Levothyroxine use and quality of life in patients with hypothyroidism

Consumo de levotiroxina y calidad de vida en pacientes con hipotiroidismo

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Abstract

Introduction: Hypothyroidism affects patients' quality of life, morbidity and mortality. The quality of life of patients taking thyroxine is greatly affected.
Objective: To determine the effect of thyroid hormone level on quality of life among patients taking levothyroxine.
Methods: A cross-sectional study was conducted, including all patients on levothyroxine treatment attending 25 family medicine clinics.
Results: the goiter symptom domain was significantly related to serum TSH and FT4 levels (P 0.036, 0.013).
Conclusions: The quality of life of hypothyroid patients receiving levothyroxine was affected independently by serum levels of thyroid function tests.

Keywords: hypothyroidism, goiter, levothyroxine, thyroid hormones, primary care. Source: DeCS
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Resumen

Introducción:El hipotiroidismo afecta la calidad de vida de los pacientes, la morbilidad y la mortalidad. La calidad de vida depacientes que toman tiroxina se ve muy afectada.
Objetivo:Determinar el efecto del nivel de hormonas tiroideas en la calidad de vida entre los pacientes que toman levotiroxina.
Método: Se realizó un estudio transversal que incluyó a todos los pacientes en tratamiento con levotiroxina que asistieron a 25 clínicas de medicina familiar.
Resultados:el dominio de síntomas de bocio se relacionó significativamente con los niveles séricos de TSH y FT4 (P 0.036, 0.013).
Conclusiones: La calidad de vida de los pacientes hipotiroideos que recibieron levotiroxina se vio afectada independientemente de los niveles séricos de las pruebas de función tiroidea.

Palabras clave: hipotiroidismo, bocio,levotiroxina, hormonastiroideas, atención primaria. Fuente:DeCS

Introduction

Thyroid disease is one of the common chronic endocrine disorders. The prevalence of primary hypothyroidism reached 5% in various populations. This chronic disorder affects patients' quality of life, morbidity and mortality. Many studies showed that the health-related quality of life of patients with benign thyroid disorders and patients taking thyroxine is greatly affected. In addition, hypothyroidism and subclinical thyroid disease are associated with an increased risk of mortality ([1,2]).

Guidelines recommend monitoring the serum thyroid stimulating hormone (TSH) level to achieve the optimal dose of hormone replacement. The medical decision on treating hypothyroidism depends mainly on the biochemical function of the thyroid. Specific clinical and epidemiological aspects related to thyroid diseases were investigated in some populations in the Middle East. Alkafajei et al. estimated a 20.8% prevalence of subclinical hypothyroidism among pregnant women[(3)]. Hashimoto's and lymphocytic thyroiditis were the most common causes of thyroiditis in patients with goiter[(4)]. This study addresses the effect of thyroid hormone level on quality of life (QoL) among patients taking levothyroxine.

Methods

A cross-sectional study was conducted that included all patients on levothyroxine treatment attending 25 family medicine and primary care clinics in Ambato from October to the end of December 2021. Pregnant women, cancer patients and those receiving immunosuppressive treatment were excluded. This study was conducted following the Helsinki declaration of 1975 (including its subsequent amendments), and informed consent was obtained from each patient after explaining all procedures. This study was approved by the Universidad Regional Autónoma de Los Andes (UNIANDES).

Demographic and clinical data, including age, sex, comorbidities, medications, smoking, duration of hypothyroidism, drug dosage and compliance, and history of structural abnormalities of the thyroid gland, were collected using a structured questionnaire. Data were extracted from medical records and confirmed by the interviewers. A participant was considered medication compliant if he or she missed fewer than two monthly doses. Other drugs were used regularly for more than three months other than levothyroxine.

The thyroid-related patient-reported outcome (ThyPRO) is a valid disease-specific questionnaire[(4)]. A trained interviewer conducted the questionnaire during patient visits to the center from October to the end of December 2021. The questionnaire had 12 domains and a final question on the overall effect of thyroid disease on the patient's life (39 items): symptoms of hypothyroid and hyperthyroid disease, goiter, eye symptoms, fatigue, cognitive problems, anxiety, depression, difficulty coping and mood changes, relationships with others, daily activities and thyroid disease, and effect on appearance. Each of the 13 ThyPRO scales was scored as a summary score and transformed into a range from 0 to 100, with higher scores indicating lower CV.

Thyroid hormone level data (TSH, free thyroxine (FT4), and triiodothyronine (T3)) were extracted from electronic records. The reference ranges accepted for FT4 and T3 are 8.5-20.5 (pmol/l) and 3.8-5.9 (pmol/l), respectively.

