Optimal levothyroxine dose to achieve euthyroidism in patients with primary hypothyroidism: analysis according to etiology

Dosis óptima de levotiroxina para lograr el eutiroidismo en pacientes con hipotiroidismo primario: análisis según etiología

Dose ideal de levotiroxina para atingir o eutireoidismo em pacientes com hipotireoidismo primário: análise de acordo com a etiologia

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La tiroides es una glándula ubicada en parte frontal y baja del cuello y su función principal es la producción de dos hormonas, T4 y T3. Estas controlan múltiples actividades del organismo, como el metabolismo, crecimiento, actividad cardíaca y muscular, entre otras tantas. Incluso, son fundamentales para el desarrollo neurológico del feto y del recién nacido. El trastorno caracterizado por la producción insuficiente de estas hormonas se denomina hipotiroidismo y el tratamiento consiste, justamente, en el uso diario de la hormona tiroidea sintética, denominada levotiroxina. El objetivo es revertir los síntomas y signos asociados al hipotiroidismo. Aunque la dosis de levotiroxina se determina según el peso corporal de la persona, puede variar según las diferentes etapas de la vida y según la causa del hipotiroidismo.

Conceptos clave:

A) ¿Qué se sabe sobre el tema?

La dosis de levotiroxina recomendada para el tratamiento del hipotiroidismo primario es de 1,6 µg/kg/día, aunque puede variar según la etiología; sin embargo, publicaciones recientes sugieren que la dosis de LT4 es menor.

B) ¿Qué aporta este trabajo?

La dosis de levotiroxina necesaria para lograr el eutiroidismo es mayor en pacientes con hipotiroidismo debido a la terapia con yodo radiactivo y la cirugía de tiroides; además, los pacientes con tiroiditis de Hashimoto requieren una dosis menor de levotiroxina que las recomendaciones actuales.

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Abstracts:

Introduction. Levothyroxine (LT4) has been considered the standard of care for treatment of hypothyroidism. Current recommendations suggest a LT4 dose between 1.6–1.8 µg/kg/day. The aim of this study was to evaluate the LT4 dose for adult patients with primary hypothyroidism of different etiologies who reached euthyroidism.
Methods. A cross-sectional study was performed from the retrospective review of the charts of patients with primary hypothyroidism in treatment with LT4. Subjects were classified according to TSH level in overtreated (TSH<0.4 µIU/ml), euthyroid (TSH 0.40-4.20), and undertreated (TSH>4.2) and according to the etiology of hypothyroidism. A stepwise logistic regression model was performed to evaluate the variables associated with TSH<0.4 µIU/ml.
Results. 955 patients were included. 75.13% of the patients had an adequate LT4 replacement. LT4 dose to achieve euthyroidism was higher in patients with a history of radioiodine therapy (1.92 µg/kg) and thyroid surgery (1.52 µg/kg), while the LT4 dose required to achieve euthyroidism in patients with Hashimoto's thyroiditis and atrophic thyroiditis was lower than that reported in previous studies (1.25 and 1.08 µg/kg, respectively). The variables that were associated with a higher probability of TSH<0.4 µIU/ml were male gender, Hashimoto's thyroiditis, radioiodine therapy, and thyroid surgery.
Major conclusion. LT4 dose required to achieve euthyroidism in patients with hypothyroidism varies according to the etiology, being higher in patients with hypothyroidism due to radioiodine therapy and thyroid surgery. Patients with hypothyroidism due to Hashimoto's thyroiditis and atrophic thyroiditis require a lower dose than current recommendations.

***Keywords**: hypothyroidism; thyroxine; Hashimoto disease*

Resumen:

