Pharmacological Reports 69 (2017) 432–437

Contents lists available at ScienceDirect

Pharmacological Reports

journal homepage: www.elsevier.com/locate/pharep

Original article

The effect of L-thyroxine treatment on sexual function and depressive symptoms in men with autoimmune hypothyroidism

Robert Krysiak*, Witold Szkróbka, Bogusław Okopień

Department of Internal Medicine and Clinical Pharmacology, Medical University of Silesia, Katowice, Poland

ARTICLE INFO

Article history:
Received 19 November 2016
Received in revised form 31 December 2016
Accepted 11 January 2017
Available online 17 January 2017

Keywords:
Depressive symptoms
Hypothyroidism
Sexual functioning
Thyroid autoimmunity

ABSTRACT

Background: Thyroid autoimmunity and mild hypothyroidism in women seem to be associated with sexual dysfunction and depressive symptoms. Data concerning similar associations in men are limited. The aim of this study was to investigate sexual functioning and depressive symptoms in men with autoimmune hypothyroidism.
Methods: The study population consisted of three groups: men with autoimmune overt hypothyroidism (group A), men with autoimmune subclinical hypothyroidism (group B) and healthy euthyroid males without thyroid autoimmunity (group C). Apart from measuring serum levels of thyrotropin and free thyroid hormones and thyroid antibody titers, all included patients completed a questionnaires evaluating male sexual function (International Index of Erectile Function-15: IIEF-15) and assessing the presence and severity of depressive symptoms (Beck Depression Inventory-Second Edition – BDI-II) before and after 6 months of levothyroxine treatment.
Results: Men with overt hypothyroidism obtained lower scores in all five domains of IIEF-15, while men with subclinical hypothyroidism only in erectile function. The total BDI-II score was higher in groups A than in groups B and C, as well as higher in group B than in group C. L-thyroxine improved erectile function and normalized intercourse satisfaction, orgasmic function, sexual desire and overall satisfaction in group A, as well as normalized erectile function in group B. In group A, L-thyroxine reduced, while in group B tended to reduce total BDI-II.
Conclusions: The obtained results suggest that autoimmune hypothyroidism in men is characterized by sexual and mood disturbances and that hypothyroid patients with sexual dysfunction and depressive symptoms benefit from L-thyroxine treatment.

Introduction

The prevalence and incidence of thyroid disorders is strongly influenced by sex, being much higher in women than in men [1]. Despite female predominance, increasingly more and more men are being diagnosed, particularly with hypothyroidism, which is by far the most common thyroid disorder in the adult population and in most men is autoimmune in origin [1,2].

Despite some discrepancies, results of few studies conducted to date suggest that thyroid disorders may have an adverse effect on male sexual functioning. Erectile dysfunction was more common in men with thyroid disorders than in healthy controls, although its frequency in this group of patients was lower than in men with type 2 diabetes [3]. Both hyperthyroidism and hypothyroidism, if untreated, were associated with impaired erectile function, which improved after the restoration of normal hypothalamic-pituitary-thyroid axis activity [4,5]. However, although the presence of overt hyperthyroidism was associated with erectile dysfunction in the study by Corona et al. [6], after adjusting for potential confounders there as no association between erectile function and primary hypothyroidism. In other studies [4,7], hypothyroidism and to a lesser extent also hyperthyroidism reduced libido. Hypothyroidism adversely affected sperm parameters, including sperm count, morphology and motility [8]. Hyperthyroidism was found to be associated with low total sperm count, lineal motility defects and progressive motility abnormalities [9]. Moreover, hyperthyroidism was found to be a common cause of acquired premature ejaculation, while hypothyroidism was associated with delayed ejaculation [4,10,11]. On the basis of these studies, we may conclude that both thyroid hypofunction and hyperfunction affect various aspects of male sexual functioning. However, conclusions

Abbreviations: BDI-II, Beck Depression Inventory-Second Edition; IIEF-15, International Index of Erectile Function-15; SD, standard deviation; TgAb, thyroglobulin antibodies; TPOAb, thyroid peroxidase antibodies.

* Corresponding author.
E-mail address: r.krysiak@interia.pl (R. Krysiak).

http://dx.doi.org/10.1016/j.pharep.2017.01.005
1734-1140/

from these studies are seriously limited by methodological problems, particularly by a small number of men participating in these studies, a retrospective nature of some studies, and assessment of only selected aspects of men's sexual response.

In our recent study, we have found that both thyroid autoimmunity and hypothyroidism deteriorated female sexual function and induced depressive symptoms and that their deteriorating effects on sexuality in women were additive [12]. These results may suggest that sexual dysfunction and depressive symptoms are more pronounced in women with thyroid hypofunction induced by autoimmune thyroiditis than in women with nonautoimmune hypothyroidism. Because similar data are not available for males, the aim of the present study was to evaluate sexual functioning and depressive symptoms in men with autoimmune hypothyroidism of various severity before and after L-thyroxine treatment.

