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Study of the level of male sex hormones in elderly patients suffering from depression

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Abstract

Introduction: Testosterone is hormone that has unique effect on man's total body. Manifestations of low testosterone level in adult may include: low sex drive, emotional, psychological and behavioral changes. There is strong relation between depression and sexual dysfunction. **Objective:** the aim was to evaluate the level of male sex hormones in elderly men suffering from depression. **Methods:** This study included 60 subjects aged ≥ 65 years who were classified into two groups. Group I included 30 elderly depressed males, group II included 30 elderly non-depressed males. All participants were subjected to detailed history taking, routine laboratory investigations, sex hormonal assessment [total testosterone, sex hormone-binding globulin (SHBG), free androgen index(FAI)=total testosterone/SHBG*100] and depression scoring using Beck Depression Inventory(BDI).

Results: There was no significant differences regarding total testosterone levels however, the level of SHBG was significantly lower in group I and free androgen index (FAI)was significantly higher in group I, there were no significant differences regarding the marital status or smoking. There were no significant correlations between the studied groups regarding age with total testosterone, SHBG or free androgen index. There were non-significant negative correlations between BDI and total testosterone or SHBG and non-significant positive correlation between BDI and FAI in group l, but in group ll there were non-significant positive correlations between BDI and total testosterone or FAI and non-significant negative correlations between BDI and SHBG in group ll. **Conclusion:** The level of total testosterone revealed no significant change but SHBG was lower and FAI was higher in depressed elderly males.

Key words: depression**,** male sex hormones, elderly.

Introduction

The prevalence of testosterone deficiency increases with age. This is partly due to decreasing testosterone levels associated with illness or disability. Hypogonadism in older men is a syndrome characterized by the presence of low testosterone levels and clinical signs and symptoms of hypogonadism as decreased libido, impaired erectile function, muscle weakness, increased adiposity, depressed mood and decreased vitality (1). The symptoms and signs of hypogonadism in aging men vary depending upon the age, severity and duration of androgen deficiency, comorbid illnesses, androgen sensitivity and previous testosterone therapy (2).

The clinical symptoms and manifestations are more difficult to recognize because they may be masked by comorbid illnesses. There had been some controversy as to the significance of falling testosterone levels with age (3). The age related decline in testosterone levels is associated with a number of mild, nonspecific symptoms including depressive symptoms. The relationship between depressive symptoms and testosterone level is confound by numerous factors, including medical illnesses, obesity, smoking, alcohol use, diet and stress. Studies have not consistently supported an integral role reduced testosterone levels in major depressive disorder, although levels may often be reduced in men with treatment refractory depression and older men with dysthymia. Testosterone replacement has demonstrated short term tolerability and efficacy in augmenting antidepressants to alleviate treatment refractory depression in adult males. Case studies support the potential need for maintenance therapy to maintain response (4). Age-related serum testosterone decline is caused by different simultaneous mechanisms, such as primary structural gonadal impairment, age-related degenerative modifications of the pituitary gland, deficits of the neuro-hypothalamic system, and primary peripheral metabolic abnormalities such as age associated increase of serum sex hormone binding globulin (SHBG) with a consequent decrease in free testosterone(FT) (5). Levels of SHBG increase at rate 1.2% per year. There are positive associations between SHBG levels and old age male depression as well as mortality (6). It is controversial whether aging is considered as the only variable linked to age related testosterone decline (7). Several factors interfere with testosterone metabolism like genetic factors (8), chronic diseases (9), chronic medications (10), obesity (11), and life style factors (12).

Despite the fact that many men with low testosterone levels are asymptomatic, many others had a partial, gradual and variable decline in testosterone associated with various clinical symptoms described as a syndrome called partial androgen deficiency of aging male(PADAM) (13). PADAM is characterized by sexual, somatic, and behavioral symptoms with insidious onset and slow progression (14): diminished sexual desire and erectile quality (15), decrease in lean body mass with associated diminution in muscle volume and strength, increase in visceral fat (16), decrease in bone mineral density resulting in osteoporosis (17), reduction in body hair and skin alteration (18), weakness, fatigue, depression, lack of motivation and energy, anxiety, irritability, insomnia and memory impairment(19,20).

