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Sexual Dysfunction

Correlation between Serum Total Testosterone and the AMS and IIEF Questionnaires in Patients with Erectile Dysfunction with Testosterone Deficiency Syndrome

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Purpose: This study was conducted to investigate the relationship between serum total testosterone levels and scores on the Aging Male's Symptom (AMS) scale and the International Index of Erectile Function (IIEF) in men with erectile dysfunction with testosterone deficiency syndrome (TDS).

Materials and Methods: From January 2005 to July 2008, 134 patients who complained of sexual dysfunction such as erectile dysfunction or decreased libido as the main symptoms of TDS with serum total testosterone levels less than 3.5 ng/ml were evaluated by independent t-test and linear regression analysis, respectively. Patients with treated hypogonadism within 6 months, with a history of taking a PDE5 inhibitor or an antidepressant for a depressive disorder, or who had metabolic syndrome were excluded from this study.

Results: The AMS scale and its 3 subdomain scores were not significantly correlated with the total testosterone level. By contrast, the total IIEF score and the score of each IIEF domain except sexual desire showed a weakly significantly positive correlation with serum total testosterone.

Conclusions: In TDS patients with erectile dysfunction, there was a low relationship between serum total testosterone levels and the AMS scale and a weakly positive correlation between total testosterone levels and all IIEF domains except sexual desire. There was a low relationship between the AMS scale, the sexual desire domain score of the IIEF, and total testosterone. We should understand these limitations when evaluating patients with erectile dysfunction with TDS. New scales should be developed for the evaluation of erectile dysfunction in these patients.

Key Words: *Erectile dysfunction; Questionnaires; Testosterone*

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INTRODUCTION

Late-onset hypogonadism or age-associated testosterone deficiency syndrome (TDS) in the aging male is defined as a clinical and biochemical syndrome characterized by a decline in levels of serum testosterone. With aging, men experience decreases in important health indicators like muscle amount, muscle power, physical activity, bone density, blood generation, and sexual drive [1]. Various research [2-4] on the decrease in blood testosterone with aging suggests that many clinical characteristics related to age, including erectile dysfunction (ED), are closely related to lack of testosterones. Recent research results indicate that testosterone and ED are closely related to one other [5,6], which suggests that supplementary therapy with testosterone may be one useful method in the treatment of ED. For such a reason, the European Association of Urology Guideline (EAU Guideline) recommends that patients who come to clinics with ED as their main complaint should all undergo testosterone value testing [7].

Although there is no established standard for the diagnosis of TDS, the 2006 recommendation by the Korean Society of Aging Male Research is a serum total testosterone level of less than 12 nmol/l (3.46 ng/ml) or a free testosterone value of less than 250 pmol/l (72 pg/ml) [8]. Furthermore, changes in male hormones with aging vary among individuals [9], and the relationship between the degree of age-related symptoms and the reduction of male hormones is not clear. Therefore, for easy clinical diagnosis of TDS, not only the concentration of blood testosterone but also subjective symptoms surveyed by questionnaire are very important.

The Aging Male's Symptom (AMS) scale is the most widely used questionnaire for the diagnosis of TDS, but the AMS has been known to be nonspecific to low testosterone [10] because it was developed on the basis of a normal aging population.

The International Index of Erectile Function (IIEF) is the most widely used questionnaire for the diagnosis and for assessing the treatment outcome of sexual dysfunction, but the IIEF has not been related to serum testosterone level because it was developed to evaluate the efficacy of phosphodiesterase-5 inhibitors (PDE5 inhibitors) in patients with ED [11,12].

Despite these limitations, the AMS and IIEF are commonly used to assess the efficacy of testosterone replacement therapy in ED patients with TDS. We performed this study to investigate the relationship between serum total testosterone levels and scores on the AMS scale and the IIEF and the threshold total testosterone level in relation to domains of the IIEF.

MATERIALS AND METHODS

This study was done on 134 outpatients in our clinics of urology with the main complaint of sexual dysfunction such as ED or decreased libido as the main symptom of TDS. The patients had a serum testosterone level less than 3.5 ng/ml and were evaluated from January 2005 to July 2008. Patients who received testosterone replacement therapy within 6 months, those taking type 5 phosphodiesterase (PDE5) inhibitors, those who were diagnosed with elderly depression and were taking anti-depressants, and those who had metabolic syndrome were excluded through gathering of disease history.

Patients underwent measurement of blood total testosterones through a blood test. Blood was collected between 07:00 and 10:00 during an outpatient visit, at which time the patients also completed the AMS and IIEF questionnaires. The AMS scale was classified into three domains (psychological, somato-vegetative, and sexual) and the IIEF questionnaire sheet into five domains (erectile function, intercourse satisfaction, orgasmic function, sexual desire, and overall satisfaction). Serum total testosterone value, AMS total points and points for the three domains, and IIEF total points and points for the five domains were respectively analyzed.

