEA) has been banned by the NCAA and the USOC because of its physiological role as a testosterone precursor (2). As an adrenal androgen, DHEA acts as a steroid precursor for gonadal and peripheral testosterone and estrogen production. Once again, performance benefits for athletes are neither documented nor proven. DHEA is “guilty” by virtue of its position in the biochemistry of gonadal hormone production.

DHEA was first identified in 1934 (3). As a precursor to testosterone and estrogen, DHEA can be converted peripherally to androstenedione, testosterone, and dihydrotestosterone and aromatized to estrogen. The degree of either the anabolic or the androgenic effect may be markedly different from one individual to another. This seems to be attributable to the many variables that affect DHEA metabolism, including age, gender, training, nutrition, genetics, and other less well-defined factors (3).

Serum concentrations of DHEA clearly reflect its role as an adrenal hormone, with increases after acute exercise stresses such as marathon running and a 26-h hockey tournament (4, 5).

Variable DHEA changes have been observed in response to chronic training or higher volume training or competition. Serum DHEA decreased after increased training volume over several weeks (6). Neither male nor female athletes involved in endurance training demonstrated a change in serum concentration of any adrenal androgen (7). Serum DHEA monitored over the course of a 7-month hockey season showed no change (8). Although serum testosterone decreased in response to a 15-day race, DHEA remained unchanged (9).

A small number of studies have looked at the effects of DHEA on performance. Welle et al. (10) supplemented a small group of young men (average age, 26 years) with 1600 mg of DHEA each day for 4 weeks. Serum DHEA increased, but no effect was demonstrated on body weight, body mass, resting metabolic rate, total energy expenditure, or proteolysis. In a study performed by Nestler et al. (11), administration of 1600 mg of DHEA each day for 4 weeks to men (average age, 24 years) produced a loss of body fat (statistically significant) and increased body mass (not statistically significant). Interestingly, serum testosterone did not change during the period of supplementation, although cholesterol dropped significantly.

After DHEA was deemed an illegal substance in 1996, studies evaluating and measuring DHEA use appeared. Dehennin et al. (12) assessed the effects of DHEA on serum testosterone. A single 50-mg dose of DHEA was administered to a group of healthy men. Labeled DHEA was converted to testosterone. As a result of their evaluation, Dehennin et al. suggested the establishment of a DHEA concentration threshold of 300 μg/L for screening for DHEA abuse.

The study by Bowers in this issue (13) indicates that oral DHEA can increase the ratio of testosterone to epitestosterone. In this study, four males were given supplements containing DHEA. The dose of DHEA ranged from 50 to 150 mg per day. Three subjects used the supplement for 4 days. The fourth used 50-, 100-, and 150-mg doses over a 6-month period. This subject showed an initial increase in urine testosterone:epitestosterone (T:E) ratios >6:1 for all three dose levels. None of the other subjects exceeded the 6:1 ratio in spite of increases in most other androgens.

As a clinician and team physician caring for interscholastic and intercollegiate athletes, I view reports such as this with a critical eye and several concerns. First, what are the implications for eligibility to participate in sports supervised by organizations in which testing is used to monitor drug use? Secondly, if “my” athletes are using DHEA, what are the risks to their health and finances? Finally, are there any proven benefits for performance?

First and foremost, DHEA is banned by the NCAA and USOC. It is likely that most athletes are unaware of the restriction imposed by these organizations. Furthermore, DHEA, although banned by the Food and Drug Administration (FDA) because of lack of proven medical value, is available at health food and nutritional supplement stores; available then, for athletes to purchase without restriction. Of equal importance is the information provided by Bowers. Although conflicting with the results of other studies, Bowers’s results demonstrated at least one participant whose DHEA supplementation dramatically altered the T:E ratio to >6:1, the accepted maximum ratio for endogenous testosterone. Not unexpectedly, other hormonal concentrations were also increased in all subjects. The other three subjects failed to increase the T:E ratio to exceed the accepted standard. These inconsistent results effectively demonstrate the unpredictable nature of DHEA supplementation. The only lesson derived from this study for my practice is to use this threat of a “positive” drug test to underscore the potential consequences for ineligibility.
Second, few if any adverse side effects related to DHEA use have been reported. Nor is the cost prohibitive when compared with the costs of other commonly used supplements.

Finally, regarding performance benefits, although DHEA may increase testosterone concentrations, no improvement in athletic performance has been proven. As with so many supplements, legal and illegal, hypothetical benefits far exceed any proven value.

Unanswered questions remain. In my review of the available information on androstenedione (14), the intricacies of the feedback mechanism remain elusive. Clearly, there are checks and balances in the conversion of DHEA to androstenedione and from androstenedione to testosterone that ultimately limit testosterone production. Their exact effects on the results of drug testing or on performance are equally elusive. Speculation suggests that complex interactions may actually increase estrogen production if athletes are challenged with too much DHEA or androstenedione.

Another issue that needs to be addressed is the effect of DHEA on epitestosterone, to improve understanding of the variables that may either increase or decrease epitestosterone, variables that may also affect the T:E ratio.

The benefit from Bowers’s study is one of education for my athletes. A positive drug test is a strong deterrent in athletes I serve. Education remains my ally in directing them toward the benefits of training and nutrition that are far more predictable in improving athletic performance.

References

Robert Johnson
Family Medical Center
5 West Lake St.
Minneapolis, MN 55408
Fax 612-827-9734