

Hypogonadism in leprosy males

Hipogonadismo em homens com hanseníase

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Abstract

Context and objective: Leprosy is a chronic systemic infectious disease caused by *Mycobacterium leprae* (Hansen's bacillus). It is a problem of public health concern mainly because of its social stigma and discrimination. Hypogonadism in male with Leprosy can occur due the involvement testicular of lepromatous disease. The aim this study here was to evaluate the gonadal function in male with chronic leprosy. **Study design:** Cross-sectional study in a leprosy outpatient clinic. **Subjects and methods:** Only the functional status of sexual hormones and male with more of 1 year of Leprosy were evaluated. Clinical data were not evaluated. Measurements were made of their serum levels of free testosterone (FT), luteinizing hormone (LH) and follicle-stimulating hormone (FSH) in 21 patients male with chronic lepromatous disease. The patients were subdivided two groups: up to 60 years (G1) and over 60 years old (G2), due to physiological decline of serum testosterone production in men over 60 years of age. **Results:** The mean age was 48.43 ± 18.65 years. Serum FT revealed low values in 37.5 % patients. Serum LH, and FSH revealed high values in 18.8 and 6.3% respectively. The mean basal LH and FSH levels were significantly elevated and the level of FT significantly reduced when compared the groups G1 and G2. Furthermore, the G1 significantly correlated with low FT levels ($P = 0.002$). **Conclusion:** This study showed a high frequency of hypogonadism among male leprosy patients. The assessment of gonadal function to detect hypogonadism should be recommended routinely screening these individuals.

Keywords: Leprosy. Hypogonadism. Gonadal function. Men. Gonadal Disorders.

Resumo

Contexto e objetivo: A hanseníase é uma doença sistêmica infecciosa crônica causada pelo *Mycobacterium leprae* (bacilo de Hansen). É um problema de saúde pública, principalmente por causa de seu estigma e discriminação social. O hipogonadismo em homens com hanseníase pode ocorrer devido ao envolvimento testicular da doença lepromatosa. O objetivo deste estudo foi para avaliar a função gonadal em homens com hanseníase. **Desenho do estudo:** Estudo transversal em um ambulatório de hanseníase. **Sujeitos e métodos:** Apenas a avaliação dos hormônios sexuais em homens com hanseníase com mais de 1 ano de evolução foram avaliados. Os dados clínicos não foram avaliados. Foram avaliados os níveis séricos de testosterona livre (FT), hormônio luteinizante (LH) e hormônio folículo-estimulante (FSH) em 21 homens com hanseníase crônica. Os pacientes foram divididos dois grupos: até 60 anos (G1) e mais de 60 anos (G2), devido ao declínio fisiológico da produção de testosterona em homens acima de 60 anos de idade. **Resultados:** A idade média dos pacientes foi de 48.43 ± 18.65 anos. A FT sérica apresentou valores reduzidos em 37.5% dos pacientes. Os níveis séricos de LH e FSH apresentaram valores elevados em 18.8 e 6.3% dos pacientes respectivamente. Os níveis basais do LH e FSH foram significativamente elevados e da FT foi significativamente reduzida quando comparados os grupos G1 e G2. Além disso, o G1 apresentou uma correlação significativa com baixos níveis de FT ($P < 0.002$). **Conclusão:** Este estudo mostrou uma elevada frequência de hipogonadismo em homens com hanseníase. Portanto, a avaliação da função gonadal nesses pacientes deve ser recomendada rotineiramente, para rastreamento de hipogonadismo.

Palavras-chave: Hanseníase. Hipogonadismo. Homens. Transtornos Gonadais.

INTRODUCTION

Leprosy is a contagious and chronic systemic granulomatous disease caused by *Mycobacterium leprae* (Hansen's bacillus) with 228.474 new cases detected worldwide during 2010 reported by 130 countries.¹

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Especially affecting the peripheral nervous, and secondarily can compromise other systems as endocrine among other.² Endocrine changes present in leprosy include hypogonadism, sterility, and osteoporosis. Leprosy is still an endemic disease more prevalent in tropical regions, and the endocrine manifestations caused by leprosy have been underestimated, even by specialists, in special the hypogonadism in male patients. In male hypogonadism it is important

determine the bone mass loss continues and increased risk of fracture.³

Hypogonadism in leprosy may be attributed to secondary gonadal dysfunction due to testicular atrophy, and also the acute orchitis of type 2 reactions leading to infertility and sexual dysfunctions development, with oligospermia or azoospermia. Leprosy can lead to hypogonadism due *Mycobacterium leprae* involvement the testicles in up to three quarters of cases of leprosy.⁴ The bacillus reaches the testicles via the lymphatic system, blood or by direct invasion through of skin adjacent tissue. Leprosy affects either the seminiferous tubules as well as the Leydig cells, and may therefore lead to isolated increases in luteinizing hormone (LH) and follicle-stimulating hormone (FSH) alone.⁵ Studies show a significant correlation between duration of disease and FSH levels, indicating that testicular dysfunction is probably cumulative and irreversible.⁶