Introducción. La levotiroxina (LT4) se considera el estándar de tratamiento del hipotiroidismo. Las recomendaciones actuales sugieren una dosis de LT4 entre 1,6-1,8 µg/kg/día. El objetivo de este estudio fue evaluar la dosis de LT4 en pacientes adultos con hipotiroidismo primario de diferentes etiologías que alcanzaron el eutiroidismo.
Métodos. Estudio transversal a partir de la revisión retrospectiva de historias clínicas de pacientes con hipotiroidismo primario en tratamiento con LT4. Los sujetos se clasificaron según el nivel de TSH en sobretratados (TSH<0,4 µUI/ml), eutiroideos (TSH 0,40-4,20) y subtratados (TSH>4,2) y según la etiología del hipotiroidismo. Se realizó un modelo de regresión logística escalonada para evaluar las variables asociadas con TSH <0,4 µUI/ml.
Resultados. Se incluyeron 955 pacientes. El 75,13% tuvo un reemplazo adecuado de LT4. La dosis de LT4 para lograr el eutiroidismo fue mayor en pacientes con antecedentes de terapia con yodo radiactivo (1,92 µg/kg) y cirugía de tiroides (1,52 µg/kg), mientras que la dosis de LT4 para lograr el eutiroidismo en pacientes con tiroiditis de Hashimoto y tiroiditis atrófica fue menor que el reportado en estudios previos (1,25 y 1,08 µg/kg, respectivamente). Las variables que se asociaron con una mayor probabilidad de TSH<0,4 µUI/ml fueron el sexo masculino, tiroiditis de Hashimoto, terapia con yodo radiactivo y cirugía de tiroides.
Conclusión principal. La dosis de LT4 necesaria para alcanzar el eutiroidismo en pacientes con hipotiroidismo varía según la etiología, siendo mayor en pacientes con hipotiroidismo por tratamiento con yodo radiactivo y cirugía tiroidea. Los pacientes con hipotiroidismo debido a tiroiditis de Hashimoto y tiroiditis atrófica requieren una dosis más baja que las recomendaciones actuales.

***Palabras clave**: hipotiroidismo; tiroxina; enfermedad de Hashimoto*

Resumo:

Introdução. A levotiroxina (LT4) é considerada o padrão de tratamento para o hipotireoidismo. As recomendações atuais sugerem uma dose de LT4 entre 1,6-1,8 µg/kg/dia. O objetivo deste estudo foi avaliar a dose de LT4 em pacientes adultos com hipotireoidismo primário de diferentes etiologias que atingiram eutireoidismo.
Métodos. Estudo transversal baseado na revisão retrospectiva de prontuários médicos de pacientes com hipotireoidismo primário em tratamento com LT4. Os indivíduos foram classificados de acordo com o nível de TSH em supertratado (TSH <0,4 µIU/ml), eutireoidiano (TSH 0,40-4,20) e subtratado (TSH> 4,2) e de acordo com a etiologia do hipotireoidismo. Um modelo de regressão logística escalonada foi realizado para avaliar as variáveis associadas ao TSH <0,4 µIU/ml.
Resultados. 955 pacientes foram incluídos. 75,13% tiveram uma substituição de LT4 adequada. A dose de LT4 para atingir o eutireoidismo foi maior em pacientes com história de terapia com iodo radioativo (1,92 µg/kg) e cirurgia da tireoide (1,52 µg/kg), enquanto a dose de LT4 para atingir o eutireoidismo em pacientes com tireoidite de Hashimoto e tireoidite atrófica foi inferior ao relatado em estudos anteriores (1,25 e 1,08 µg/kg, respectivamente). As variáveis que se associaram à maior probabilidade de TSH <0,4 µIU/ml foram sexo masculino, tireoidite de Hashimoto, radioiodo e cirurgia da tireoide.
Conclusão principal. A dose de LT4 necessária para atingir o eutireoidismo em pacientes com hipotireoidismo varia de acordo com a etiologia, sendo maior em pacientes com hipotireoidismo devido ao tratamento com iodo radioativo e cirurgia da tireoide. Pacientes com hipotireoidismo devido à tireoidite de Hashimoto e tireoidite atrófica requerem uma dose mais baixa do que as recomendações atuais.

***Palavras-chave**: hipotireoidismo; tiroxina; doença de Hashimoto*

INTRODUCTION

Hypothyroidism is a common condition resulting from thyroid hormone deficiency.[1,2] The prevalence of hypothyroidism varies according to the region. Levothyroxine (LT4) has been considered the standard of care for treatment due to its efficacy in resolving its symptoms, long-term experience of its benefits, favorable side effect profile, ease of administration, good intestinal absorption, long serum half-life, and low cost. TSH serves as a surrogate marker of euthyroidism. Achieving a serum TSH within the normal age adjusted reference interval is desirable for all patients.[3]