PADAM as a clinical entity is still controversial, because it is very difficult to

distinguish to what extent the symptoms attributed to PADAM are due to the natural and unavoidable consequences of aging and how much to androgen deficiency. Behavioral aspects of PADAM may overlap with signs of depression (21).

Objective:

The aim of this study was to evaluate the level of male sex hormones in elderly men suffering from depression.

Subjects:

This study included 60 subjects aged ≥65 years who were classified into two groups: Group I included 30 elderly depressed males and group II included 30 elderly non-depressed males who were attending Geriatrics outpatient clinics Alexandria Main University Hospital during the period from January till Decemder2017.

The exclusion criteria:

Subjects that were suffering from diabetes mellitus, renal failure, liver failure, endocrinal diseases related to sexual dysfunction, cerebrovascular stroke, drug therapy that induce sexual dysfunction as a side effect, neurological deficit or drug induced depression were excluded from the study.

Methods:

This prospective study included 60 subjects that were recruited after obtaining informed consent then thorough history taking and complete physical examination were done. Routine laboratory investigations including [complete blood count, blood urea, serum creatinine, liver function tests (Serum glutamic pyruvic transaminase (SGOT), Serum glutamic oxalacetic transaminase (SGPT), serum albumin), fasting and post prandial blood glucose, serum uric acid and Thyrotropin binding globulin (TSH)].

Total testosterone measurement by ELISA technique (22). The level of sex hormone-binding globulin(SHBG) was measured and Free androgen index (FAI) (23) was calculated: FAI=total testosterone/SHBG*100.

Depression scoring: Beck Depression Inventory (BDI) (24) was used to assess the presence and severity of depression. BID was used as it was considered one of the most widely psychometric tests for measuring the severity of depression. The BDI questionnaire consists of 21 groups of statements and the participants read each group and then picked out the statement in each group that best described the way they had been feeling during the past two weeks including the day of assessment. If several statements in the group seemed to apply equally well, they had to choose the highest number for that group. The questionnaire included the following symptoms: sadness, pessimism, past failure. Loss of pleasure, guilty feelings, punishment feelings, self-dislike, self-criticalness, suicidal thoughts or wishes, crying, agitation, loss of interest, indecisiveness, worthlessness, loss of energy, change in sleeping pattern, irritability, changes in appetite, concentration difficulty, tiredness or fatigue and loss of interest in sex. Each question had a set of at least four possible responses, each answer being scored on a scale value of zero to three. Scores can range from 0 to 63. Depression was diagnosed on BDI score more than 10.

Statistical analysis

Data entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences

(SPSS software package version 18.0 Baseline characteristics of the study population were presented as mean values and standard deviations (SD) or median and interquartile range (range). For comparison of data, Chi-Square test was used to compare two independent groups of qualitative. For quantitative data, Independent-Samples t-test was used. Mann-Whitney U test were used to compare two groups of parametric and non-parametric quantitative data respectively. For all tests, P values <0.05 are considered significant. Spearman correlation coefficients were used to assess the significant relation between two quantitative parameters in the same group. All results were interpreted at 5% level of significance where the difference between the study groups is considered significant if P is ≤ 0.05.

Results:

The current study the mean age of group l was (74.53±7.24) and in group ll was (75.65±5.97) with no statistically significant difference (t=0.655, p=0.515). There was no statistically significant difference between the studied groups regarding the marital status (z=0.034, p=0.973) table (1).

The results of the current study showed no statistical significant differences between the studied regarding the routine laboratory investigations (table2). The mean level of total testosterone was (4.07±1.28) in group l and (3.87±1.07) in group ll (t=0.660, p=0.512) with no statistically significant difference. SHBG mean level in group l was (54.43±31.34) and in group ll (74.52±39.16) with statistically significant difference between the studied groups (z=2.049, p=0.049). The mean value for FAI in group l was (36.70±33.83) and in group ll (23.08±13.89) with statistically significant difference between the studied groups (z=2.208, p=0.027) (table3). There was no statistically significant difference between the studied groups regarding smoking (X^2=0.012, p=0.912) (table 4).

There were no significant correlations between the studied groups regarding age with total testosterone, SHBG, and free androgen index (table 5). There were non-significant negative correlations between BDI and total testosterone or SHBG and non-significant positive correlation between BDI and FAI in group l, but in group ll there were non-significant positive correlations between BDI and total testosterone or FAI and non-significant negative correlations between BDI and SHBG in group ll (table 6).