The hypogonadism due to immune response has been a hypothesis, because the finding of testicular germinal cell antibodies in lepromatous leprosy has been evaluated, and testicular microsomes, presumably derived from immature spermatozoa, would be the most likely antigen.⁷ Also have been documented that inflammatory cytokine family can influence in secretory activity of the hypothalamic–pituitary–gonadal axis at different levels secondary to attack of testicles by Hansen's bacillus.^{8,9}

The present study was undertaken to assess the changes in sexual hormones in males with leprosy.

MATERIALS AND METHODS

Study design

Male leprosy patients of all ages, irrespective of duration of the disease and treatment, were selected from the leprosy clinic of National Health Foundation Itabuna, Bahia, Brazil. The functional status sexual hormones of all patients were evaluated by tests that included free testosterone (FT), LH, and FSH.

This study was conducted at the National Health Foundation Itabuna, Bahia, Brazil, and all patients gave their informed consent to participate. The study was approved by the ethical committee of Faculdade de Tecnologia e Ciências, Salvador, Bahia, Brazil, in accordance to the Declaration of Helsinki.

Study patients

Our study included 21 patients with chronic lepromatous disease accompanied in ambulatory of the National Health Foundation Itabuna, Bahia, Brazil. The eligibility criteria were: male of all ages, and duration of Leprosy more than 1 year.

The clinical examinations of testes were not performed, and the patients were subdivided two groups: up to 60 years old (G1) with 11 participants and over 60 years old (G2) with 10 participants, due to decline of serum testosterone production in men over 60 years of age.

Hormonal analysis

Only the functional sexual hormones were evaluated. Serum concentration of FT was measured using enzyme immunoassay techniques (ELISA) (DRG Free Testosterone ELISA kits) in a DYNEX DS2 Automated ELISA System (reference normal range of 8.8 - 27.0 pg/ml), serum FSH and LH levels were estimated by the ELISA method (Diagnostics Systems Laboratories, Webster, Tex, USA) (reference normal range of 1.0 - 14.0 mIU/ml and 1.24 - 8.62 mIU/ml respectively).

Statistical analysis

Data are expressed as mean \pm SD for those variables that were normally distributed. The variables were compared using Pearson's chi-square or Fisher's exact test where appropriate.

Statistical analysis was performed using SPSS® version 17.0 for Windows (SPSS Inc, Chicago, Ill), and a p-value < 0.05 was considered statistically significant.

RESULTS

Mean age of the 21 patients was 48.43 ± 18.65 years (range: 21-79 years). Other major characteristics of the studied patients are shown in Table 1.

Table 1. Clinical and demographic profile of patients with leprosy

Clinical Form	N	%	Age mean	range
Tuberculoid leprosy	4	19.10	54.75	32–71
Lepromatous leprosy	5	23.80	38.40	21–54
Dimorphic leprosy	12	57.10	50.50	24–79

LH, FSH, FT levels determinations

The levels serum LH, FSH presented high values in 18.8 and 6.3% respectively, whereas the levels serum FT revealed low values in 37.5 % patients.

The serum LH and FSH levels weren't significantly elevated when patients compared of G1 and G2 group with the clinical forms of leprosy (LH: G1, 5.25 ± 1.96 mIU/ml; G2, 6.41 ± 4.81 mIU/ml; and FSH: G1, 6.68 ± 3.50 mIU/ml; G2, 8.50 ± 1.26 mIU/ml). The FT levels weren't significantly elevated when patients compared of G1 and G2 group with the clinical forms of leprosy (LH: G1, 14.40 ± 4.20 pg/ml; G2, 7.26 ± 2.91 pg/ml).

Correlation between LH, FSH and FT

The mean basal LH and FSH levels were significantly elevated and the level of testosterone significantly reduced in individuals with hypogonadism when compared the groups G1 and G2. Furthermore, the G1 significantly correlated with low FT levels ($P = 0.002$).

Correlation between LH, FSH, FT and clinical form leprosy

In the lepromatous dimorphic the basal plasma gonadotropin levels were significantly increased (FSH 8.24 ± 2.56 mIU/ml; LH 6.96 ± 4.45 mIU/ml). The plasma gonadotropins were in the normal range in tuberculoid leprosy (FSH 6.45 ± 3.02 mIU/ml; LH 4.25 ± 0.83 mIU/ml). In lepromatous leprosy, the basal mean plasma FSH was 6.88 ± 3.02 mIU/ml, whereas LH levels were 3.53 ± 1.02 mIU/ml.

