The Role of Hypothyroidism in Male Infertility and Erectile Dysfunction

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Purpose: To evaluate the effect of hypothyroidism on erectile function and sperm parameters.

Materials and Methods: This study was conducted on 24 patients with hypothyroidism and 66 normal individuals. Serum levels of hormones, including thyroid stimulating hormone (TSH), thyroxin (T4), follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), and testosterone, were measured and semen analysis was done in all the participants. Erectile function was evaluated using International Index of Erectile Function (IIEF-5) questionnaire.

Results: The mean IIEF-5 total score was 11.75 [95% confidence interval (CI): 9.70 to 13.79) and 20.81 (95% CI: 20.02 to 21.6) for hypothyroid group and normal subjects, respectively ($P = .005$). Furthermore, serum concentrations of PRL and seminal parameters were significantly different between two groups ($P < .001$).

Conclusion: Hypothyroidism adversely affects erectile function and sperm parameters, including sperm count, morphology, and motility. In patients with sperm abnormalities and erectile dysfunction, measurement of thyroid hormones is recommended.

Keywords: hypothyroidism, infertility, erectile dysfunction, semen

INTRODUCTION

Hyper and hypothyroidism are the main thyroid diseases with adverse effects on male reproductive system. Short-term hypothyroidism has no significant effect on male reproduction in adults, while severe, prolonged hypothyroidism may impair the reproductive function.[1] Although the effects of the thyroid dysfunction on female gonadal function have been clearly established, its impact on male reproductive function remains controversial.[2,3]

Thyroid hormone disorders cause some sexual dysfunctions that normalizing the thyroid hormone levels can reverse them.[4] El-Sakka and colleagues reported that low serum testosterone (15%), hyperprolactinemia (13.7%), and hypothyroidism (3.1%) are the most frequent endocrine abnormalities seen in patients with sexual dysfunction. They also reported a significant association between sexual dysfunction and endocrine imbalance.[5]

Furthermore, hypothyroidism has an adverse effect on human spermatogenesis; as Griboff showed that morphology is significantly affected and motility may be less affected.[6] On the other hand, histological abnormalities in all testicular biopsies have been reported.[7,8]

The aim of this study was to evaluate erectile functions, serum levels of hormones, and sperm parameters in male patients with hypothyroidism and normal subjects. We hypothesized that hypothyroid state has an adverse effect on the erectile function and sperm parameters in men.

MATERIALS AND METHODS

Between January 2009 and June 2010, 24 consecutive hypothyroid patients (group A), who were referred to the outpatient endocrine clinic of Sina Hospital, affiliated to Tehran University of Medical Sciences, were enrolled in this study.

The inclusion criteria were as follows: age range of 20 to 70 years, not being investigated or treated for sexual dysfunction before the onset of thyroid symptoms, and being married for more than 1 year. Patients with diabetes mellitus, cardiovascular diseases, including history of myocardial infarction, coronary angioplasty, or coronary artery bypass grafting, or urological diseases were excluded from the study.

Group A, with the mean age of 43.1 ± 11.6 years (range, 20 to 63 years), were complaining from clinical symptoms of hypothyroidism. They had documented hypothyroidism. The control group, group B, consisted of 66 healthy normal hospital staff, with the mean age of 41.5 ± 69.0 years (range, 21 to 69 years). All participants provided written informed consent and the study was approved by the Medical Ethics Committee of Tehran University of Medical Sciences.

Serum levels of free thyroxin (FT4), thyroid stimulating hormone (TSH), free testosterone, prolactin (PRL), follicle-stimulating hormone (FSH), and luteinizing hormone (LH) were measured using immunoassay commercial kits in both groups. The normal reference ranges for thyroid hormones were as follows: TSH, 0.3 to 5.0 IU/mL and T4, 4.5 to 12.5 g/dL.

Erectile dysfunction was evaluated using International Index of Erectile Function (IIEF-5) questionnaire.[9] This is a 5-item version of the 15-item IIEF questionnaire for diagnosing the presence and severity of erectile dysfunction (ED). These items focus on erectile function and intercourse satisfaction. Possible scores for the IIEF-5 range from 5 to 25. This questionnaire was translated into Persian language and its validity and reliability have been tested previously in our center.

Semen analyses were done according to the World Health Organization guidelines.[10] Semen was obtained by masturbation after 3 to 7 days of sexual abstinence. Semen sample was collected into a sterile container, using no lubricant jelly. Reference limits of semen parameters are as follows: total sperm number, 39 million per ejaculate (range,

Table 1. Characteristics, hormonal, and seminal parameters of participants

	Hypothyroid group	Normal group		
	Mean ± SD	Mean ± SD	*P*	95% Confidence Interval
Participants, n	24	66	-	-
Age, y	43.1± 11.6	41.5 ± 69	.45	-4.09 to 7.19
IIEF-5 score	11.75 ± 4.84	20.81 ± 3.21	.005	-10.82 to -7.31
FSH, mU/mL	8.70 ± 4.17	7.51 ± 7.37	.342	-1.29 to 3.67
LH, mU/mL	7.40 ± 3.70	6.58 ± 2.62	.327	-0.85 to 2.49
Free testosterone, pg/mL	5.40 ± 2.27	17.73 ± 98.09	.311	-36.45 to 11.80
Prolactin, ng/mL	359.41 ± 77.57	290.13 ± 96.86	.001	29.48 to 109.08
Sperm count, million/mL	28.04 ± 25.72	72.98 ± 42.72	.000	-59.82 to -30.05
Sperm motility, %	30.08 ± 18.53	67.39 ± 12.20	.000	-45.61 to -29.00
Sperm morphology, %	35.12 ± 13.87	65.10 ± 11.28	.000	-36.38 to -23.57

SD indicates standard deviation; IIEF-5, International Index of Erectile Function questionnaire; FSH, follicle-stimulating hormone; and LH, luteinizing hormone.