Table (1): Comparison between the two studied groups according to demographic data.

	Group I Depressed (N=30)	**Group II Non depressed (n=30)**	**T**	**P**
Age (years)				
Min- Max	65.0-85.0	65.0-85		
Mean± SD	74.53±7.24	75.65±5.97	0.655	0.515
Median	76.0	75.0		
			Z	**P**
Marital status				
Min-Max	1.0-2.0	1.0-2.0		
Mean±SD	1.07±0.25	1.06±0.25	0.034	0.973
Median	1.0	1.0		

t: student t-test
Z:Z for Mann Whitney test
p: p value for comparing between the studied groups
*:Statistically significant at p≤0.05

Table (2): Comparison between the two studied groups according to routine laboratory investigations.

	Group I Depressed (n=30)	Group II Non depressed (n=30)	t	P
HB (g/dl)				
Min-Max	11.0-14.0	11.0-14.0		
Mean±SD	12.28±0.88	12.37±0.93	0.392	0.696
Median	12.20	12.30		
BUN (mg/dl)				
Min-Max	7.0-15.0	6.0-15.0		
Mean±SD	10.57±2.53	10.81±2.89	0.344	0.732
Median	10.0	11.0		
Creatinine (mg/dl)				
Min-Max	0.40-1.20	0.50-1.20		
Mean±SD	0.86±0.20	0.84±0.20	0.415	0.680
Median	0.90	0.90		
Uric acid (mg/dl)				
Min-Max	4.0-7.0	3.0-7.0		
Mean±SD	5.40±0.92	5.36±0.99	0.185	0.854
Median	5.15	5.30		
SGOT (U/L)				
Min-Max	40.0-45.0	40.0-45.0		
Mean±SD	42.27±1.82	42.65±1.66	0.849	0.400
Median	42.50	43.0		
SGPT (U/L)				
Min-Max	30.0-45.0	30.0-45.0		
Mean±SD	38.13±5.10	38.84±4.54	0.571	0.570
Median	39.0	40.0		
FBG (mg/dl)				
Min-Max	100.0-126.0	100.0-125.0		
Mean±SD	115.80±7.74	112.45±8.21	1.638	0.107
Median	118.50	113.0		

t: Student t-test
p: p value for comparing between the studied groups
*: Statistically significant at p≤0.05
HB: Hemoglobin
BUN: blood urea nitrogen
SGOT:Serum glutamic pyruvic transaminase
SGPT: Serum glutamic oxalacetic transaminase
FBG: Fasting blood glucose

Table (3): Comparison between the two studied groups according to sex hormones.

	Group I Depressed (N=30)	**Group II Non depressed (n=30)**		
			T	**p**
Total testosterone ng/ml Min-Max Mean± SD Median	 0.90-8.0 4.07±1.28 3.80	 0.50-5.10 3.87±1.07 4.0	 0.660	 0.512
			Z	**p**
SHGB (nmol/l) Min-Max Mean±SD Median	 10.0-150.0 54.43±31.34 50.0	 22.0-170.0 74.52±39.16 65.0	 2.049*	 0.049*
FAI Min-Max Mean±SD Median	 11.53-191.0 36.70±33.83 30.13	 2.42-63.10 23.08±13.89 20.10	 2.208*	 0.027*

t: Student t-test
Z: Z for Mann Whitney test
p: p value for comparing between the studied groups
*: Statisstically significant at p≤0.05
SHGB: sex hormone-binding globulin
FAI: Free androgen index

Table (4): Comparison between the two studied groups according to smoking.

	Group I Depressed (N=30)		**Group II Non depressed (n=30**		X^2	P
	No.	**%**	**No.**	**%**		
Smoking						
Smoker	17	56.7	18	58.1	0.012	0.912
Non -smoker	13	43.3	13	41.9		

X^2: Chi square test

Table (5): Correlation between age with sex hormones in each group.

	Age Group I Depressed		**Age** Group Non depressed	
	r	p	r	p
Total testosterone	-0.209	0.269	-0.277	0.131
SHBG	0.257	0.170	0.071	0.703
Free androgen index	-0.308	0.098	-0.279	0.128

r: Pearson coefficient

Table (6) correlation between BDI with hormones in each group.

