Original Article

# Serum testosterone and gonadotropins levels in patients with premature ejaculation: A comparison with normal men

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## Abstract

**Background:** To investigate the role of testosterone (T) in the pathogenesis of ejaculatory symptoms, particularly premature ejaculation (PE).

Materials and Methods: A total of 41 male patients with PE as well as 41 controls with no sexual dysfunction were recruited in this cross-sectional study. We used the stopwatch measurement to monitor the intravaginal ejaculatory latency time (IELT). Patients with mean IELT values lower than 60 s were considered to have PE. Serum levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), total testosterone (TT) and free testosterone (FT) were measured in patients as well as controls. Patients with thyroid dysfunction, hypogonadism, hypertension and dyslipidemia were excluded from the study.

**Results:** The serum levels of FT and FSH were significantly higher in cases ($P = 0.036$ and 0.003, respectively). There was no significant difference between TT, LH and PRL levels of the two groups.

**Conclusion:** Patients with PE have higher FT and FSH levels compared with normal men. The causative relationship between these entities and also the clinical importance of this finding has to be determined by more comprehensive studies.

**Key Words:** Follicle stimulating hormone, free testosterone, luteinizing hormone, premature ejaculation, testosterone

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## INTRODUCTION

Premature ejaculation (PE) is the most common form of sexual dysfunction in men.[1] National and international epidemiologic studies have shown that 20-30% of men are suffering from PE. Despite its high prevalence, this condition rarely motivates the patient for seeking medical consultation and referring to a recent study, only 9% of the patients sought help.[2] The definition of PE is still changing; the term, however, is mainly used when "persistent or recurrent ejaculation occurs with a minimal stimulation before, on or shortly after penetration and before the individual is willing for it. The individual has little or no voluntary control over the condition and therefore it may lead to distress in the sufferer and/or his partner".[3]

A significant correlation has been shown between the serum thyroid stimulating hormone (TSH)

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and mean intravaginal ejaculatory latency time (IELT) values; as a result, one would expect a considerable improvement in IELT by treating thyroid dysfunction.[4] Testosterone (T) is another hormone that controls ejaculation. For sexual activity to take place, synchronized transmission of sexual desire is needed. It arises from the brain and is transmitted to the periphery, resulting in penile erection, necessary for sexual intercourse. T has long been considered as an essential hormone in regulating this process, acting both at central and peripheral levels.[5]

Lifelong PE is defined as "early ejaculation in the majority of intercourse attempts with nearly every partner from the first sexual encounter onward that is probably the manifestation of neurobiological phenomenon."[6] It may have a genetic etiology or be related to disturbances in central serotonergic neurotransmission.[7]

To the best of our knowledge, only one study has reported the higher serum levels of T in PE patients. In the very study, Corona *et al*. linked delayed ejaculation (DE) with lower levels of the male hormone.[8]

In the current study, we compared the serum levels of T and some other hormones in lifelong PE patients with a control group.

## MATERIALS AND METHODS

This cross-sectional study was conducted on a series of 41 patients diagnosed with PE between April 2008 and January 2011 and 41 controls, from patients referred to the same out-patient clinic for reasons other than sexual dysfunction, including asymptomatic individuals with a positive history of resolved renal stone who came to the clinic for follow-up.

Patients with lifelong PE who had never received any treatment for their condition were enrolled. Those with sexual dysfunction secondary to erectile dysfunction due to using sympatholytic drugs or diabetes mellitus and to ejaculatory dysfunction because of prostatitis or multiple sclerosis, along with individuals with hyperthyroidism,[4] hypogonadism (defined as having total testosterone (TT) levels below 350 ng/dl), hypercholesterolemia,[9] hypertension[10] and those taking drugs, such as serotonin reuptake inhibitors or tricyclic antidepressants that may influence ejaculatory time were excluded from the study.

Committee of Ethics approved the protocol and all participants signed an informed written consent.