The etiology of a patient's hypothyroidism affects his dose of LT4 probably reflecting the amount of residual functional thyroid tissue.[4] We recently demonstrated in a study involving 586 patients that LT4 dose needed to achieve euthyroidism correlated more adequately with actual body weight (ABW) than with ideal body weight (IBW) and that patients with Hashimoto's thyroiditis they require a higher dose to reach the euthyroid state (1.2 µg/ kg/day versus 1.03 µg/kg/day).[5] Although previous studies demonstrated that weight-based LT4 dose in patients with atrophic thyroiditis (1.26±0.07 µg/kg/day) was lower than in patients with Hashimoto's thyroiditis (1.59±0.07 µg/kg/day),[6] it can be observed that the requirements are higher than those reported in our cohort. Some studies estimate higher doses of 2.0–2.1 µg/kg/day for some patient groups.[7] Furthermore, current guidelines suggest a LT4 dose between 1.6–1.8 µg/kg/day of ABW.[1]

Therefore, the primary aim of this study was to evaluate the mean daily replacement dose of LT4 for adult patients with primary hypothyroidism of different etiologies who reached a state of biochemical euthyroidism. The secondary objective was to evaluate the percentage of patients with excessive or deficient LT4 substitution according to the etiology of the primary hypothyroidism. Finally, we compared the mean LT4 dose necessary to achieve euthyroidism obtained in our analysis with that reported in the literature.

MATERIALS AND METHODS

STUDY DESIGN

A cross-sectional study was performed from the retrospective review of charts of adult patients over 18 years of age from four Endocrinology services in the cities of Rosario and Casilda (Argentina) during the period between January 2017 and December 2019. Approval from the teaching and ethics committee was obtained before the study began.

SUBJECTS

All patients older than 18 years, of both sexes, with previous diagnosis of primary hypothyroidism in treatment with LT4 and with a stable dose of LT4 during the last six months were included.

Patients with primary hypothyroidism with follow-up and/or irregular treatment, pregnant or lactating women, patients with a history of thyroid cancer, and central hypothyroidism were excluded from the study. Patients under treatment amiodarone, lithium, proton pump inhibitors, iodine, corticosteroids, iron or calcium supplements, patients with severe chronic diseases (congestive heart failure, NYHA III-IV congestive heart disease, hypercapnia and/or hypoxemia lung disease, chronic kidney disease), pituitary disease and/or malabsorptive gastrointestinal diseases (celiac disease, inflammatory bowel disease, lactose intolerance, bariatric surgery) were also excluded from the analysis.

DATA COLLECTION

Sex, age, ABW (kg), previous hyperthyroidism, thyroid surgery, and radioiodine therapy were recorded. Gender was classified into three distinct groups: men, premenopausal women, and menopausal women. The mean T4 dosage per day per body weight was derived using the total T4 dosage per week divided by 7 and their respective ABW. TSH and thyroid autoantibody status [thyroid peroxidase antibodies (TPOAb) or antithyroglobulin antibody (TgAb)] were recorded.

TSH assays used by the clinical laboratories employed a third-generation ultra-sensitive immunochemiluminometric assay with a sensitivity of 0.01 µIU/ml (reference ranges approximately 0.4–4.2 µIU/ml). Because some patients had more than one TSH value available during the study period, we decided to choose the last TSH determination value available with stable LT4 dose during the study period. Subjects were classified into 3 groups based on TSH level: overtreated (TSH<0.4 µIU/ml), euthyroid (TSH from 0.40 to 4.20µIU/ml, and undertreated (TSH>4.2 µIU/ml).

Patients were also classified according to the etiology of their hypothyroidism: Hashimoto's thyroiditis, thyroid surgery (total thyroidectomy), post-radioiodine therapy, and atrophic thyroiditis.

STATISTICAL ANALYSIS

Statistical software R version 4.0.4 was used. Continuous variables were expressed as means and standard deviations (mean±SD). Categorical variables were expressed as counts and percentages (%). The t-test or analysis of variance (Bonferroni post-test), as appropriate, was used to compare continuous measures between groups. Chi-square or Fisher exact test was used for categorical variables (Holm post-test). One-sample t student test was used to compare the LT4 dose to achieve euthyroidism obtained in our study with that reported in previous studies according to different causes of primary hypothyroidism. Correlations analyses were made with the Pearson correlation coefficient. Variables that reached significance of $p<0.05$ in the exploratory analysis were entered into a stepwise logistic regression model to determine their association with low TSH (<0.4 µIU/ml) compared to the normal TSH group. The selection of the final model was made using the p-value. The likelihood ratio was expressed as Odds Ratio (OR) and 95% confidence interval (CI95%). Differences were considered significant if $p<0.05$. This study was performed in line with the principles of the Declaration of Helsinki. The study was approved by the Ethics Committee of our institution. This research has not received specific aid from agencies of the public sector, commercial sector, or non-profit entities

RESULTS

A total of 1562 charts of patients were reviewed. Of this total, 955 patients met the inclusion criteria. Most of the participants were women (842 women and 113 men). Of the 842 women, 358 were of reproductive age and 484 were post-menopausal. The status of TPOAb and/or TgAb was verified in 547 patients (301 patients with positive antibodies and 246 patients with negative antibodies).

