Research Article

PSA and Testosterone Serum Levels in the Middle East; Is there a Difference?

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Abstract

Objective: To evaluate the difference between testosterone and total prostate specific antigen (TPSA) serum levels between Arabic and Turkish people in the Middle East.

Material and methods: The study included 3 groups of healthy men; Group I included 119 patients with a mean age of 52.73 ± 7.53 years from east of Turkey. Group II consisted of 196 patients with a mean age of 50.32 ± 7.84 years from west of Turkey. Group III consisted of 388, with mean age of 51 ± 6 years from west bank in Palestine. The mean values of PSA and testosterone were calculated for each groups and a comparison were carried out. The relationships among testosterone and TPSA levels and patients' age were investigated.

Results: The mean TPSA levels for Group I, Group II and group III were 1.11 ± 0.78 ng/mL and 1.75 ± 1.06 ng/mL and $1.1+8$ ng/ml respectively ($p=0.5$, $p=0.7$, $p=0.8$ respectively). The mean testosterone levels in Group I (386.4 ± 154.6 ng/dL), Group II (383.9 ± 170.6 ng/dL) and group III (380 ± 230 ng/L) showed no significant difference ($p=0.89$, $p=0.29$, $p=0.7$). In Group I there was a positive correlation between age of the patients and testosterone level ($r=0.22$, $p=0.015$); however, in Group II, and group III there were significant negative correlation between age and serum testosterone levels ($r=-0.16$, $p=0.022$ and $r=-0.29$, $p=0.01$). Serum testosterone level showed no significant correlation with TPSA level in all groups.

Conclusion: Testosterone or TPSA levels did not change among the groups. However, the effect of age on testosterone levels varies according to different geographical regions.

ABBREVIATIONS

TPSA: Total Prostate Specific Antigen; DRE: Digital Rectal Examination; DHEA: Deydroepiandrosterone; TRT: Testosterone Replacement Therapy; LOH: Low Onset of Hypogonadisim;

INTRODUCTION

The sordid past of testosterone began in 1941 when Charles Huggins demonstrated that metastatic prostate cancer (PCa) was activated by androgens and inhibited by their absence [1]. Since then, many reports have documented the importance of serum androgen in the progression and control of prostate cancer. However, there is a controversy regarding the role of androgen in the pathophysiology and clinical treatment of men at risk of prostate cancer. Testosterone is essential for health and well-being of humans. It has been postulated to play role in the cognitive function and Alzheimer disease, as well [2]. There

is variation in the serum level of testosterone and PSA along the life of the human being; while PSA value increase with age, testosterone serum level goes down. The national and geographic variation in testosterone is also well known. The American black are known to have high serum testosterone level and more aggressive advance prostate cancer [3,4]. In a recent study we have investigated the difference in serum testosterone level between two different geographic regions in Turkey and we have found no difference neither in testosterone serum level nor in the TPSA values [5]. The relation between the testosterone level and prostate cancer is well established but ill defined. However the expected relation between TPSA and serum testosterone is unclear; PSA goes down with castration and low testosterone serum level, however the opposite is not correct. Therefore in another recent study we have investigated the relation between PSA serum level and testosterone level [6]. We couldn't detect any correlation between PSA and serum testosterone serum

level in healthy men [6]. Here in we investigated the difference between the serum levels of testosterone and TPSA between Turkish and Arabic people and we evaluated the relation between testosterone serum levels and TPSA values in both people.

MATERIALS AND METHODS

The study included three separate groups of healthy men from two geographically distinct regions in Turkey and the third group from Palestinian people. Group 1 included 119 patients with a mean age of 52.73±7.53 years who visited Osmaniye State Hospital in the east of Turkey for routine check-up between January 2006 and January 2007. Group 2 consisted of 196 patients with a mean age of 50.32±7.84 years who visited the outpatient clinics in Izmir Ataturk Teaching Hospital in the west of Turkey between July 2008 and July 2009. Group III consisted of 388, with mean age 51±6 years who visited Palestinian state hospitals in west bank in Palestine between November 2011 and May. 2012. In general Osmaniye region is characterized by a low socioeconomic level, high fat diet and hot climate. Izmir district is characterized by high socioeconomic level, low fat diet, and high fruit and vegetables consumption. The inclusion criteria for all groups were the same; males aged 40-60 years old, men with PSA level less than 4 ng/ml, normal urine analysis, normal urine culture, normal digital rectal examination (DRE) for men older than 50 years old, normal kidney function test, normal liver function test and no previous prostatic surgery. The blood sample for serum testosterone and TPSA levels were taken in the morning. The mean values of TPSA, testosterone and age were calculated for each group. A comparison between the mean values of the groups was done. The relation between TPSA and testosterone in each group was also investigated.