The database and statistical processing of the data were performed and analyzed in the SPSS 26 statistical program (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used for the results collection, presentation, and interpretation. Patient characteristics were described by frequency and percentage for categorical variables and mean ± standard deviation (SD) for continuous variables. TSH, free T4 and T3 were classified into quartiles according to the latest results during the last year. A Student's t-test or ANOVA was performed to compare the quality of life domain scores. A p-value of less than 0.05 was considered statistically significant.

Results

Out of a total of one hundred and fifty patients who received levothyroxine treatment, twenty-three patients were excluded following the exclusion criteria. Most of the patients were female and under 60 years of age. The main comorbid conditions were hypertension, diabetes, and dyslipidemia. Almost two-thirds of

the patients had no structural thyroid problems and levothyroxine was the only drug with a high compliance rate. The TSH level was within the reference range for 55.9% of patients, while 77.9% and 77.1% were within the reference range of FT4 and FT3, respectively. However, the mean TSH level was outside the reference range, while it was within for FT4 and T3.

All domains were affected among all patients. In descending order, the most affected domains of the ThyPRO were fatigue, emotional susceptibility, and anxiety. At the same time, the least affected was the goiter symptoms domain.

Across the 13 ThyPRO domains, only the goiter symptoms domain was significantly related to serum TSH and FT4 levels (P 0.036, 0.013) (Table 1) and T3 (data not shown). The goiter domain score from the first to the third quartile of TSH worsened but improved in the fourth, and the opposite for free T4. However, after the bivariate correlation test, there was no significant correlation between serum TSH levels and the goiter symptom scale (Pearson correlation = 0.124, p = 0.166). Furthermore, when comparing the means of VC domain scores between the groups, which have TSH within and outside the reference range, there were no significant differences across the 13 ThyPRO domains (p > 0.05). A weak inverse correlation was observed between serum FT4 levels and the goiter symptom scale (Pearson correlation = -0.238, p = 0.012).

Table 1. TSH levels (mU/l) in quartiles related to ThyPRO questionnaire scores for patients receiving levothyroxine.

ThyPROProficiencyScale	TSH < 1.33 (n = 30) Mean (SD)	TSH = 1.33-2.75 (n = 33) Mean (SD)	TSH = 2.76-5.38 (n = 32) Mean (SD)	TSH > 5.38 (n = 32) Mean (SD)	P-value
Symptomsofgoiter	9.80 (10.19)	18.36 (18.12)	23.03 (23.72)	19.13 (16.98)	0.036
Symptomsofhyperthyroidism	26.03 (16.58)	30,52 (22,22)	30.19 (19.46)	31,16 (21,90)	0.749
Symptomsofhypothyroidism	31.04 (23.98)	33,71 (24,20)	35.35 (25.08)	35,55 (25,82)	0.884
Ocular symptoms	21,90 (20,87)	31.48 (25.05)	21,34 (20,76)	31,19 (24,73)	0.134
Fatigue	50,07 (25,77)	58,79 (23,44)	57,00 (28,58)	59,44 (21,24)	0.436
Cognitive problems	37,90 (26,93)	45,36 (23,84)	42,53 (29,67)	44,09 (27,26)	0.717
Anxiety	45,03 (30,57)	53,91 (26,21)	47,91 (22,65)	54,53 (23,48)	0.392
Depression	43.53 (30)	44,76 (24,87)	37,16 (25,72)	42.41 (26.14)	0.680
Emotionalsusceptibility	50,40 (22,85)	54,09 (22,79)	52,00 (24,61)	52,25 (19,63)	0.935
Deteriorated social life	22,47 (24,90)	26,97 (25,79)	25,78 (27,34)	24.92 (26.05)	0.915
Impairmentofdailylife	25,63 (26,62)	34.00 (27.06)	31,88 (28,22)	34,31 (27,29)	0.573
CosmeticComplaints	38,63 (29,61)	34,52 (27,83)	42,66 (32,79)	37,59 (25,92)	0.730
General qualityoflife	38,33 (35,80)	34,85 (33,04)	45,31 (38,33)	40,63 (35,21)	0.689

Source: statistical analysis, SD (standard deviation), milliunits per liter (mU/l), p ≤0.05.

