

The power of the ketoconazole test

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Introduction

The ketoconazole test is recognized as a powerful test in order to determine whether a high ratio of the glucuronides of testosterone (T) and epitestosterone (E) is of an endogenous or of an exogenous origin [1,2]. Especially, if the T/E ratio is in the range of 6 to 10, this test may be of interest. It has been shown for instance, that after ketoconazole administration, the T/E ratio of subjects with a high endogenous ratio decreases, because the E excretion is in a lesser extent suppressed, than the T excretion. However, if the high T/E ratio of a subject is caused by T administration, the ratio will increase due to exogenous T and the suppressed E excretion. Based on these opposite effects, the test is indeed a powerful test.

We report the results of a 'short' ketoconazole test performed on an athlete with a history of anabolic androgen abuse. Also some plasma and urine hormonal data were available during a presumed anabolic androgen free period. The T/E ratio was in that period in the range of 2 to 3. Because of practical reasons, the so-called 'short' test protocol [3] was used.

Experimental

The protocol of the 'short' ketoconazole test consists a total of 3 days (Table 1). The first day is a 'blank' day and at the second day 2 x 200 mg ketoconazole is given. The third day is a follow-up day. Urine samples are collected during these periods at certain 4 h intervals or on spontaneous voiding of the bladder beyond these intervals. Blood sample are drawn also at certain 4 h intervals. In the obtained plasma, the concentration of T and

luteinizing hormone (LH) are determined and urine the glucuronides of T and E, respectively.

Table 1 Protocol of the 'short' ketoconazole test

day	time	sampling	miscellaneous
01	0900 h	urine	start of sampling
	1200 h	blood and urine	
	1600 h	blood and urine	
	2000 h	blood and urine	
	overnight	urine on spontaneous voiding	
02	0800 h	blood and urine	200 mg ketoconazole
	1000 h	blood and urine	200 mg ketoconazole
	1200 h	blood and urine	
	1600 h	blood and urine	
	2000 h	blood and urine	
	overnight	urine on spontaneous voiding	
03	0800 h	blood and urine	end of sampling

Results and discussion

After the administration of ketoconazole the concentration of T in plasma (Figure 1), of T and E in urine and the respective T/E decreased (Figure 2). Normally, these results would indicate, that the high T/E ratio as observed in the urine samples of the athlete, was of an endogenous origin. However, the data were not in agreement with the former obtained hormonal data. Compared to these older data, the T/E ratio was elevated and the plasma T significantly suppressed. The concentration of LH in plasma, although in the normal range, was risen (Figure 1) and indicated a rebound effect of the negative feedback system [4]. A doping control test for anabolic androgens was negative.

It may be concluded, that the urinary data of the ketoconazole test were according to subjects with a high endogenous ratio and the plasma data assumed anabolic androgen abuse. Former hormonal data pointed out the last assumption, although no definite prove was obtained. It has however been reported before, that the use of anabolic androgens may alter the urinary excretion of metabolites of endogenous steroids [5].

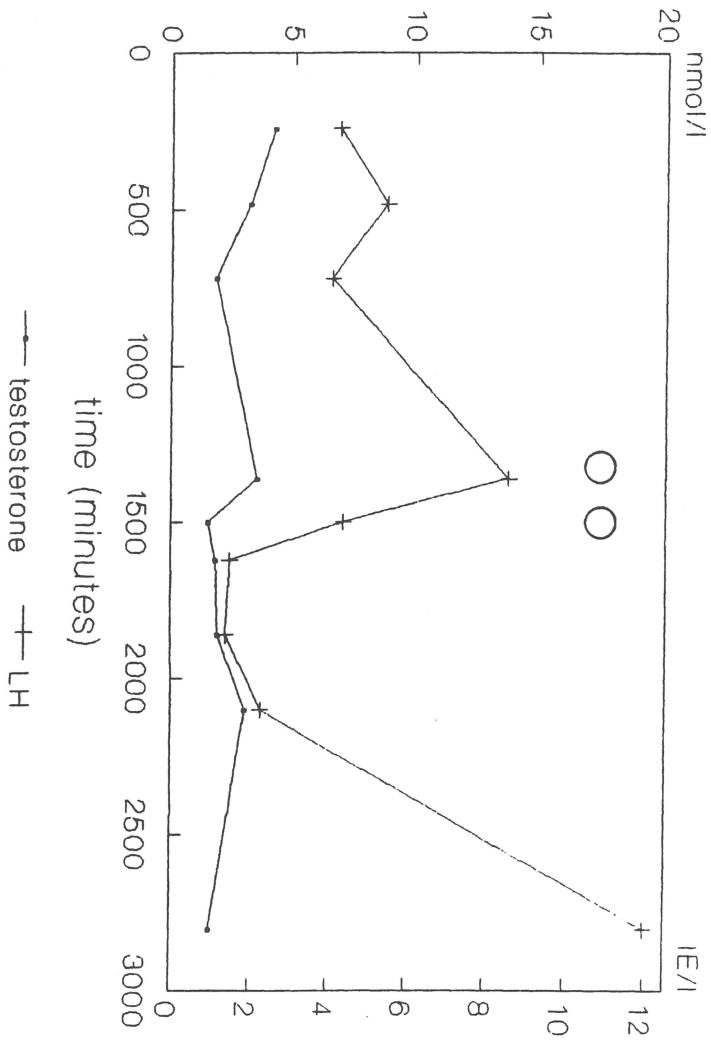
As it could at least not be excluded that the athlete had administered anabolic androgens prior to the ketoconazole test, it may not be concluded that the subject studied had a high endogenous T/E ratio. The 'short' ketoconazole test may be less powerful, than it seemed to be. In this special case, a additional follow-up will be necessary.