Statistical analysis

All data were expressed as mean ± standard deviation (SD). Independent sample t-test was used to compare the blood test values between groups. Pearson correlation test was applied to estimate the correlation between testosterone levels and TPSA values. The SPSS for Windows 10.0 was use for statistical analysis and P value less than 0.05 were considered statistically significant.

RESULTS

The mean values of TPSA, testosterone for all groups were similar. The mean TPSA levels for Group I, Group II and group III were 1.11±0.78 ng/mL and 1.75±1.06 ng/mL, 1.1+8 ng/ml respectively (p=0.5, p=0.7, p=0.8 respectively). The mean testosterone levels in Group I (386.4±154.6 ng/dL), Group II (383.9±170.6 ng/dL) and group III (380±230 ng/L) showed no significant difference (p=0.89, p=0.29, p=0.7). The mean values of ages, serum testosterone levels and TPSA values are summarized in table 1. In Group I there was positive correlation between age of the patients and testosterone level (r=0.22, p=0.015). However in group II there was significant negative correlation between patient age and serum testosterone level (r=-0.16, p=0.22). Similarly in group III there was negative significant correlation between patient age and testosterone level (r=-0.29, p=0.01). Regarding the relation between TPSA and testosterone, there was no significant correlation in all groups. The association between serum testosterone level, age, and TPSA was demonstrated in table 2. The Pearson's correlation coefficients (r) and p values in group I, group II, group III were (r=0.03, p=0.72), (r=-0.04, p=0.67), (r=0.05, p=0.34) respectively.

DISCUSSION

It is well known that there is variation in testosterone level in individual. It is likely that multiple factors are involved, including socioeconomic, environmental, dietary, and genetic factors. Black men present with more advance disease at younger age than white men with prostate cancer. The difference in androgen level between black and white American was noted only in men less than 40 years old. There was no difference in serum testosterone level detected in men with and without prostate cancer [7]. In our present study we couldn't detect any significant difference between all groups in term of serum testosterone level. Although we had ethnic, geographic and dietary differences among the groups. But this doesn't mean not to have difference in the serum level of testosterone in all age groups. Because our age group was limited to men between 40 and 60 years old and as we know the surge of testosterone level appear before 40 years old. Therefore to make sure whether there is a difference in serum testosterone

Table 1: Mean values of age, testosterone serum levels and TPSA for all groups.

	Patient (n)	Age (year)	Testosterone (g/dL)	TPSA (ng/mL)
Group I	119	52.73±7.53	386.4±154.6	1.11±0.78
Group II	196	50.32±7.84	383.9±170.6	1.75±1.06
Group III	388	51±6	380±23	1.1±0.8
P		>0.05	>0.05	>0.05
N: Number of the patient, TPSA: Total Prostate Specific Antigen				

Table 2: Pearson correlation coefficient (r) between serum testosterone level, age and TPSA.