The diagnosis of PE was confirmed based on the IELT values; those with average last 3 IELTs values lesser than 60 s were diagnosed with the condition.[11] Patients' partners performed stopwatch measurements for a month to monitor IELT values.

Patient's weight, height and blood pressure values (mean of three measurements 5 min apart, in a sitting position with a standard sphygmomanometer) along with his smoking and ethanol and opium use habits were recorded. Blood samples to assess the serum levels of TT, free testosterone (FT), prolactin (PRL), follicle stimulating hormone (FSH), luteinizing hormone (LH), triglyceride (TG) and total cholesterol (TC) were drawn in the morning after an overnight fasting. All tests were performed by *chemiluminescent* method and Advia Siemens Centaur kits (Siemens Healthcare Diagnostic Inc., Malvern, Pennsylvania, USA), except FT measurement that was performed by the enzyme-linked immunosorbent assay method using the Monobind kits (Monobind Inc., California, USA).

Since thyroid function has a relationship with IELT, TSH was a measure to rule out thyroid dysfunction as a confounding factor. PRL, FSH and LH were measured to evaluate the integrity of the hypothalamus-pituitary-gonadal axis and discover the cases with hypogonadism. Hyperlipidemia was assessed by measuring cholesterol and TG, because these entities were among our exclusion criteria.

Baseline assessments included the evaluation of ejaculatory complaints, erectile function status and hormonal assessment. Patients were asked about organic causes of ejaculatory dysfunction and a through physical examination was performed for possible neurological diseases and prostate inflammation/infection. The volume of the right testis was measured using Prader orchidometer, whereas that of the left one was ignored as its measurement is often biased because of concomitant varicocele.[12]

Collected data were analyzed with SPSS software V.13. Quantitative variables were presented using mean ± standard deviation. They were compared using the paired *t*-test. *P* values lower than 0.05 were considered as significant.

## RESULTS

The subjects and controls were matched for characteristics such as age, body mass index, TG and TC. Apart from FT and FSH, there was no significant difference between the hormone levels in the studied groups. The hormonal status in either of the two groups is summarized in Table 1.

**Table 1: Characteristics and hormonal status of the studied patients**

| Characteristics | Group | *N* | Mean (SD) | *P* value |
|---|---|---|---|---|
| Age (year) | Premature | 41 | 35.66 (9.37) | 0.45 |
| | Control | 41 | 37.63 (10.20) | |
| Weight (kg) | Premature | 41 | 79.15 (12.31) | 0.8 |
| | Control | 41 | 80.46 (13.74) | |
| Height (cm) | Premature | 41 | 176.88 (8.56) | 0.221 |
| | Control | 41 | 177.17 (9.83) | |
| TT (ng/dL) | Premature | 41 | 483.93 (123.59) | 0.177 |
| | Control | 41 | 455.49 (116.95) | |
| FT (pg/dL) | Premature | 41 | 24.10 (4.86) | 0.036 |
| | Control | 41 | 22.05 (4.07) | |
| TC (mg/dL) | Premature | 41 | 173.34 (25.76) | 0.114 |
| | Control | 41 | 174.80 (22.82) | |
| TG (mg/dL) | Premature | 41 | 132.78 (56.32) | 0.235 |
| | Control | 41 | 130.88 (60.31 | |
| FSH (mIU/mL) | Premature | 41 | 4.939 (1.23) | 0.003 |
| | Control | 41 | 3.971 (1.89) | |
| LH (mIU/mL) | Premature | 41 | 4.368 (2.45) | 0.498 |
| | Control | 41 | 4.185 (2.09) | |
| PRL (ng/mL) | Premature | 41 | 8.91(3.69) | 0.109 |
| | Control | 41 | 9.11 (4.06) | |

TT: Total testosterone, FT: Free testosterone, TC: Total cholesterol, TG: Triglyceride, FSH: Follicle stimulating hormone, LH: Luteinizing hormone, PRL: Prolactin, SD: Standard deviation

There was no significant difference between TT, LH and PRL values between the two groups, whereas higher levels of FT and FSH were reported in the PE group (Panel A and B $P = 0.036$ for FT and $P = 0.003$ for FSH).