The basal plasma FT levels were in dimorphic leprosy of 10.51 ± 5.48 pg/ml, lepromatous leprosy of 11.53 ± 4.31 pg/ml, and tuberculoid leprosy of 16.103 ± 6.51 pg/ml.

DISCUSSION

This study reports the frequency of changes in gonadotropins and testosterone in males with chronic leprosy. The frequency of hypogonadism was 37.50% in our study, and demonstrates a significant correlation between serum gonadotropins levels high with and low FT levels in males with chronic leprosy up to 60 years old individuals.

The prevalence of hypogonadism has increased in recent years. The hypogonadism has been reported that 12%, 19%, 28%, and 49% of men greater than 50, 60, 70, or 80 years of age respectively.¹⁰ Male hypogonadism can be primary or hypergonadotropic hypogonadism, and secondary or hypogonadotropic hypogonadism. The primary hypogonadism is characterized by low levels of circulating testosterone with high levels of LH and FSH, as occurs in Klinefelter's, infection, trauma, drug use and exposure to chemotherapeutic agents or radiation. The secondary hypogonadism is due defect in the hypothalamus or the pituitary resulting of decreased of LH and FSH as in Kallman's syndrome.

Testosterone is most important testicular androgen in men, and 50 - 60% is bound with high affinity to sex hormone-binding globulin (SHBG) while 40-50% is bound to albumin, and 1-3% is unbound so called of FT.¹¹ Androgen levels decrease by approximately 1% per year after the age of 40 and the levels of SHBG increase with age, resulting in reduced bioavailable FT.¹² Low testosterone levels in the male can be associated with hypogonadism and your consequences. The signs and symptoms of low testosterone include loss of libido, erectile dysfunction, diminished intellectual capacity, depression, lethargy, osteoporosis, loss of muscle mass and strength, and some regression of secondary sexual characteristics.¹³ In our study only the functional status of sexual hormones were evaluated. Clinical data were not evaluated.

Hypogonadism in male patients with leprosy is common and elevations of serum gonadotropin and deficient testosterone levels were found in a male with Hansen's disease whose insufficient erections were

secondary to atrophic testes.¹⁴ In the present study, FT serum levels were inversely correlated with serum gonadotropin levels, featuring a hypergonadotropic hypogonadism. Generally the testicular damage is the result of direct invasion by leprosy bacilli via the blood stream, leading to functional abnormalities that are not always associated with histological lesions.^{15,16} In addition, both humoral and cellular immune components are involved in the pathogenesis of orchitis in leprosy.^{7,17} The hormone serum levels reported here are in accordance with the studies that reported increased plasmatic levels of LH and FSH and decreased levels of FT in patients with leprosy.^{6, 18}

Under physiological conditions, serum LH levels in men are kept within a range, due the balance between stimulation by Gonadotropin-Releasing Hormone and inhibition by gonadal sex steroids. In men, serum LH values are relatively constant from puberty to old age, and high serum LH value with a low serum testosterone in a male is an abbreviated endocrine test diagnostic of primary hypogonadism. The mean basal LH levels were significantly elevated found in leprosy carriers with hypogonadism in this work was in accordance with the findings of previous studies and also in accordance with other reports of leprosy studies performed in different countries.¹⁹

FSH is a glycoprotein dimer secreted by the adenohypophysis that stimulates gametogenesis in both males and females. Serum FSH levels is a sensitive indicator of spermatogenesis in adolescents and young adults, and can be used to evaluate the etiology of low sperm counts, amenorrhea, menstrual irregularities, pituitary disorders, precocious or delayed puberty, and ovarian/testicular dysfunction.^{20,21} The mean basal serum FSH levels were significantly elevated in our study.

Studies showed that in lepromatous leprosy the basal plasma gonadotropin levels are significantly increased, the plasma gonadotropins are normal range in tuberculoid leprosy, and in borderline leprosy the basal mean plasma FSH are normal, whereas LH levels are significantly increased. Furthermore, the basal plasma testosterone levels are significantly decreased in lepromatous leprosy, in tuberculoid leprosy and in borderline leprosy.¹⁹ Our results the associations between elevated levels of gonadotropins and low concentration of FT no present association significant with clinical form of leprosy.

The results of the present study indicate a high frequency of gonadal dysfunction in male Leprosy patients which can be associated with complications of hypogonadism requiring of prevention with testosterone replacement therapy. Therefore, whenever leprosy is diagnosed, there need for routine assessment of gonadotropins and testosterone levels to detect hypogonadism and prevent their consequences.

Conflict of interest: All authors declare to have no conflict of interest.

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