THE RELATIONSHIP OF SERUM TESTOSTERONE TO ERECTILE FUNCTION IN NORMAL AGING MEN

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ABSTRACT

Purpose: We evaluated the variation in serum testosterone in normal aging men and its relationship with erectile function.

Materials and Methods: In a study that was not community based and during a free screening program for prostate cancer, 1,071 men were invited to complete a sexual activity questionnaire, that is the abridged 5-item version of the International Index of Erectile Function (IIEF-5), as a diagnostic tool for erectile dysfunction. Possible scores on the IIEF-5 are 1 to 25 and erectile dysfunction was classified into 5 categories based on the scores, namely severe—1 to 7, moderate—8 to 11, mild to moderate—12 to 16, mild—17 to 21 and none—22 to 25. Serum total testosterone was measured between 8:00 and 10:00 a.m. in all men.

Results: Of the 1,071 men registered, 965 (90.1%) were included in this study, of whom 88% were white and 12% were black. Mean age was 60.7 years. In this sample the prevalence of all degrees of erectile dysfunction was estimated to be 53.9%. The degree of erectile dysfunction was mild in 21.5% of cases, mild to moderate in 14.1%, moderate in 6.3% and severe in 11.9%. According to age the erectile dysfunction rate was 36.4% in the 40 to 49, 42.5% in the 50 to 59, 58.1% in the 60 to 69, 79.4% in the 70 to 79 and 100% in the 80 years and older groups (p < 0.05). The variation in mean serum total testosterone in the age groups was not statistically significantly different (p > 0.05).

Conclusions: Erectile dysfunction showed a clear association with aging but no consistent correlation of total testosterone with erectile condition was identified.

KEY WORDS: penis, impotence, testosterone, questionnaires, aging

Accompanying the aging process are certain critical conditions that are often associated with decreased testosterone, such as decreased muscle tissue mass, increased body fat mass, decreased bone mass, osteoporosis, decreased sense of well-being, depression, decreased libido and increased erectile dysfunction. The decrease in serum androgen associated with aging in normal males is accompanied by a decline in testicular function, including lower serum testosterone and bioavailable testosterone, and increased androgen binding to the sex hormone globulin. Because of these aspects, the decrease in non sex hormone binding globulin bound testosterone, called bioavailable testosterone, is often much greater than the decrease in total testosterone. Another aspect is the fact that is unknown whether the age related decline in serum testosterone in men is universal.

Normal male sexual function depends on a complex interplay of psychological, neurological, vascular and endocrine factors. There is considerable controversy on the relative importance of each factors in the initiation and maintenance of erection, especially the role of serum testosterone. Several studies show that aging in men is associated with decreased sexual interest and activity, particularly with an increased prevalence of erectile dysfunction.

Generally androgens enhance libido and the frequency of sexual acts but a causal relationship between altered androgen levels and erectile dysfunction has not been proved. However, recent data support the theory that androgens, mainly free testosterone, have a beneficial effect on sexual function. On the other hand, the real relationship of total testosterone and sexual function, more specifically erectile function, is less clear. We assessed serum total testosterone in normal aging men and determined its association with self-reported erectile function.

MATERIALS AND METHODS

The ethics committee at our hospital approved this study. Patients were previously informed of the research details and they agreed to participate in the study. This noncommunity based series included 1,071 men who were invited to participate during a free screening program for prostate cancer, that is Prostate Cancer Awareness Week at Santa Casa Hospital-Porto Alegre, Brazil, from July 26 to 30, 1998. This number of men was previously established without any type of selection criteria by the program. This aspect needs careful consideration regarding its possible influence on the results, mainly due to the extremes of age. In addition to questions on urinary symptoms and physical examination, all men who presented completed a sexual activity questionnaire, that is the abridged 5-item version of the International Index of Erectile Function (IIEF-5), as a diagnostic tool for erectile dysfunction. They were not asked about sexual function, risk factors or co-morbidities. As previously described by Rosen et al, this questionnaire consists only of 5 questions and each IIEF-5 item is scored on a 5-point ordinal scale, on which lower values represent poorer sexual function.
Thus, a response of 1 on a question was considered least functional, whereas a response of 5 was considered most functional. Possible scores on the IIEF-5 are 1 to 25. Scores above 21 were considered normal erectile function and scores at or below this cutoff were considered erectile dysfunction. Erectile dysfunction was classified into 4 categories based on IIEF-5 scores, namely severe—1 to 7, moderate—8 to 11, mild to moderate—12 to 16, mild—17 to 21 and none—22 to 25. Total testosterone determined by a commercially available radioimmunoassay kit was the only serum hormone measured. Blood samples were obtained between 8:00 and 10:00 a.m. Normal total testosterone was 241 to 827 ng/dl.

The screening was advertised in print and electronic media, and participants were self-selected after responding to this publicity. The media were only directed toward prostate publicity. The media were only directed toward prostate

...variables IIEF-5 score and age showed a statistically significant inverse or negative relationship (r = −0.3449, p < 0.05).