	Group I	Group II	Group III
Age versus testosterone	R=0.22, p= 0.015	R=-0.16, p= 0.02	R=-0.29,p=0.01
TPSA versus testosterone	R=0.032,p=0.72	R=-0.04,p=0.67	R=0.05,p=0.34
Age versus TPSA	R=0.25,p=0.25	R=0.19,p=31	R=0.2,P=0.34
TPSA: Total Prostate Specific Antigen			

level we should examine testosterone level in men with ages less than 40 and we should determine the weights of the patients in all groups, because weight and waist circumference have significant impact on testosterone level [7]. In group II and III there was continuous decline in the serum testosterone level. This finding correlates with the data in the literature. Aging results in an increase in sex hormone binding globulin, testosterone, deydroepiandrosterone (DHEA), estrogen, and free biologically active androgen [8]. Between the age of 30-80 years old the mean free testosterone index (the ratio of serum total testosterone to sex hormone binding globulin) decrease by as much as 50% in men [9]. In group I there was positive correlation between serum testosterone level and age of the patients. This finding deserve to be evaluated, because this is opposite to the known in the literature and the increment in serum testosterone level may have effect on a lot of diseases which have relation with testosterone. Despite decades of research on the relationship between testosterone and related disease, like cognitive function, Alzheimer disease, urological disease, TPSA and prostate cancer many questions remained [2]. Regarding the prostate cancer some studies support the role of testosterone in initiation of prostate cancer as in the black American [7]. Two theories have been proposed to explain the relationship between prostate cancer and serum testosterone level: suppression theory which sate that malignant cells secrete androgen inhibitors and saturation theory which state that levels of serum androgen above baseline level are sufficient to stimulate prostate growth (benign or malignant). Some studies have claimed that low testosterone level might be relate to worse clinical outcomes, including risk of prostate cancer, [10], higher gleason score [11,12], and worse pathological stage [13,14]. Therefore increase effort toward patient's awareness and TPSA screening are certainly warranted. We recommend DRE and TPSA screening test for group I and further studies to investigate the difference in the testosterone level. In men with high testosterone level like black American, the threshold of TPSA for prostate biopsy should be is 2.5 ng/ml [15].

The relationship between serum TPSA and testosterone levels is still controversial. In our study there was no association between TPSA values and serum testosterone level in our study. In some studies TPSA was reported to be increased in response to all types of testosterone replacement regardless of whether the testosterone level was raised endogenously or exogenously [16]. Rastrelli et al., investigated the relation between serum testosterone level and TPSA and he concluded that PSA is a marker of T concentrations and it may represent a new tool in confirming hypogonadism [17]. However some studies showed that TPSA remain stable after the normalization of testosterone level [18]. This findings was supported by the study of Marks et al who investigated the effect testosterone replacement therapy (TRT) and suggested that TRT for 6 months in patients with low onset of hypogonadism (LOH) cause no significant on the prostatic tissue [19]. This may be justified by the fact that intraprostatic tissue is not under the direct effect of serum testosterone rather than it is under the effect of DHEA and 5 alpha reductase enzymes. There is no evidence that higher endogenous testosterone increases the risk of prostate cancer nor induces it. Our study differs from the previous mention studies in that it was conducted in healthy men and not in hypogonadism patients who receive TRT. Our aim

was to detect if there is need to adjust the TPSA value in those high serum level. Even in group I where there was increase in testosterone level there was no correlation detected between TPSA and serum testosterone. This mean that TPSA is a valid biomarker for prostate cancer, but it can't predict the unclear but established effect of sex hormone on prostate cancer. Whether low or high serum level of testosterone the variation in the sex hormone level should be investigated thus the management of some diseases which are reported to be with direct relation of this hormone can be adjusted accordingly. People with high serum testosterone can be considered as risk group for the development of prostate cancer with more aggressive oncologic features. Thus screening test with TPSA and DRE should be recommended for such men. Hopefully the result of such program would be to increase the percentage of men diagnosed with organ confined prostate cancer especially in people located in high risk group. Therefore we do recommend the determination of sex hormone concentration for each nation incase variation in the testosterone level may be present thus different characteristic of many urological and non urological disorders are expected.

The low number of patients, not including patients with ages less than 40 years old, absence of determination of weights, serum levels of free testosterone, and prostatic tissue level, of testosterone and DHEA can be considered to be limitations of our study.

CONCLUSION

Testosterone or TPSA levels did not change among different nations or different geographical regions in the Middle East. However, the effect of age on testosterone levels varies according to different geographical regions. The impact of geographic and national variations on the oncologic features of prostate cancer and other urologic and non urological diseases should be investigated. Further studies with more patients from different nations in the region are needed to confirm these preliminary results.

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