Tabla 1 shows the clinical characteristics of the study population based on their biochemical classifications using TSH levels. 75.13% of the patients had an adequate LT4 replacement, while 9.65% and 15.22% were overtreated and undertreated, respectively. A negative correlation was observed between TSH levels and LT4 dose ($r=-0.236$, $p<0.001$).

	TSH <0.4 (n= 92)	**TSH 0.40-4.2 (n= 716)**	**TSH >4.2 (n= 145)**	**p-value**
Age (years)	52.64±14.70	54.42±15.65	52.85±16.51	ns
Pre-menopausal women (%)	33 (9.4)	263 (75.1)	54 (15.4)	<0.0001*
Menopausal women (%)	46 (9.7)	376 (79)	54 (11.3)	
Male (%)	11 (9.7)	66 (58.4)	36 (31.9)	
Body weight (kg)	75.27±17.11	76.08±17.96	82.10±17.83	0.0007**
LT4 dose (µg/kg/day)	1.53±0.50	1.21±0.47	1.15±0.45	<0.0001***
* Chi-square test (Holm post-test): p<0.001 male vs pre-menopausal and vs menopausal				

Table 1. Clinical characteristics of study population

The mean daily LT4 dose according to the different etiologies was higher in those with a history of radioiodine therapy **(Figure 1)**.

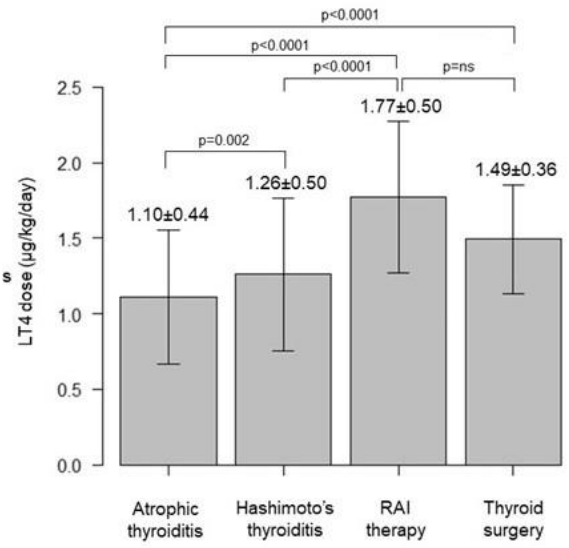

Figure 1. LT4 dose according to etiology of hypothyroidism (ANOVA. Bonferroni post-test)

Among patients in the euthyroid state, the mean daily LT4 dose varied according to the different etiologies of hypothyroidism, being higher in those patients undergoing radioiodine therapy and thyroid surgery, and lower in patients with atrophic thyroiditis. **¡Error! No se encuentra el origen de la referencia.** shows the mean LT4 dose according to the TSH range and the different causes of primary hypothyroidism. There was no correlation between the mean LT4 dose and age in euthyroid patients (r=-0.037, p=0.31).

	Atrophic thyroiditis	**Hashimoto's thyroiditis**	**RAI therapy**	**Thyroid surgery** (n= 145)	*p value*
LT4 dose (µg/kg/day)	1.09±0.42*	1.25±0.48**	1.92±0.58***	1.52±0.36	<0.0001
ANOVA. Bonferroni post-test					
* p=0.004 vs Hashimoto's thyroiditis; p<0.0001 vs RAI therapy and vs thyroid surgery					
** p<0.0001 vs RAI therapy; p=0.005 vs thyroid surgery					
*** p=0.03 vs thyroid surgery					

Table 2. LT4 dose in euthyroid patients

A one-sample t student test was performed with the alternative hypothesis that the mean LT4 dose in patients with Hashimoto's thyroiditis and atrophic thyroiditis obtained in our study is lower than that reported in the literature (1.59 µg/kg/day and 1.26 µg/kg/day, respectively). This hypothesis is corroborated for both Hashimoto's thyroiditis and atrophic thyroiditis (p <0.0001).