To determine the correlations of serum testosterone levels with scores on the IIEF and AMS scale, linear regression analysis was used and correlation coefficients and p-values were determined. To determine the threshold testosterone level, independent t-tests were also used with SPSS ver. 13.0 (SPSS Inc., Chicago, IL, USA). p-values of less than 0.05 were considered to be statistically significant.

RESULTS

The average age of the patients was 56.1±9.39 years, and the average value of serum total testosterones was 2.71±0.76 ng/ml. In the AMS, the average value of the psychological symptom, somato-vegetative symptom, and sexual symptom domains were, respectively, 8.76±4.13, 14.7±5.80, and 14.2±4.48, and the average total points was 37.6±12.5. In the IIEF, the average values of each domain were, respectively, 11.9±7.54 for erectile function, 4.76±3.42 for

TABLE 1. Characteristics of the patients

Variables	Mean±SD
Age (yr)	56.1±9.39
Testosterone (ng/ml)	2.71±0.76
AMS scale	
Psychological factor	8.76±4.13
Somatovegetative factor	14.7±5.80
Sexual factor	14.2±4.48
Total score	37.6±12.5
IIEF questionnaire	
Erectile function	11.9±7.54
Intercourse satisfaction	4.76±3.42
Orgasmic function	4.61±3.40
Sexual desire	4.52±1.94
Overall satistaction	4.14±1.90
Total score	29.9±16.1

SD: standard deviation, AMS: Aging Male's Symptoms, IIEF: International Index of Erectile Function

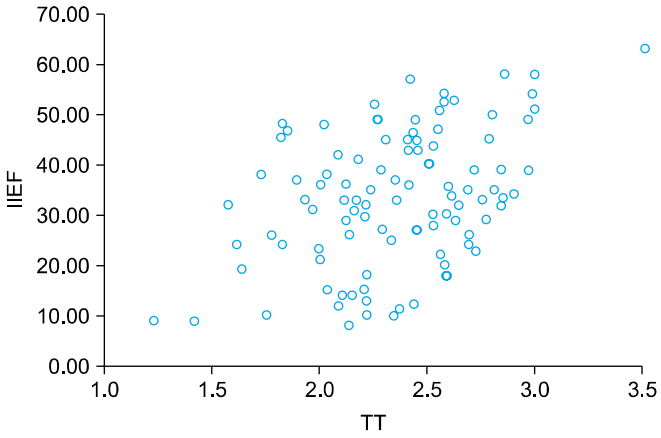

FIG. 1. Correlation of serum total testosterone and IIEF scores. TT: total testosterone, IIEF: International Index of Erectile Function.

TABLE 2. Correlations of testosterone and multi-vocal factors in TDS patients

	Correlation coefficient	p-value
AMS scale		
Psychological factor	0.131	0.168
Somatovegetative factor	0.101	0.289
Sexual factor	0.015	0.875
Total score	0.095	0.318
IIEF questionnaire		
Erectile function	0.141	0.021
Intercourse satisfaction	0.126	0.049
Orgasmic function	0.173	0.018
Sexual desire	0.127	0.561
Overall satisfaction	0.099	0.040
Total score	0.124	0.034

TDS: testosterone deficiency syndrome, AMS: Aging Male's Symptoms, IIEF: International Index of Erectile Function

sexual satisfaction, 4.61±3.40 for orgasmic function, 4.52± 1.94 for sexual drive, and 4.14±1.90 for overall satisfaction with sexual life, and the average total points was 29.9±16.1 (Table 1).

In the correlation analysis, serum total testosterone was not significantly correlated with the AMS total score or its 3 subdomains ($p > 0.05$). Serum total testosterone showed a significant weakly positive correlation (r=0.124, p=0.034) with the IIEF total score (Fig. 1), and among the 5 domains, the domains of erectile function, intercourse satisfaction, orgasmic satisfaction, and overall satisfaction with sexual life also showed significant weakly positive correlations with serum total testosterone ($p < 0.05$). However, the sexual drive domain did not show any correlation with serum total testosterone (Table 2).

DISCUSSION

Reduction in blood total testosterones with aging was described for the first time by Hollander et al in the late 1950s and was verified in various cross-sectional studies and longitudinal studies [13-18]. Reduction of androgen accompanied by aging can cause physiological, somato-vegetative, and sexual symptoms, and the sexual symptoms include hyposexuality, ED, reduction of orgasmic function, and reduction of ejaculation amount and ejaculation force [19-21]. Testosterone deficiency causes sexual dysfunction and anatomical, physiological, and biochemical substrate damage of erectile function and affects the erection mechanism in the penis organ but can be recovered through testosterone supplementation therapy. Some study results have indicated that aged males require higher concentrations of testosterones for normal sexual function than do young people. These findings support the importance of male hormones as represented by testosterone regarding the sexual dysfunction that occurs with aging [22].