## DISCUSSION

The normal sexual response cycle in men can be functionally divided into five interrelated stages that occur in a defined sequence: Libido, erection, ejaculation, orgasm and detumescence. Functional classification of the male sexual cycle is the most physically quantifiable one;[13] therefore, we considered it as the basis of the current discussion.

Several lines of evidence have suggested an important role for the central dopaminergic neurotransmission in mediating sexual behavior and erection in animal and human males.[14] Corona *et al*. showed a facilitating role for T in controlling ejaculatory reflex, independent of central or peripheral problems.[8] Furthermore, the role of T in promoting copulation seems to be mediated by an increase in the release of dopamine in the medial preoptic area, possibly through up-regulation of nitric oxide (NO) synthesis.[14]

Mooradian *et al.*[15] have reviewed the critical role of androgens in regulating the sexual behavior in human males. Only in healthy elderly men, do higher serum T levels appear to be associated with improved sexual activity.[16,17] Furthermore, higher levels of serum T may also shorten the latency of erection in individuals exposed to erotic material.[18] Likewise, restoration of sexual interest, a reduction in latency time and an increase in the frequency and magnitude of nocturnal penile tumescence could be expected after T replacement in hypogonadal males.[19,20] Recent studies have proved the fact that gonadal androgens exert their effect on penile erection through local regulation of NO secretion.[21]

While 75% of adult men are capable of controlling their ejaculation, a wide spectrum of ejaculation disorders ranging from mild premature to severely retarded or absent ejaculation exists.[22]

Researchers believe that T is the main synchronizer in sexual activity that acts by regulating libido and such enzymes as nitric oxide synthase (NOS) and phosphodiesterase type 5 (PDE5), which are essential for the erectile process. In fact, NOS increases the levels of cyclic guanosine monophosphate while PDE5 has an opposite effect. Considering the fact that T positively controls the initiation as well as termination of penile tumescence, its net effect on erection is null. In fact, penile tumescence may occur even in the absence of T.[5]

Normalizing T values improves libido and erectile function in most hypogonadal men; it may, however, take 12-24 weeks before the effects of the treatment become evident.[23] Therefore, one could concluded that T plays a pivotal role in male sexual response, affecting both central and peripheral levels of the hormone.[5,23-25]

In 2008, Corona *et al*. reported for the 1st time that different T levels might lead to various severities of ejaculatory disturbances. In line with previous studies, they added that T levels clearly affect sexual desire.[6,26-29] They also reported higher TT and FT levels in their youngest subjects (aged between 25 and 40 years) suffering from PE while the oldest age group (55-70 years) with DE had lower TT and FT levels. Accordingly, hypogonadism was more prevalent in patients with PE compare with subjects with DE (12% vs. 26%). These investigators suggested a facilitatory role for T in the control of the ejaculatory reflex.

In our study, however, TT level was not significantly different in the two groups, whereas similar to Corona's study, higher FT levels were observed in PE patients.

While it does not seem that androgen suppression be an acceptable treatment for PE, androgen replacement is being studied as a means of treating DE.[8]

The small sample size is the major limitation of the present study. Besides, we did not include patients with DE. In order to generalize the present data, further large-scale studies are needed to be conducted on PE patients with a broader age range with both PE and DE.

## CONCLUSIONS

We found that patients with PE had the higher FT and FSH levels compared with the normal men, supporting the facilitator effect of T in the control of the ejaculatory reflex. T can exert its effect through both central and peripheral mechanisms. To find a causative relationship between these entities, larger scale studies are needed. It is not yet known whether this finding could be translated into a solution for PE; however, androgen replacement for the treatment of DE merits further evaluation.

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