Original Article

Gonadal Hormones and Gonadotrophins in healthy males beyond forty years

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Abstract

Objective: To determine and compare the sex hormones, gonadotrophins and sex hormone binding globulin (SHBG) in healthy males of different age groups.

Methods: One hundred eighty five consecutive healthy nonobese males of age 40-90 years were studied. Serum samples were assayed for total testosterone, estradiol, LH, FSH and SHBG estimation by radioimmunometric method. The subjects were divided into five age groups and the mean serum concentrations of each parameter were compared among the groups.

Results: No significant difference in the mean serum concentrations of total testosterone, SHBG, LH and FSH was found among the different age groups($p > 0.05$ by Anova). Significant age related decrease was found in the serum estradiol concentration ($p < 0.05$) by both Anova and Pearson's Correlation test.

Conclusion: There is no significant age related change in serum total testosterone, gonadotrophin and SHBG concentrations in healthy males beyond forty years. Significant age related decrease in serum estradiol needs further studies. (JPMA:56:203;2006)

Introduction

Though it is generally held that serum testosterone in males decreases with age, how real is andropause or male menopause is, still not decided. This is mostly due to insufficient and conflicting reports on the age related changes in gonadal hormones, their hypothalamopituitary regulation and SHBG concentrations that determine the availability of free hormones in the circulation.[1-8] There is no doubt about the rapid increase of serum androgen levels during puberty. However, much controversies still exist regarding the changes in gonadal hormones and their regulatory hormones in the elderly males.[5,7,9] Some authors consider age related decrease of gonadal function and serum concentration of sex hormones to the extent justifying andropause as the male counterpart of menopause while others report no significant age related decline in gonadal functions. Alteration in the SHBG in the blood is also reported by some studies.[1,10,11] The availability of the sex hormones in the body is the resultant effect of all these factors. Chronic systemic illnesses and exposure of the body to medications are often associated with aging subjects that can affect the gonadal hormone levels and their regulation. The number of studies in this field are not sufficient to have a clear conclusion about the age related changes in male gonadal hormones. The reports are also contradictory. It is probable that the earlier reports differ to each other in subject selection and also in laboratory procedures as sensitivity and specificity of the available assay procedures improved over time. In fact due to insufficient and conflicting reports regarding age related changes in gonadal hormones and their regulations andropause as the male counterpart of menopause still remains controversial. On this background we thought that studies on healthy males and using sensitive assay procedures can give results that could be useful in solving these controversies. Accordingly the aim of the study was to determine the sex hormone levels, gonadotrophins and SHBG in healthy males beyond 40 years of age and to compare the means of the measured variables among the different age groups.

Subjects and Methods

Healthy males of age 40 -90years, BMI 23.13 ± 0.38Kg/m²) were selected from the male visitors attending Dhaka Medical College, Bangabandhu Medical University, and Bangladesh Medical College Hospital between January 2003 to July 2003. An informed written consent for participation in this study was taken from each and the study procedure was approved by BMRC (Bangladesh Medical Research Council) Ethical Committee. Out of 210 provisionally selected males , 185 completed the study. A detailed clinical and laboratory examination was done on each subject and only the healthy males were included. Every possible efforts were made to exclude the subjects with diabetes, hypertension, obesity, cardiac, liver, renal and other systemic diseases and subjects with history of taking medication within six weeks before sample collection. Benign prostatic hyperplasia, history of trivial illnesses like common cold, nonspecific rheumatism were ignored. Blood samples were collected from upper limb veins between 8 and 9 am. Serum was separated by centrifugation and preserved at -40°C in the Department Of Biochemistry, Bangabandhu Sheikh Mujib Medical University, Dhaka until laboratory analysis. Laboratory analysis were done in the Popular Diagnostic Laboratory, Dhaka within 3 months of collection. Reagent kits were supplied by Diagnostic Products Corporation, 5700 West 96th Street, Los Angeles, USA. Assays were done by Chemiluminiscent technique and IMMULITE 2000 Analyzer.

Serum total testosterone, Estradiol, SHBG, LH and FSH concentrations were measured from each sample. The sensitivity of the tests were 0.3 nmol/L for total testosterone, 1.5pg/mL for estradiol, 0.1mIU/mL for LH and FSH and 0.02nmol/L for SHBG

The subjects were divided into five age groups: group 1 from 40-50 years, group 2 from 51-60 years, group 3 from 61-70 years, group 4 from 71-80 years and group 5 from 81-90 years. The results were expressed as Mean±SEM until otherwise stated. Mean and SEM of each group for every measured variable was determined. For each variable means of all age groups were compared among each other by Anova test. Correlation coefficient of each variable with age was also determined by Pearsons's correlation test [13] p-value < 0.05 was considered significant. Data entry and statistical analyses were done by the software program FOXPRO and SPSS version 10.