Tabla 3 shows the number and percentage of patients according to the different TSH categories and the etiology of hypothyroidism.

	TSH <0.4 (n= 92)	**TSH 0.40-4.2 (n= 716)**	**TSH >4.2** (n= 145)	*p value*
Hashimoto's thyroiditis (%)	33 (11)	212 (70.4)	56 (18.6)	0.00118*
Thyroid surgery (%)	8 (15.1)	36 (67.9)	9 (17)	
RAI therapy (%)	5 (20.8)	15 (62.5)	4 (16.7)	
Atrophic thyroiditis (%)	10 (4.7)	182 (85.4)	21 (9.9)	
Chi-square (Holm post-test)				
* p=0.02 atrophic thyroiditis vs Hashimoto's thyroidectomy; p=0.018 atrophic thyroiditis vs RAI therapy; p=0.02 atrophic thyroiditis vs thyroid surgery.				

Table 3. Percentage of patients according to TSH level and etiology of hypothyroidism

To evaluate the variables involved in overtreated with LT4, variables that showed differences according to the different TSH categories were included. Therefore, gender, body weight, etiology of hypothyroidism, and mean LT4 dose were included in the initial model. The variables that were associated with the highest probability of TSH <0.4 were LT4 dose, Hashimoto's thyroiditis, and thyroid surgery. In the final model, the only variable associated was LT4 dose with OR 2.80 (95% CI 1.64-4.77, p=0.0002). **¡Error! No se encuentra el origen de la referencia.** summarizes the initial and final model, OR (95% CI) and p-value.

	OR	**95% CI**	**p-value**
Initial model			
Body weight (kg)	1.01	0.99-1.03	0.32
Pre-menopausal women	0.96	0.35-2.65	0.94
Menopausal women	0.85	0.33-2.19	0.73
LT4 dose (µg/kg/day)	2.48	1.33-4.64	0.004
Hashimoto's thyroiditis	2.78	1.27-6.05	0.01
RAI therapy	4.30	0.87-21.2	0.07
Thyroid surgery	2.84	1.11-7.24	0.03
Final model			
LT4 dose (µg/kg/day)	2.80	1.64-4.77	0.0002

Table 4. Multivariate logistic regression analysis

DISCUSSION

LT4 treatment is considered the standard treatment in patients with primary hypothyroidism due to its efficacy when administered orally and its long serum half-life that allows daily or even weekly administration. The goal of this treatment is to normalize the signs and symptoms of hypothyroidism, including the biological and psychological markers of the disease, and to achieve TSH level within the reference range for age, avoiding overtreatment, especially in elderly patients.[1]

Inadequate hypothyroidism treatment has been shown to be associated with health consequences. A population-based study showed that patients with a high (>4 µIU/ml) or suppressed TSH (<0.03 µIU/ml) had an increased risk of cardiovascular disease, dysrhythmias, and fractures, but patients with a low but unsuppressed TSH (0.03-0.4 µIU/ml) did not.[8] In contrast, in primary hypothyroidism patients under LT4 treatment whose TSH levels were within the reference range no clinically significant differences were observed in long-term health outcomes, including mortality.[9] In our cohort, 75% of the patients had an adequate LT4 replacement while 15.22% were undertreated and 9.65% were overtreated. This percentage of patients with TSH levels within the normal range is higher than that reported in other cohorts.[8,10-14]

The etiology of primary hypothyroidism affects LT4 requirements, reflecting the different degrees of residual functional thyroid. Patients who are athyreotic because of thyroidectomy generally require a higher LT4 dose.[1,6] Our analysis showed that patients with a history of radioiodine therapy received higher doses of LT4, followed by patients undergoing thyroid surgery, Hashimoto's thyroiditis, and lastly, atrophic thyroiditis. Typically, LT4 replacement after thyroidectomy for benign conditions uses an empirical dose of approximately 1.6 µg/kg/day, with subsequent adjustments based on thyroid function test results.[15] In our cohort, thyroidectomized patients required a mean dose of LT4 to achieve euthyroidism like that previously reported (1.52±0.36 µg/kg/day). Patients who have received radioactive iodine therapy for Graves's disease may have a variable need for LT4, depending on the remaining functional autonomic thyroid. However, the studies that analyzed the LT4 dose necessary to achieve euthyroidism in these subjects are scarce. Gordon et al. showed that the mean LT4 dose in patients with hypothyroidism after radioiodine treatment increased from 0.87 µg/kg/day at 6 months to 1.57 µg/kg/day at 7 years of follow-up.[6] In our study, the mean dose of LT4 in patients with euthyroidism was slightly higher (1.92 ± 0.58), which may reflect a lower thyroid functional reserve.