Materials and methods

Patients

The participants of the study were recruited among adult men (aged 18–50 years) with symptoms or signs suggestive of thyroid dysfunction. Hashimoto's thyroiditis was diagnosed if the patient had positive thyroid peroxidase antibodies (TPOAb) (>100 U/mL) and reduced echogenicity of the thyroid parenchyma on thyroid ultrasonography. All sonographic examinations were performed by the same person. Only patients unaware of their thyroid function and not taking any drugs were included in the study. Based on thyroid function test, the patients were enrolled into one of two groups, each consisting of 12 individuals: patients with overt hypothyroidism (plasma thyrotropin levels above 20 mU/L and free thyroid hormone levels below the lower limit of the normal laboratory range) (group A) and men with subclinical hypothyroidism (serum thyrotropin levels more than 4.5 mU/L but below 20 mU/L and normal free thyroid hormone levels) (group B). The control group included 12 age- and weight-matched healthy men without thyroid disease (Group C). These patients were characterized by serum thyrotropin levels between 0.45 and 4.5 mU/L, free thyroid hormone levels and thyroid antibody titers within the reference range and no abnormalities on thyroid ultrasound.

The exclusion criteria were as follows: hypogonadism, prolactin-secreting tumors, diabetes, multiple sclerosis, prostatitis, psychiatric problems, cardiovascular disease, impaired renal or hepatic function, vasculogenic or neurogenic disorders known to impair male sexual function, developmental or acquired anomalies of the male reproductive system, as well as previous operations that might have affected sexual function. The study protocol was approved by our institutional review board and subjects gave written, informed consent to participate in the study.

Study design

Patients with both overt and subclinical hypothyroidism were then treated with L-thyroxine, which was administered at a starting dose of 50 μg once-daily and gradually (over 4–8 weeks) titrated to obtain thyrotropin levels in the range between 0.45 and 4.5 mU/L. The target daily dose of this agent was administered for the following 6 months, and no changes in dosage were allowed during this time.

Laboratory assays

Venous blood samples were drawn from the antecubital vein between 8.00 and 9.00 a.m., at least 12 h after the last meal and assessed in duplicate. Serum levels of thyrotropin, free thyroxine and free triiodothyronine were measured with electrochemiluminescence immunoassay reagents from Roche Diagnostics (Lewes, United Kingdom). Serum levels of prolactin, as well as titers of TPOAb and thyroglobulin antibodies (TgAb), were determined by enzyme-linked immunosorbent assays using reagents purchased from DRG Instruments GmbH (Marburg, Germany) and IBL International (Hamburg, Germany). Intra- and interassay coefficients of variation were less than 6.0 and 8.6%, respectively. Thyroid ultrasound was performed with a 5- to 12-MHz linear array transducer.

Questionnaires

The men were asked to complete a questionnaire assessing their demographic characteristics, smoking, physical activity, education, occupation, stress exposure, the number of sexual partners, the number and duration of marriages, as well as systolic and diastolic blood pressure. Sexual function and depressive symptoms were assessed in all men considered for enrollment immediately after blood collection and the ultrasound. However, only data of the participants of the study were included in the final analyses. Sexuality was evaluated using the International Index of Sexual Function-15 (IIEF-15) for heterosexual men, consisting of five collective sexual domains: erectile function, intercourse satisfaction, orgasmic function, sexual desire and overall satisfaction from sexual activity over the preceding 4 weeks. This self-administered questionnaire, composed of 15 items, is regarded as a reliable, cross-culturally valid, and psychometrically sound measure of male sexual function [13]. Each answer was rated on a scale ranging from 0 to 5 or 1 to 5, with a higher score corresponding to better sexual function. Total scores for each of the domains were calculated separately by summing up individual question scores. Erectile function was evaluated based on 6 questions (questions 1 to 5 and 15), yielding a maximum score of 30 points. An overall erectile function below 26 indicated erectile dysfunction. Erectile dysfunction was scored as follows: severe erectile dysfunction for score no more than 10, moderate erectile dysfunction for score 11–16, mild to moderate erectile dysfunction for score 17–21, and mild erectile dysfunction for score 22–25. Intercourse satisfaction was evaluated based on 3 questions (questions 6–8), yielding a maximum score of 15 points. Orgasmic function (questions 9 and 10), sexual desire (questions 11 and 12) and overall satisfaction (questions 13 and 14) were evaluated using two questions, yielding a maximum score of 10 points. Minimum scores were: 0 for intercourse satisfaction and orgasmic function, 1 for erectile function, and 2 for sexual desire and overall satisfaction [14].

The presence of depression symptoms and depression severity were evaluated using the Beck Depression Inventory-Second Edition (BDI-II), which is a valid and reliable measure of depressive state [15], corresponding well to a clinical diagnosis of depressive disorders outlined in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* [16]. Each item was rated on a 4-point scale from 0 (not present) to 3 (severe) and the scores were added to yield the total score, which can range from 0 to 63, with higher values indicating more severe depressive symptoms. According to manual guidelines [15], the total score of 0–13 was regarded as minimal range, 14–19 as mild, 20–28 as moderate, and 29–63 as severe depression.

Statistical analysis

Because of the skewed distributions, values for hormones and thyroid antibodies were natural-log transformed to achieve normality and homogeneity of variance. Comparisons between the groups were performed using analysis of covariance followed by Bonferroni *post hoc* tests after consideration of age, smoking,