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Research Article

Marital Status and Serum Level of Testosterone: In Relation to Serum Level of Cortisol

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Abstract

Purpose: To explore the association between marital status and testosterone, and cortisol serum levels in 119 healthy men aged 45 to 60 years representing the general population.

Material and Methods: Data on men's age, waist circumference, body mass index, smoking, alcohol consumption, and marital status were collected. Serum levels of LH, testosterone, and cortisol were also measured. Two groups were identified according to marital status: paired (married, living together, and living apart) and unpaired men (divorced or separated).

Results: The participants had a mean age of 55 (± 4.0 years). Testosterone level was significantly lower in paired as compared to unpaired men (14 nmol/L *vs.* 19 nmol/L, $p = 0.01$). The opposite trend was found regarding cortisol levels (350 nmol/L *vs.* 293 nmol/L, $p = 0.01$). No significant differences between the two groups were found regarding men's age, body mass index, waist circumference, and LH level ($p > 0.05$). Using a multivariate regression analysis test adjusted for men's age, body mass index, waist circumference, smoking, and alcohol consumption; a significant negative association between marital status and testosterone level (β = -04.00; 95% CI = -7.00, -1.00; $p = 0.01$), and a significant positive association between marital status and cortisol level (β = 47.00; 95% CI = 6.00, 89.00; $p = 0.03$) were found.

Conclusions: Paired men were associated with lower testosterone levels. These findings might be partially explained by the concomitant higher cortisol level found in this group of men.

Introduction

Testosterone is not only essential for male reproductive function and virilization [1,2] but also for cognitive health and well-being [3]. Luteinizing Hormone (LH) is considered as a good marker of testicular function, in this line negative significant correlations were found between LH and testicular volume, and testosterone level [4-6].

The association between marital status and testosterone levels has been subjected to analyses in a large number of studies, and paired men were found to have lower levels of testosterone compared to unpaired men. Several theories were previously used to explain this association including relationship orientation [7], male pair bonding status and fatherhood [8-11], and changes in the hypothermic-pituitary-gonadal system due to an adjustment to life changes [12].

Cortisol is essential in stress-response mechanisms and unpaired men were found to have higher levels of salivary cortisol as compared to paired men [13,14]. The difference in cortisol levels was explained by interpersonal stress experienced by the unpaired men as compared to paired men [13].

Herein, the possible impact of marital status on serum levels of testosterone and cortisol is investigated based on data from 119 healthy men aged 45 years – 60 years representing the general population considering covariables such as men's age, Body Mass Index (BMI), waist circumference, smoking, and alcohol consumption in the analyses.

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Material and methods

Participants

The present study is a part of a large study carried out to explore the relationship between male sexual function and risk of early cardiovascular disease based on data from 119 healthy men aged 45 to 60 years, representing the general population collected between the years 2006 and 2011. A detailed information was published by Elzanaty, et al. 2017 [15].

Exclusions criteria

Men were excluded if they indicated a history of medical disease, including cardiovascular disease, hypertension, diabetes, inflammatory/or infectious disease, and psychological illnesses, or were taking regular medications during the last 6 months before the start of the study. Exclusion criteria include also men aged from 45 to 60 years at the time of inclusion.

Collected data

Information about men's age (years), height (cm), weight (cm), BMI (kg/cm²), waist circumference (cm), smoking (never, past/current), alcohol consumption (yes, no), and marital status were collected. Fasting blood samples were taken from men who were found illegible for the study to measure the concentrations of serum LH, testosterone, and cortisol. Blood samples were delivered between 07:00 and 10:00 AM.

Hormonal analyses

Plasma samples were stored in the biological bank at -80 °C. Serum testosterone, LH, and cortisol concentrations were measured using a Two-step competitive method with ElectroChemiLuminiscenceImmunoassay (ECLIA) detection method based on Ruthenium (Ru) derivatives, which has an intra-and interassay coefficient of variation (CV) of 5%. With measuring range: 0.087 – 52.0 nmol/L, 0.10 – 200 IE/L, 1.5 – 1750 nmol/L, respectively, and reference range: 5.0 – 30 nmol/L, 1.7 – 8.6 IE/L, 133 – 537 nmol/L, respectively. Missing data were found on these variables: testosterone [number = 11 (9%)], and LH & cortisol [number = 13 (11%)].

Marital status

Paired men including those who are married, not married but living together, and not married but living apart together. Unpaired men including those who are divorced or separated at least 6 months from the time of inclusion. The main outcome measure was the impact of marital status on serum levels of testosterone and cortisol.