	BDI Group I Depressed		**BDI** Group II Non depressed	
	r_s	p	r_s	p
Total testosterone	-0.062	0.745	0.048	0.797
SHBG	-0.309	0.096	-0.121	0.516
Free androgen index	0.352	0.056	0.121	0.517

r_s: Spearman coefficient

Discussion:

The current study was performed on 60 elderly subjects aged ≥65 years who were attending Alexandria Main University Hospital and were divided into two groups: group I included 30 elderly depressed males and group II included 30 elderly non depressed males. The results of this study revealed that there were no statistical significant differences between the two studied groups regarding age (t=0.655, p=0.515), or total testosterone level (t=0.660, p=0.512). In agreement with these results the study performed by Mario, et al (25) who summarized current knowledge on depressive symptoms correlated with PADAM and on the potential benefit of testosterone on mood and they found that, there were no statistical significant differences between their studied groups regarding age or total testosterone level.

In contrast to this result, the study performed by Westly et al (26) who found that aging men whose testosterone drop had increased risk for depressive disorder. Also longitudinal analyses in men revealed inverse associations between total testosterone (TT) and depressive symptoms in 5 and 10-year follow-up, but only in age-adjusted models. The link between low TT and depressive symptoms is described in previous meta-analysis and observational research, which suggest that low TT concentrations are associated with an earlier onset and greater incidence of depressive illness in older men (27).

In this study there were statistical significant differences between the two studied groups regarding SHBG level which was lower in group I than group II (z=2.049, p=0.049) and Free androgen index which was significantly higher in group I (z=2.049,

p=0.049). These results were similar to the study done by Hanna Kische et al (28) who found inverse relationship between SHBG and depression. Contrarily, even in older men a study on androgen concentrations and androgen receptor polymorphism did not support a link between androgens and depressive symptoms based on the Geriatric Depression Scale (29). Also in contrast to this study the results of the study performed by Samuel Yet al (30) who reported that there was no significant difference between depressive symptoms and SHBG or free androgen index. In contrast to these results the study performed by Hintikka et al (31) who examined the association between hypogonadism (laboratory diagnosis was based on free testosterone (FT)<4.6ng/dl), erectile dysfunction, sexual desire, and long term and current depressive symptoms in population based sample of Finnish middle-aged men. The inclusions of that study were based on self-reported adverse mental symptoms prevailing at baseline and at three year follow up. They found that men who reported long-term adverse mental symptoms had higher depression but lower FT levels than asymptomatic men

There was no statistical significant difference between the two studied groups regarding the marital status (z=0.034, p=0.973). In contrast with these results the study done by Philip Donalad (32) who stated that married men had lower level of depressive symptoms than unmarried men. In this study there was no statistical significant difference between the studied groups regarding smoking and this came in contrast to the study performed by Shuai Yuan (33) who found that smoking was causally associated with depression.

There was no significant correlation between the studied groups regarding age with total testosterone, SHBG, and free androgen index in this study. These results were partially similar to the study performed et al by Yasuhiro (34) who investigated the associations between depression and serum testosterone levels in the eldery and they stated that there was no significant correlation between testosterone and depression scores or age.

In the current study there were non-significant negative correlations between BDI and total testosterone or SHBG in group l and this was partly similar to the study performed by Seidman et al (35) who found negative correlation between total testosterone and depression scores. Also in agreement with these results the study done by Almeida et al (36) who stated that there was negative correlation between testosterone level and depression scores. In contrast to the results of this study the results of the studies done by Wu FCW et al (37) and Kische H et al (38) who stated that there was no association between testosterone level and depressive symptoms. In this study there was non-significant positive correlation between FAI and BDI and this was in contrast to the studies performed by Delhez et al (39) who found negative correlation between free testosterone and BDI. Previous studies of sex hormones and depression in elderly men, including clinical trials, had yielded mixed results, possibly

reflecting the different patient populations and androgen assays.

Conclusion: The level of total testosterone revealed no significant change but SHBG decreased and FAI increased in depressed elderly males

Limitation of the study: Sample size is small. Body mass index and nutritional

assessment were not performed. Patients recruited from one hospital in Alexandria, so our results could not be generalized.

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