

Original article

Comparison of the Values of Free Testosterone with Free Androgen Index

(Serbest androjen indeksi ile serbest testosteron değerinin karşılaştırılması)

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Amaç: Testosteron erkeklerde birincil ve ikincil seks karakterlerinin gelişmesinden başlıca sorumlu hormondur. Ancak birçok biyokimyasal parametrede olduğu gibi testosteronun biyolojik aktif olan kısmı, serbest olanıdır. Serbest androjen indeksi; total testosteronun, seks hormon bağlayıcı globüline oranıdır. Bu çalışmada biz, rutin laboratuarda serbest testosteronun ölçülemediği durumlarda, plazma serbest androjen indeksi değerlerinin serbest testosteron yerine kullanılıp kullanılmayacağına araştırmayı amaçladık.

Materyal ve Metot: Çalışmaya total testosteron ve serbest testosteron parametreleri ölçüm istemi yapılmış 92 kişi dahil edildi. Bu kişilerden total testosteron ve seks hormon bağlayıcı globülin parametreleri kemilüminesans yöntemi ile ölçülerek serbest androjen indeksi hesaplandı. Yine bu kişilerden radyoimmünoassay ile serbest testosteron ölçülerek, serbest androjen indeksi ile kıyaslandı.

Bulgular: Çalışma grubuna alınan kişilerde; hesaplanan serbest androjen indeksi ile, ölçülen serbest testosteron değerleri arasında istatistiksel anlamlı ilişki bulundu.

Sonuçlar: Serbest testosteron düzeylerinin belirlenmesinde serbest androjen indeksi maliyet etkin alternatif bir yöntemdir.

Anahtar Kelimeler: Serbest androjen indeksi; seks hormonu bağlayıcı globülin; serbest testosteron

ABSTRACT

Background: Testosterone is primarily responsible for the development of male primary and secondary sex characters. However, like many biochemical parameters, biologically active portion of testosterone is the free one. Free androgen index is the ratio of the total testosterone to sex hormone-binding globulin. In this study, we aimed to investigate possibility of using free androgen index instead of the free testosterone when the free testosterone can not be measured routine laboratory.

Material and Methods: Measurement of the total testosterone and free testosterone parameters asked 92 people were included in the study. Total testosterone and sex hormone-binding globulin parameters of these people measured with the chemiluminescence method by these parameters the free androgen index was calculated. Free testosterone measured by radioimmunoassay, and compared with the free androgen index among these people.

Results: Statistically, significant relationship was found between calculated with the free androgen index and the measured free testosterone values among the study groups.

Conclusions: Free androgen index is an alternative cost-effective method and may be used to evaluate the free testosterone levels.

Key Words: Free androgen index; sex hormone-binding globulin; free testosterone

INTRODUCTION

Testosterone is an important gonadal hormone that is primarily responsible for the development of primary and secondary sex characters in men and women. Testosterone is produced mainly in the testes Leyding cells in men, and the adrenal glands, ovaries and peripheral conversion from androstenedione in women¹.

Ninety-eight percent of testosterone is bound to its carrier protein and only 1-2% remains unbound in circulation².

The biologically active portion of the testosterone is the free one. Testosterone-binding proteins are sex hormone-binding globulin (SHBG), albumin and cortisone-binding proteins³. SHBG is a glycol-protein and it is synthesized in the liver. Unlike the others, it is strictly bound to testosterone. A small fraction of testosterone that is not bound to SHBG is called as bioavailable testosterone⁴.

Free androgen index (FAI) or free testosterone index is the ratio of total testosterone concentration to SHBG concentration. Previous studies, have reported low and high testosterone amounts, FAI might correlation with free testosterone (FT)^{5,6}.

Equilibrium dialysis, ultracentrifugation, radioimmunoassay (RIA) methods are used to measure FT⁷. In this study, we aimed to investigate the

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relationship between the FAI and the FT measured by RIA.

MATERIAL and METHODS

Total testosterone and FT levels of 92 persons were included in the study. The study group included 32 male (35.5%) and 60 female (64.5%) patients. The serum samples were stored at -70°C until analysis. All parameters in this study were measured at the same time.

Measurements of total testosterone and SHBG were performed with Immulite® [DPC (Diagnostic Products Corporation), Los Angeles, USA] immune auto analyzers using DPC measurement kits through chemiluminescence. The measurement of the FT was performed in the laboratory of RIA. Coat-A-Count Free Testosterone kit of the DPC Company was used. To separate the group into sub-groups, FT reference values were used. Reference value ranges of the FT is shown in Table 1.

Table 1. FT reference Values

| Years | Men (pg/mL) | Women (pg/mL) |
|-------|-------------|---------------|
| 20-39 | 8,8-27 | 0,06-2,57 |
| 40-59 | 7,2-23 | 0,04-2,03 |
| 60-80 | 5,6-19 | 0,03-1,55 |

Statistical Analysis

Statistical analysis was performed using SPSS for Windows 16.0 (SPSS Inc. Chicago, IL, USA).