Results

No statistically significant difference in the means of total testosterone, LH, FSH and SHBG was found among the different age groups (p > 0.05 for each parameter by Anova test). In case of serum

Table 2. Correlations of the measured variables with age. (n =185)

Variables	Correlation coefficient	P - value
Total testosterone	-.0619	.403
Estradiol	-.1544	.036*
LH	.0250	.735
FSH	-.0429	.562
SHBG	-.0867	.241

* Significant (p<0.05)

estradiol means of different age groups were significantly different and there was significant negative correlation with age (p < 0.05 in both Anova and correlation test) (Table 2). The means of total testosterone and estradiol in different age groups have been shown in Figure 1. A downward trend in the mean concentration with advancing age was found in both testosterone and estradiol but in case of testosterone it was not statistically significant. The means of other variables have been shown in Table 1
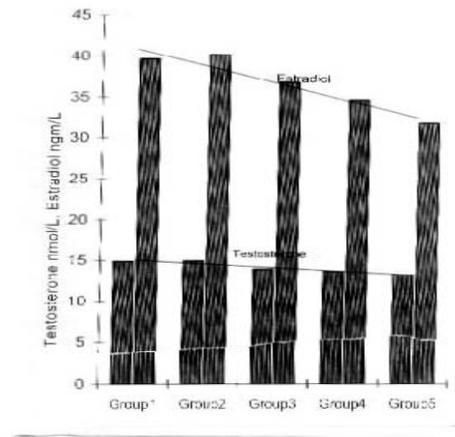
Figure 1. Mean serum concentration of total testosterone(left in each group) and estradiol (right in each group) of different age groups. Group 1-(40-50yrs), Group 2- (51-60yrs), Group 3-　(61-70yrs), Group 4-(71-80yrs) and Group 5- (81-90yrs). A downward trend with age is found for both estradiol and　testosterone but it is statistically significant only in case of　estradiol.

Table 1. Mean and SEM of the measured variables in different age groups.

Measured variable	Group-1 40-50 yrs (n=42)	Group-2 51-60 yrs (n=56)	Group-3 61-70 yrs (n=40)	Group-4 71-80yrs (n=28)	Group-5 81-90yrs (n=19)	p by Anova
Total testosterone						
nmol/L	14.91± .63	15.03 ± .53	14.08±.49	13.90± .61	13.53±.57	>.05
Estradiol						
ngm/L	9.72± 1.19	40.28± 1.21	36.91± 1.81	34.92± 1.39	32.18± 1.60	<.05
LH						
mIU/mL	7.67±.37	7.56± .42	7.92± .39	7.98± .43	8.85± .58	>.05
FSH						
mU/mL	8.28± .44	8.09± .49	8.23± .57	8.50± .49	8.83± .52	>.05
SHBG						
nmol/L	65.06± 2.51	64.51± 1.96	63.98± 2.08	64.85±2.11	63.06± 2.75	>.05

and the correlation coefficients of each measured variable with age in Table 2. Except with estradiol orrelations of each with age was statistically insignificant. In case of estradiol a statistically significant negative correlation with age (p < 0.05 in Pearson's test) was found.

Discussion

No significant change in total testosterone in advancing ages as has been found in our study is consistent with the results of similar studies done by several others.[9,14,16,17] However, most of the earlier studies reported age related decrease in testosterone concentration and apparently contradict with our findings.[4,5,6,17] Vermeulen et al divided all these studies in two groups one reporting decrease and the other reporting no change in serum testosterone in aging males.[5] These apparent discrepancies are

probably due to differences in the cinical characteristics of the study subjects and the laboratory methods employed in different studies.

Decreased serum testosterone has been found to be associated with different diseases like dyslipidemia, CHD, obesity and mental disorders of different intensities.[18,19] These diseases may remain subclinical and undiagnosed in elderly males. Inclusion of these subjects in the study can result in decreased testosterone concentration as has been reported earlier. Most studies reporting age related decrease in serum testosterone did not attempt to exclude such illnesses from their study population. The age ranges over which the observations were made in those studies also differ from our study and this may also partially account for the differences in the results of different studies. Most of the available studies included subjects as young as 20 years in contrast to our study where males of age > 40 years only were included.[6,7] It is probable that age related decline in testosterone as reported in some studies might have occurred in earlier age i.e., before 40 years and there was no or minimal decline in testosterone concentration after 40 years that is consistent with our finding. Few such studies found age related decline in testosterone concentration only when compared between the age groups > 40 with that of < 40 years.[20,21] However, a downward trend not sufficient to be statistically significant has also been found in our study. The inclusion of only the healthy subjects and observation over the age range >40 years are the two probable reasons that explain our finding of no age related decline in testosterone concentration.

No change in gonadotrophin levels as has been found in our study indicates no change in the pituitary gonadal axis with age among our study population. This finding is consistent with no change in testosterone concentration as was also found. For the healthy males, as included in our study, we considered this finding as expected. The increased SHBG in elderly males, reported in some studies differs from our results where no significant change was found.[10,11] This was also due to meticulous exclusion of subjects with any form of liver disease from our study. We think that there is no reason other than unrecognized or undiagnosed liver disease that can explain elevated SHBG in elderly males as has been reported by others.

A negative correlation of serum estradiol with age, found in our study, is also reported by Ferrini et al. and others.[23,24] Several earlier studies reported age related increase and in some studies no change with age in estradiol concentration.[23,25] It is known that estradiol in males are mainly derived from   peripheral aromatization of circulating androgens and obesity is a known factor determining the rate of aromatization. As our subjects were nonobese (Mean BMI 22-24 Kg/m^2 in different groups) and aged   subjects had significantly lower BMI (correlation of BMI with age -.15, p= 0.03) this might be one reason of lowered serum estradiol in our subjects.

It is concluded that no significant age related change occurs either in total serum testosterone, their pituitary regulation and in their serum binding by SHBG in males beyond forty years. Age related decline in serum estradiol needs more research.

Acknowledgements

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