**DISCUSSION**

Data in this study do not represent a randomly selected population from within a community. Study participants sought medical attention in a free screening program. Therefore, it is possible that these data may not represent national or even regional status. Individuals seeking medical attention in a screening program may be more concerned with health than the general population. On the other hand, patients with co-morbidity and low quality of life may have no interest in participating in this type of program.

The National Institutes of Health recommends routine measurement of serum testosterone in men with erectile dysfunction. However, studies show that this recommendation is irrational because of the overall low yield of clinically significant endocrine abnormalities. The current study and others confirm this finding.

In men there is a gradual decrease in androgen with aging. There is great variability among individuals in the degree of this reduction and not all aging men have hypogonadism to a clinically significant degree. Nevertheless, little is known about the true incidence of hormonal abnormalities in an unselected group of men with erectile failure and, in addition, there is confusion concerning the effects that hormonal abnormalities have on erectile function.

**TABLE 1. Prevalence of normal erectile function and erectile dysfunction in the study population**

<table>
<thead>
<tr>
<th>Erectile Function (IIEF-5)</th>
<th>No. Pts. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>445 (46.1)</td>
</tr>
<tr>
<td>Dysfunction:</td>
<td>529 (53.9)</td>
</tr>
<tr>
<td>Mild</td>
<td>208 (21.5)</td>
</tr>
<tr>
<td>Mild–moderate</td>
<td>136 (14.1)</td>
</tr>
<tr>
<td>Moderate</td>
<td>61 (6.3)</td>
</tr>
<tr>
<td>Severe</td>
<td>115 (11.9)</td>
</tr>
</tbody>
</table>

**TABLE 2. Prevalence of erectile dysfunction according to age group**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>No. Pts.</th>
<th>No. Erectile Dysfunction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–49</td>
<td>11</td>
<td>4 (36.4)</td>
</tr>
<tr>
<td>50–59</td>
<td>470</td>
<td>200 (42.5)</td>
</tr>
<tr>
<td>60–69</td>
<td>334</td>
<td>194 (58.1)</td>
</tr>
<tr>
<td>70–79</td>
<td>131</td>
<td>103 (79.4)</td>
</tr>
<tr>
<td>80 or older</td>
<td>19</td>
<td>19 (100)</td>
</tr>
</tbody>
</table>

*Statistically significant difference among all age groups, except 40 to 49 and 50 to 59 years (ANOVA and Bonferroni test p < 0.05).**

**RESULTS**

Of the 1,071 men 965 (90.1%) were included in the study. A total of 106 men (9.9%) were excluded from analysis because of failure to complete all protocol criteria. Of the respondents 850 (88%) were white and 115 (12%) were black. Mean age was 60.7 years (range 45 to 90).

In this sample the prevalence of all degrees of erectile dysfunction was estimated to be 53.9%. Erectile dysfunction was mild in 21.5% of cases, mild to moderate in 14.1%, moderate in 6.3% and severe in 11.9% (table 1). According to age the erectile dysfunction rate was 36.4% in the 40 to 49, 42.5% in the 50 to 59, 58.1% in the 60 to 69, 79.4% in the 70 to 79 and 100% in the 80 years and older group. This rate was statistically different among all age groups (p < 0.05) except in the 40 to 49 and 50 to 59-year-old groups (p > 0.05, table 2).

Table 3 lists mean total testosterone per individual in the various decades of life. The variation in mean serum total testosterone in the age groups did not show any statistically significant difference (p > 0.05). However, we observed a greater percent of men with subnormal total testosterone in the 80-year-old and older group (p < 0.05) compared with the other age groups. Men 70 years old or older more often presented with subnormal total testosterone compared with those 40 to 49 years old (p < 0.05, table 4).

When considering only the 144 men with the maximum score of 25 points on the IIEF-5, we observed that 143 (99.3%) had normal total testosterone and only 0.7% showed a subnormal level of the androgen. The Pearson coefficients of the variables age and total testosterone did not reveal any significant correlation (r = 0.00376, p = 0.907). Furthermore, no correlation was noted of IIEF-5 score with total testosterone (r = 0.0163, p = 0.612, see figure). However, analysis of the
Testosterone production is regulated by the hypothalamic-pituitary-testis axis and there is no clear consensus on the endocrine mechanism of the rather modest decline in androgen with aging. Several studies indicate that aging is associated with changes at all 3 levels of the axis but probably most predominantly at the testicular level. Furthermore, there is increased binding of testosterone to its carrier proteins, resulting in a lower level of free, biologically active testosterone. Nickel et al reported a 17.5% incidence of hypothalamic-pituitary-gonadal axis abnormalities in patients with an initial diagnosis of erectile failure, although in only 12.1% did abnormalities clearly contribute to this condition.

However, plasma testosterone below the lower normal limit occurs only in a minority of elderly men, including 7% in the 40 to 60, 20% in the 60 to 80 and 35% in the older than 80 years old group. When compared with the rate of erectile dysfunction in the various decades of life (table 2), these data show much lower values. Erectile dysfunction data in other studies, such as the Massachusetts Male Aging Study (MMAS), indicate a higher rate of this condition in the various decades of life than the rate of hormonal abnormalities. These aspects show that other significant conditions have a significant influence on sexual condition.