There were no significant differences between ThyPRO domain scores and age, duration of hypothyroidism and levothyroxine compliance (p > 0.05). In terms of sex, the mean

hypothyroidism symptom scale score was higher in females (36.25 ± 24.84) than in males (19.12 ± 16.61) (p = 0.001). However, other domains of the ThyPRO scales showed no significant differences between males and females (p > 0.05). Current smokers had a higher mean depression scale score (43.50 ± 26.39) than non-smokers (27.17 ± 24.06), p = 0.042. Patients with structural thyroid abnormalities (goiter, nodule, cyst, or thyroiditis) reported higher levels of fatigue with a mean (±DE) score of 68.72 (±19.94) and aesthetic complaints (49.32 ± 32.10) compared to those without (53.43 ± 25.09; 35.62 ± 27.59, respectively) with p = 0. 005; p = 0.033, respectively.

Among patient comorbidities, the presence of hypertension was significantly associated with higher mean (±DE) ThyPRO multiple domain scores compared to non-hypertensive patients: goiter symptoms 19.56 (±19.38) versus 8.86 (±8.67) (p < 0.001); hyperthyroidism symptoms 31.30 (±20.63) versus 21.14 (±14.87) (p = 0.010); fatigue 58.43 (±23.81) versus 46.95 (±28.01) (p = 0.049); daily life impairment 34.17 (±27.25) versus 19.14 (±23.83) (p = 0.018); and appearance 40.75 (±28.84) versus 26.68 (±26.98) (p = 0.037). Diabetic patients were associated with a higher goiter symptom score of 19.16 (±19.02) compared to non-diabetic patients at 6.87 (±6.57) (p < 0.001). Also, dyslipidemia was associated with higher emotional susceptibility of 53.93 (±21.46), daily living impairment of 33.44 (±27.78) and appearance scores of 40.

Discussion

In this study, thyroid hormone levels were evaluated in addition to their effect on the quality of life among patients receiving levothyroxine at the primary health care level.

In the current study, 55.9% of patients had TSH levels within the reference range. This rate is higher than that found in a research setting, where the percentage of normal TSH levels among patients with hypothyroidism was 32.2 %[5]. On the other hand, the Colorado Thyroid Disease Prevalence Study revealed that 40 % of patients taking thyroid medications had abnormal TSH levels[6].

All patients in our study ranked fatigue at the top of all affected domains. In addition, there were higher means of emotional susceptibility and anxiety. This finding is similar to what prospective trials and cross-sectional studies documented[7,8].

The least affected domains were goiter symptoms, social life impairment and ocular symptoms. Findings from other studies were almost similar for goiter symptoms, impairment of social life[9] and ocular symptoms[10]. Some gynecological and fertility concerns had the lowest frequency in the two studies[5,11], but these concerns do not exist in the short version of ThyPRO. Overall, QoL was negatively influenced by all patients. Also, other investigators reported a similar finding[12,13].

The analysis according to quartiles of TSH, free T4 and T3 stated that none of the ThyPRO domains had a significant relationship with hormone levels, except for the goiter symptoms domain. However, this statistically significant relationship did not go with a precise explanatory rhythm. Therefore, it did not have clinical significance. Two trials used the ThyPRO questionnaire to assess patient quality of life[7,10]. The first stated that quality of life in patients with Hashimoto's thyroiditis and benign goiter was impaired independently of biochemical control. The other trial showed no significant relationships between ThyPRO scores and blood hormone levels before and after levothyroxine treatment. In addition, investigators using different VC questionnaires detected a weakened relationship between hormone levels and clinical symptoms[14,15].

While no significant relationship was found between ThyPRO domain scores and duration of hypothyroidism, the association with the presence of a structural thyroid problem was significant. Kelderman-Bolk et al. found no difference in the quality of life for both[14], but others reported the effect of duration of hypothyroidism on certain patients' complaints, such as swelling of the hands and feet[11]. In addition, certain comorbid illnesses were significantly associated with higher scores on specific domains of our questionnaire. This link with worse quality of life has been stated by other articles[16].

The findings point out that the complaints of these patients still exist despite levothyroxine therapy and are independent of thyroid hormone levels. This may be clarified by the concept of hypothyroidism at the cellular level[17], and may be related to other factors

such as weight gain[14], or comorbid diseases and medications[18] , as QoL could be affected. However, many physicians' experience indicates that CV-related concerns persist in treated hypothyroid patients[19,20].

Conclusions

The quality of life of hypothyroid patients receiving levothyroxine was affected independently by serum levels of thyroid function tests. Therefore, we cannot rely solely on TSH or free T4 as a marker of optimal treatment outcome, as it does not reflect the patients' state of concern. It is recommended to consider treating comorbid conditions when treating these patients. Increased attention to alleviation and satisfaction of patient complaints could be the main dependent variable of therapy.

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