References

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3. Oftebro H. Personal communication 1991.
4. Harrison, L.M., D. Martin, R.W. Gotlin and P.V. Fennesey. Effect of extended use of single anabolic steroids on urinary steroid excretion and metabolism. *J. Chromatogr.* 489: 121-126, 1989.
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Figure 1:

Concentration of Testosterone (T) and Luteinizing Hormone (LH) in plasma during the 'short' ketoconazole test (○) tablet of Opalidon®)



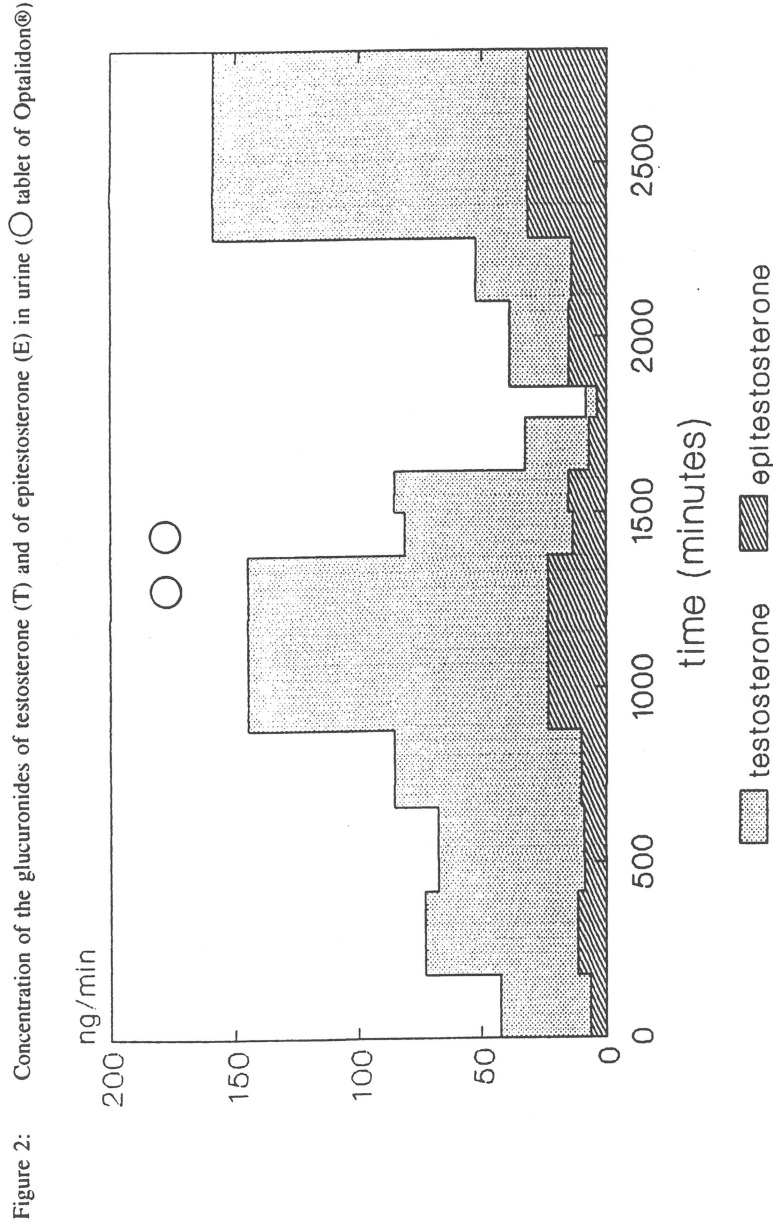


Figure 3:

The T/E ratio during the 'short' ketocconazole test (○ tablet of Opalidon®)