Sexual hormones are widely studied under the assumption that sexual dysfunction symptoms are related to the conditions of sexual hormones, but some patients with sexual dysfunction remain within the normal range of blood testosterone values [19-21]. Therefore, the correlation between high age itself and symptoms caused by aging leaves potential for argument, because aging-related symptoms can be affected by various causes such as hereditary factors, living habits, physical activity, nutritional status, and chemical dosage and accompanying diseases as well as endocrine changes. For such reasons, whether a patient's symptoms are alleviated as well as blood testosterone concentration is marked in a self-administered symptom score table, but in practice there is no internationally recognized method of diagnosis that can be used for the determination of diagnosis and treatment progress.

The most frequent reason that patients with reduced male hormone visit a urologist is sexual dysfunction, such as hyposexuality or reduction of sexual drive, and in this regard, the IIEF of Rosen et al and the sexual area of the AMS of Heinemann can be used [10,11]. In the present study, the AMS total score and the 3 subdomains showed a positive but not a significant correlation ($p > 0.05$) with total testosterone.

In 2005 Morley et al specified male hormone deficiency condition as 70 ng/ml or less of bioavailable testosterones and compared the questionnaires of the Androgen Deficiency in Aging Males (ADAM), the AMS, and the Massachusetts Male Aging Study (MMAS). The diagnostic sensitivities of each questionnaire were, respectively, 98%, 83%, and 60%, and the specificities were, respectively, 30%, 39%, and 59% [23]. It was reported that the patients who showed a positive reaction in each questionnaire showed a significant difference in free testosterone and bioavailable testosterones but did not show any difference in total testosterones. In addition, in 2005 Basar et al determined more than 29 points in the total score of the AMS to be a positive reaction accompanied with aging and defined less than 26 points in the IIEF as hyposexuality in 348 persons [24]. In the AMS survey, patients with a positive reaction had significant differences in age, DHEA-A, estradiol, and AMS total points and points for each range compared with patients who did not have a positive reaction. Patients with hyposexuality had significant differences in age, DHEA-S, FTI, IIEF points, and AMS points. However, total testosterone was not associated with any variable. As mentioned above, the AMS survey is often used to screen patients with a lack of male hormone by total testosterone, but has low singularity and is not associated with total testosterone. These results may be because in the AMS survey, the items are questions associated with aging and do not reflect deficient status of testosterone, and the male hormone value is not considered in the judgment of results. In the future, it is necessary to reevaluate the questions of the AMS survey and to correct and supplement them translated in Korean as a tool for the diagnosis and evaluation of age-associated TDS.

The IIEF was designed to measure erection ability and to evaluate a medical effect of impotence. In 2006, Zitzmann

et al analyzed the relationship between male menopause and blood testosterone values in 434 males aged 50-86 years old who suffered from the male menopause syndrome and reported that, according to reduced blood total testosterone value, syndromes such as sexual disinclination, obesity, lack of concentration, somnipathy, and impotence were significantly increased [25]. The study also disclosed that there were significant positive correlations between blood total testosterone and IIEF total points and the points in the four ranges of erection ability, sex satisfaction, orgasm, and general satisfaction for sex life. However, with regard to sexual desire, the testosterone value was not correlated and many patients had normal sexual desire. Actually, it is reported that the numerical testosterone value required to maintain sexual desire is somewhat low. Some have reported that the numerical value of testosterone was not largely associated with sexual desire, although others strived to disclose a correlation between the numerical value of testosterone and sexual desire [26]. Therefore, to evaluate sexual desire, the relationship of blood total testosterone with psychological factors such as stress and melancholy and chronic disease such as lack of sleep should be considered.

This study analyzed correlations between blood total testosterone value and scores related to sexual function syndromes in hospital visitors with hyposexuality such as impotence and sexual disinclination. Our study differs from the existing domestic research carried out with male persons of more than a fixed age. It is a limit of the study that this was a quantitative analysis of the numerical value of male hormone with only the AMS and IIEF as tools for measuring syndromes. Our study does not reflect the diverse endocrine changes that had an effect on the syndromes because we measured only blood total testosterone as a method of biochemical diagnosis. Male hormone replacement therapy is now the main therapy of age-associated TDS. Therefore, it is thought that it is necessary to carry out a large-scale research study on the correlations between male hormone values and survey results before and after carrying out male hormone replacement therapy. There are many reports that other hormones such as free testosterone, bioavailable testosterone, E2, and DHEA-S are associated with clinical syndromes such as impotence. Therefore, it is necessary to carry out research including the above in the future.

CONCLUSIONS

In TDS patients with ED, there was a low relationship between serum total testosterone levels and the AMS scale and a weekly positive correlation between the total testosterone level and IIEF scores, except for sexual desire. Because there was a low relationship between the AMS, the sexual desire domain score of the IIEF, and total testosterone, we should understand these limitations of evaluating TDS patients with ED and develop a new scale to be used in the evaluation of these patients.

Conflicts of Interest
The authors have nothing to disclose.

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