The relationship between FT and FAI was performed using Pearson's correlation analysis. $P < 0.05$ was considered statistically significant.

RESULTS

The male group ($n=32$) was divided into two groups according to FT values; <9 pg/mL ($n=16$) and ≥ 9 pg/mL ($n=16$). The female Group ($n=60$) was divided into two groups according to FT values; <1 pg/mL ($n=39$) and ≥ 1 pg/mL ($n=21$).

Table 2. The FAI and FT Values According To Groups

| | FAI | FT pg/mL | p value | Group |
|---------------------------|-------------------|----------------------|---------|--------|
| FT <9 pg/mL n=16 | 31.97 \pm 24.76 | 4.88 \pm 2.99 | p<0.01 | Male |
| FT ≥ 9 pg/mL n=16 | 98.24 \pm 51.59 | 16.62 \pm 10.93 | p<0.01 | Male |
| FT <1 pg/mL n=39 | 4.11 \pm 2.57 | 0.74 \pm 0.16 | p<0.01 | Female |
| FT ≥ 1 pg/mL n=21 | 14.65 \pm 17.40 | 2.12 \pm 2.10 | p<0.01 | Female |

Table 2 shows the FT and FAI values obtained from these groups as mean \pm standard deviation. Scatter plot graphs of these groups were shown in Figure 1 A-D.

There were statistically significant correlations between FAI and FT values of each group ($p < 0.01$ for all). Correlation more pronounced in the male group although the female group with FT >1 pg/mL had the strongest correlation. Although there were statistically significant correlations in the female group with FT <1 pg/mL, this relationship was weaker than the other groups.

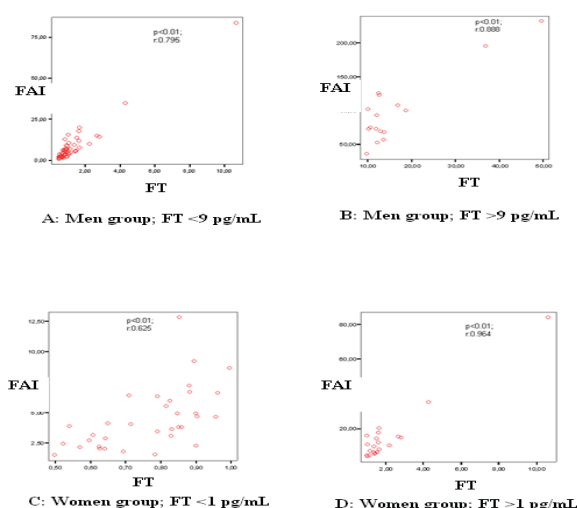


Figure 1. Correlations between FT and FAI in male and female groups

DISCUSSION

The FT measurement has considerable importance in androgen metabolism disorders. Determining the status of androgen, especially in hypogonadism, FT or bioavailable testosterone values give more precise information. First measurement procedures were performed to determine the amount of testosterone about 60 years ago⁸.

However, direct measurement of FT is time-consuming, labor intensive and a costly process⁹.

The FT measurement can not be performed easily in ordinary biochemistry laboratories. Therefore, the concept of FAI to determine the amount of FT was introduced in the clinical laboratory^{10,11}. Morley et al. reported that FAI as the most effective method when evaluating hypogonadism¹².

In the present study, significant correlations were found between the FAI and FT values especially in subgroups with lower FT values. This value indicated that FAI might be used in determining the amount of FT in subjects with lower FT values.

Likewise, patients with androgen oversecretion, serum FT values give much more precise information than the total testosterone values¹³.

In subgroups with higher FT values, we also found a significant correlation between the FAI and FT. In people with higher FT value, FAI can be used in determining the amount of FT. Similar studies have also shown that high FAI may be a sign of polycystic ovarian disease¹⁴⁻¹⁶. In a same way, FAI may be higher in the cases of hirsutism in women^{17,18}.

Wehr E. et al. reported a significant association between vitamin D and higher total testosterone amounts and FAI¹⁹. Creatsa M. et al. reported that in healthy menopausal women, higher total testosterone and the FAI were correlated with subclinical atherosclerosis²⁰. In these clinical trials, increasing or decreasing FAI values and FT amounts in the same direction, may support the results of the present study.

In some studies, FAI was criticized for the lack of reference values specifying a variety of physical situations²¹.

Our aim is to investigate whether there is a relationship between the FAI with FT. Therefore

we have included the subjects regardless of their clinical diagnoses in the study. We found statistically significant relationship between FT and FAI between male and females. The strongest association was among women with FT value 1-10 pg/mL. Further studies are necessary to confirm our preliminary data.

In conclusion, according to this study, FAI is an alternative cost-effective method and may be used to predict FT values. In clinics that can not measure FT, FAI can be used to assess the androgen status. Reference value studies according to gender and age ranges for the guidelines would be useful to standardize clinical use.

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Conflict of interest statement none declared.

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