33 to 46); sperm concentration, 15 million per mL (range, 2 to 16); vitality, 58% live (range, 55% to 63%); progressive motility, 32% (31% to 34%); total (progressive + nonprogressive) motility, 40% (range, 38% to 42%); and morphologically normal forms, 4.0% (range, 3.0% to 4.0%).[10]

Statistical Analysis

Each variable, including age, serum levels of hormones, sperm parameters, and IIEF-5 scores, was assessed using a univariate analysis by independent sample *t* test, Mann-Whitney *U* test, and Pearson correlation, where appropriate. The Kolmogorov–Smirnov test was used to check if IIEF-5 scores had a normal distribution. Variables that were significantly related to hypothyroidism ($P < .05$) were assessed in a multivariate analysis with a logistical regression procedure and forward stepwise selection. The dependent variable was coded as zero for absence and one for the presence of hypothyroidism.

RESULTS

While age was not significantly different between the two groups ($P = .465$), a significant difference was found in IIEF-5 scores ($P < .001$). Serum PRL level, sperm count, sperm motility, and morphology were significantly different between two groups ($P = .001$, $P < .001$, $P < .001$, and $P < .001$, respectively; Table 1). Multivariate analysis showed that hypothyroidism affected the morphology of the sperm more than other parameters (OR = 75.3; Table 2). In the hypothyroid group, TSH and FT4 were 15.02 ± 3.30 IU/mL and 2.91 ± 1.40 g/dL, respectively. There was no correlation between serum TSH levels and severity of ED (IIEF-5), serum testosterone levels, and sperm parameters (Table 3).

DISCUSSION

The effects of thyroid hormone alterations on the reproductive system have been studied extensively in animals, which showed that abnormal thyroid function resulted in decreased fertility and

Table 2. Multivariate analysis of IIEF-5 and sperm parameters.

Variables	*r*	*P*	Odds ratio
IIEF-5	-93.953	.989	0.000
Sperm count	1.079	.991	2.942
Sperm motility	.502	.992	1.652
Sperm morphology	4.322	.985	75.307

IIEF-5 indicates International Index of Erectile Function questionnaire.

Table 3. Correlation analysis of TSH levels in the hypothyroid group

Variables	*r*	*P*
Free Testosterone	-0.182	.396
IIEF-5	0.088	.681
Sperm count	-0.154	.472
Sperm motility	-0.135	.529
Sperm morphology	0.098	.650

*Correlation is significant at the 0.05 level (2-tailed).

TSH indicates thyroid stimulating hormone; and IIEF-5 International Index of Erectile Function questionnaire.

impaired sexual activity.[11,12] In animals, if hypothyroidism occurs soon after birth, delay in sexual maturation will be observed.[13] In male Pax8-/- mice with congenital hypothyroidism, the efferent ducts and epididymis are either absent or the efferent ducts lumen are reduced, which leads to impaired testicular drainage and absence of spermatozoa.[14] Moreover, in male rats with transient gestational onset hypothyroidism, post-testicular sperm maturation is impaired in the epididymis. In these cases, androgen bioavailability, its receptor expression, and function are subnormal; however, there are no lower serum levels of androgen.[15]

In the current study, patients with hypothyroidism had significantly higher level of serum PRL and lower IIEF-5 score, which means more erectile problems. Serum levels of FSH, LH, and free testosterone were not significantly different. In hypothyroid subjects, high levels of PRL may affect sexual drive and result in ED.[16,17] On the other hand, hypothyroidism in women decreases serum level of sex hormone-binding globulin (SHBG) and increases the PRL secretion by affecting the ovarian function. Thyroxin administration can improve fertility and reverses hormonal abnormalities.[18,19] In addition, primary hypothyroidism causes decreased serum levels of SHBG and total testosterone. It has been shown that thyroid hormone administration to men with hypothyroidism increases both SHBG and total serum testosterone.[20] We did not observe significant difference in serum testosterone, LH, and FSH levels between two groups. It may be due to subnormal bioavailable androgen and abnormal receptor expression and function, as shown in the animal studies or small sample size of study.[15]

Not all of the patients with thyroid diseases do experience sexual dysfunction. Moreover, all of the patients with hyper or hypothyroidism reaching euthyroid state do not recover from sexual dysfunction. These observations show that sexual dysfunctions are almost always multifactorial (physical and psychological factors).[4]

In the current study, there are some potential confounders, such as body mass index, smoking habits, etiology of hypothyroidism, abstinent time for semen analysis, season, and time of the day that sampling happened. They may affect serum levels of hormones and sperm parameters. In addition, only a single sample of semen and blood were collected in a small group of patients. Therefore, it is needed to conduct studies with higher degree of evidence, such as cohort studies, on larger number of participants to clarify the effects of hypothyroidism on male reproductive system.

CONCLUSION

Hypothyroidism adversely affects erectile function and semen quality in men. Further large scale studies are needed to replicate our results.

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CONFLICT OF INTEREST

None declared.

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