The present study protocol was reviewed and approved by the institutional review board of Lund University Hospital (Reg. No. 400/2005). Informed consent was submitted by all subjects when they were enrolled.

Statistical analyses

Statistical analyses were done using the SPSS software, version 20 (SPSS, Inc; Chicago, IL). Nonparametric Mann-Whitney U test was applied to compare men's age (years), BMI (kg/cm²), waist circumference (cm), levels of LH (IE/L), testosterone (nmol/L), and cortisol (nmol/L) between the study groups (paired men versus unpaired men).

To test the impact of marital status with paired men as a reference group on serum levels of LH (IE/L), testosterone (nmol/L), and cortisol (nmol/L); a multivariate regression analysis model adjusted for men's age (continuous years); BMI (continuous kg/cm²); waist circumference (≤ 99, > 99 cm), smoking (never, past/current); and alcohol consumption (0 – 10, 10 – 20, >20 cL/week) was conducted.

Results

Table 1 summarizes the demographic statistics of the study population. Serum level of testosterone was significantly lower in paired men as compared to unpaired men (14 nmol/L *vs.* 19 nmol/L, $p = 0.01$). While, serum level of cortisol was significantly higher in paired men than in unpaired men (350 nmol/L *vs.* 293 nmol/L, $p = 0.01$). On the contrary, no significant differences between groups regarding men's age (years), BMI (kg/cm²), waist circumference (cm), and serum levels of LH (IE/L) were found ($p > 0.05$) (Table 2).

A significant negative association between marital status and serum level of testosterone (β = -04.00; 95% CI = -7.00, -1.00; $p = 0.01$), and a significant positive association between marital status and serum level of cortisol (β = 47.00; 95% CI = 6.00, 89.00; $p = 0.03$), were found. On the other hand, no association between marital status and serum level of LH was found ($p > 0.05$) (Table 3).

Table 1: Descriptive statistics of the study population.

Variables	n	Mean (±SD) or %	Range
Age (years)	119	55 (±4.0)	46 - 60
BMI (kg/cm²)	117	27 (±3.0)	20 - 38
Waist circumference (cm)	118		
≤ 99	59	93 (±4.0)	79 - 99
> 99	59	108 (±7.0)	100 - 132
Relationship status:	118		
Paired	95	80%	-
Unpaired	24	20%	-
Smoking:	118		
Never	61	52%	-
Past/current	57	48%	-
Alcohol consumption (cL/week)	116		
0-10	56	47%	-
20-Oct	41	34.50%	-
> 20	22	18.50%	-
Biochemical markers:			
LH (IE/L)	106	4.4 (±2.0)	1.5 - 11
Testosterone (nmol/L)	108	15 (±7.0)	0.6 - 32
Cortisol (nmol/L)	106	339 (±92)	132 - 662

Data are mean (±SD) or (%), range. BMI = Body Mass Index; LH: Luteinizing Hormone

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Table 2: The demographic and biochemical markers according to the marital status obtained from 119 middle-aged men from the general population.

Variables	*n*	Normal range	Marital status		*p*
			Paired n = 95	Unpaired n = 24	
Age (years)	119	-	55 (±4.0)	56 (±4.0)	0.2
BMI (kg/cm²)	117	-	27 (±3.0)	26 (±4.0)	0.5
Waist circumference (cm)	118	-	100 (±9.0)	101 (±13)	0.9
LH (IE/L)	106	1,5 - 9,3	4.4 (±2.0)	4.5 (±2.0)	0.6
Testosterone (nmol/L)	108	5,7 - 25,2	15 (±6.0)	19 (±8.0)	0.01
Cortisol (nmol/L)	106	133 - 537	350 (±93)	297 (±75)	0.03

Data are mean (±SD). Statistical analysis was done using the Mann-Whitney U test. *p* - values below 0.05 are considered statistically significant.

Table 3: Associations between marital status and serum levels of LH, testosterone, and cortisol obtained from 119 middle-aged men from the general population.

Variables	Marital status			
	β	*p*	95% CI Lower	95% CI Upper
LH (IE/L)	-2	0.1	-3	0.4
Testosterone (nmol/L)	-4	0.01	-7	-1
Cortisol (nmol/L)	47	0.03	6	89

Statistical analysis was done using multivariate regression analysis model adjusted for age of subjects (continuous years), BMI (continuous kg/cm²), waist circumference (≤ 99, > 99 cm), smoking (never, past/current), and alcohol consumption (0-10, 10-20, >20 cL/week). *p* - values below 0.05 are considered statistically significant.