It seems safe to say that when androgen values are within the reference range, they are not a significant factor in erectile dysfunction in aging men. Sexual function decreases with age but hormonal changes are not the major determining factor in this decline. Korenman et al stated that hormonal hypogonadism without compensatory gonadotropin elevation is common in older men. Erectile dysfunction, which is also common in aging men, is independent of gonadal status. Because there is usually no cause and effect relationship of low testosterone and erectile dysfunction, it was suggested that the 2 conditions should be evaluated separately because they are separate entities or it may indicate that the process is more complex and factors other than testosterone alone are involved.

Others, such as Nieschlag et al, did not observe any correlation of testosterone with sexual activity in vigorous elderly men. However, Davidson et al clearly noted a significant but weak correlation of sexual activity with free testosterone. Similarly Tis touras et al reported higher mean testosterone in men with high sexual activity.

Another interesting aspect is that the effects of androgen replacement on sexual activity and erectile function are rather disappointing, which is not surprising in view of the complexity of the factors determining sexual activity, whereas erectile function in elderly men rarely has an endocrine but more often has a vascular or neurological origin. Study results show a more consistent impact of testosterone on behavior related directly to libido and not on erectile function which, on the other hand can be retained when serum androgen decreases below the normal range.

In absolute terms testosterone in aging men is almost always within the normal reference values despite the possibility of a significant decrease during an individual lifetime. In the MMAS median free testosterone at ages 40 and 70 years was 0.23 and 0.16 nmol/l., respectively, with a within-group standard deviation of 74%. Thus, a substantial number of elderly men continue to have serum testosterone within the wide range present in much younger men. Notably normal total testosterone assay results are widely variable at 241 to 827 ng/dl. This aspect and the relatively small numbers in the youngest and oldest age groups may have skewed the results and may explain the lack of a positive relationship in the current study. Another aspect is the possible lack of a relationship of total testosterone in the aging process with sexual function, as described by others, as well as the possible influence on this type of androgen by another factor, such as sex hormone binding globulin. As described previously, sex hormone binding globulin increases with aging and this fact results in a lower decrease in serum total testosterone than in nonsex hormone binding globulin bound testosterone. Further longitudinal studies with longer followup would probably explain many doubts regarding this situation.

Another aspect that must be considered is the widely recognized major influences of androgen in the sexual desire domain. A possible skewing effects of this aspect on our results was possible because the IIEF-5 determines only the erectile condition of sexual function. However, the actions of libido over the other sexual functions is well known. Unfortunately we did not evaluate this aspect in the current study.

In the MMAS, Feldman et al did not note any consistent correlation of erectile dysfunction with testosterone but there was a significant association of this condition with decreased dehydroepiandrosterone. Others investigated the relationship of androgens to sexual function. The most common conclusions indicate that testosterone correlates positively with sexual desire and sleep related erection but not with erectile dysfunction or the frequency of coitus. The latter finding confirms evidence in androgen replacement studies in hypogonadal men that androgen is more important for sustaining sexual desire and sleep related erection than for maintaining the erectile response to external stimuli.

Pearson correlation of total testosterone with IIEF-5 scores (r = 0.01623, p = 0.615)
The age associated decrease in androgen varies highly among individuals. Many elderly men have an androgen level that is in the normal range of young men, and so there is no reason to treat them with androgens whatever their complaints may be. Moreover, few controlled studies have assessed the effects of androgen substitution on clinical signs generally attributed to androgen deficiency, such as asthenia, lack of energy, decreased bone mass and osteoporosis, decreased libido and sexual activity, and erectile dysfunction. There are enormous variations in testosterone values among men of all ages. We did not detect any significant variations in these levels in the current study. No significant correlation with erectile function was identified but there was a consistent relationship of the latter with age. Another aspect is that the free testosterone fraction and not total testosterone, which was considered in this study, or the possible relationship of various levels of androgen may possibly be more useful in erectile function.

As noted by Sternbach, it would be erroneous to attribute erectile dysfunction to decreasing testosterone when there are other variables that must be considered as the etiology of complaints related to diminished libido, erectile and ejaculatory dysfunction, and reduced sexual activity. Such variables include availability of a partner, fear of performance failure, impaired penile perfusion, chronic illness, depression, medications, neuropathy, smoking, and alcohol and drug abuse.

CONCLUSIONS

This study does not confirm a positive relationship of erectile dysfunction and low serum total testosterone. However, it shows a direct relationship of an increased prevalence of erectile dysfunction and low serum testosterone. However, there is a consistent relationship of the latter with age. Another variable is that the free testosterone fraction and not total testosterone was a consistent relationship of the latter with age. Another aspect is that the free testosterone fraction and not total testosterone, which was considered in this study, or the possible relationship of various levels of androgen may possibly be more useful in erectile function.

REFERENCES

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