Discussion

Paired men had significantly lower testosterone levels and significantly higher cortisol levels compared to unpaired men. These findings were further confirmed in a multivariate regression analysis test adjusted for men's age, BMI, waist circumference, smoking, and alcohol consumption, thus marital status showed a significant positive association with cortisol and a significant negative association with testosterone. The present results are in line with previous findings that paired men are associated with lower levels of testosterone [7-12]. The lower levels of testosterone among paired men might be partially related to the higher levels of serum cortisol.

The age, BMI, and waist circumference did not differ significantly between paired and unpaired men, thus the differences in testosterone levels in this study seem not related to differences in the aging process or changes in body configurations between men in the two groups. Moreover, no significant difference between paired and unpaired men regarding serum levels of LH which supports the previous suggestion that the difference in testosterone levels between paired and unpaired men did not reflect significant differences in testicular function between men in the two groups [12].

Interestingly, paired men in the present study had significantly higher levels of serum cortisol compared to unpaired men in disagreement with previous documentation [13,14]. Cortisol levels were measured in serum in the present study, whereas in previous studies it was measured in saliva. Salivary cortisol reflects approximately 50% of serum cortisol due to the conversion of the biologically active cortisol to cortisone by 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) enzyme in parotid and submandibular tissues [16,17]. The degree of activity of the 11β-HSD2 enzyme affects the levels of salivary cortisol [18], for this reason, it is believed that salivary cortisol is a less sensitive mirror of serum cortisol levels [19].

Exposure to chronic stress is suggested to induce higher HPA activity [20] resulting in increased serum cortisol levels and to induce lower HPG activity [21] resulting in decreased serum testosterone levels. In this line, Li, et al. observed higher serum cortisol and lower testosterone levels in 15 rats exposed to stress by placing them beside a cage containing native cats without direct contact, compared to the control group. Interestingly, the authors observed lower cortisol and higher testosterone levels in another 15 rats which exposed to a similar stress but received 2.5 g/kg of the Chinese medicine Schisandra chinensis (known to have a sedative effect) by intragastric administration twice per day for one week before modeling, compared to the exposed top stress. LH did not differ significantly between groups [22].

Previous works have attributed the lower testosterone levels in paired men to different theories including relationship orientation [7], male pair bonding status and fatherhood [8-11], and changes of the hypothermic-pituitary-gonadal system due to an adjustment to life changes [12,23]. In addition, one could argue that being pair-bonded buffers men against stressors, and as such paired men have higher average serum cortisol concentrations and lower average serum testosterone concentrations than unpaired men. Unfortunately, the design of the present study was not able to provide information on how much stress participants were experiencing at the time of the study, for which reason it was not possible to confirm whether the higher levels of cortisol observed in paired men were related to exposure to a higher level of chronic stress more so than would unpaired men. Therefore, the present results should be interrupted with caution.

Different factors have been postulated to affect circulating testosterone levels including diurnal variation where testosterone levels are highest in the early morning between 07.00 and 11.00 AM and lowest in the evening [24]. Available data regarding the impact of intermittent fasting on testosterone levels are inconsistent where some researchers recommended fasting samples [25], while others did not find significant differences in testosterone values between men with paired fasting versus non-fasting samples [26]. The same trend was found regarding circulating cortisol with the lowest values reported when people sleep, then rise upon awakening and peak approximately 40 min later [27], cortisol level then declines across the day reaching a nadir in the evening or during the night [28]. Intermittent fasting was found to have no impact on serum cortisol levels [29]. In accordance, in the present study samples were collected between 07:00 and 11.00 AM and all participants were fasting.

The present study has some weaknesses; the number of participants is small and is based on one analysis of testosterone and cortisol. Low testosterone values should be further confirmed by at least one more measurement. However, a single measurement of serum testosterone is considered

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sufficient to reliably reflect the annual mean testosterone level in healthy middle-aged men as previously reported [30]. Moreover, missing data for testosterone (9%), LH, and cortisol (10%) were found. Missing data is a common problem in most studies. In this matter, it has been stated that bias is likely in statistical analyses reported more than 10% missing data [31]. Our study groups are unbalanced with paired men representing 80% while unpaired men representing 20% of the study subjects. However, there is no standard definition of the number of subjects for the ideal small group, for which reason we believe that our results are still statistically valid.

Conclusion

Paired men were associated with significantly higher cortisol and lower testosterone levels compared to unpaired men. These novel findings suggest a possible link between marital status and the levels of these two hormones. We believe that the impact of marital status on testosterone levels is a complex process where several factors are involved. A large number of future studies are needed to investigate such factors simultaneously.

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