Hashimoto's thyroiditis is the most common cause of primary hypothyroidism in iodine-sufficient areas. In our study, patients with Hashimoto's thyroiditis required a higher LT4 dose to achieve euthyroid state than patients with atrophic thyroiditis (1.25±0.48 µg/kg/day *versus* 1.09±0.42 µg/kg/day). This is in line with a previous study that demonstrated that weight based LT4 dose in patients with atrophic thyroiditis (1.26±0.07 µg/kg/day) was lower than in patients with Hashimoto's thyroiditis (1.59±0.07 µg/kg/day).[6] However, when we compare the dose reported in previous studies with that obtained in our population, we confirm that the LT4 requirements to reach the euthyroid state are lower. Recent studies[16,17] support our finding and highlight the need for a review of current recommendations for the treatment of patients with hypothyroidism.

Factors that can commonly lead to LT4 dose adjustments include non-compliance, changes in the LT4 formulation, dosing errors, increased serum T4-transporter globulin levels, changes in body weight, dietary habits, or concomitant intake of calcium supplements, ferrous sulfate, proton pump inhibitors, bile acid sequestrants, or sucralfate.[18,19] We previously demonstrated that the LT4 dose required to achieve euthyroidism correlates better with ABW body weight rather than ideal BW. Likewise, we show that the daily requirements of LT4 do not vary according to age when analyzing according to age ranges (18-44 years 1.18 µg/kg/day, 45-65 years 1.07 µg/kg/day, >65 years 1.11 µg/kg/day), or gender (male 0.97 µg/kg/day, premenopausal 1.16 µg/kg/day, menopausal 1.13 µg/kg/day).[5] In the current study we corroborate that the LT4 dose (µg/kg/day) does not correlate with age. In our analysis, patients under treatment with calcium, iron, amiodarone, lithium, iodine, corticosteroids, and proton pump inhibitors were excluded.

Several factors can affect the LT4 requirements necessary to normalize TSH levels. A study carried out on a cohort of 1037 patients with hypothyroidism showed that males and younger age are associated with insufficient replacement with LT4, while a longer duration of treatment is associated with overtreatment.[10] The authors did not analyze the etiology of hypothyroidism as a confounding factor. Another study demonstrated that overtreated subjects received a higher dose of LT4 than those in the euthyroid state (1.4 µg/kg/day versus 1.1 µg/kg/day).[17] Our initial analysis showed that the variables involved in the patient's overtreated (TSH <0.4 µIU/ml) were higher LT4 dose, male gender, lower BW, and higher frequency of radioiodine therapy, Hashimoto's thyroiditis, and thyroid surgery. Therefore, we performed a logistic regression analysis to evaluate the variables involved with a TSH level <0.4 µIU/ml and we observed that LT4 dose and history of thyroid surgery and Hashimoto's thyroiditis were initially associated with a greater probability of overtreatment. Considering that a higher dose of LT4 is associated with a higher risk of overtreatment, it is contradictory that patients with Hashimoto's thyroiditis, who a priori required lower LT4 dose to achieve euthyroidism compared to those patients with a history of radioiodine therapy, present a higher risk of overtreatment compared to these. However, the cause of hypothyroidism does not seem to be the most influential factor since, in the stepwise logistic regression model, only the LT4 dose was associated with a greater probability of overtreatment, which is consistent with previous studies.[17] This finding would allow the stratification of patients who need a closer biochemical follow-up.

The strength of our study is the large population size included in the analysis, the confirmed compliance with the medication, the exclusion of factors that could affect the LT4 dose and the analysis of the LT4 dose according to different etiologies of primary hypothyroidism. The limitations arise from the cross-sectional nature of the study that did not allow analysis. For example, we did not record the time between radioiodine therapy and the inclusion of patients in the study. Hypothyroidism develops in as many as 90% of patients within the first year after therapy, with a continuing rate of 2% to 3% per year thereafter. This issue is important as hypothyroidism is an unavoidable consequence of radioiodine therapy.[20] Another limitation was that determinations of TSH levels were not carried out in a centralized laboratory. However, a third-generation ultra-sensitive immunochemiluminometric assay was employed in all cases. Finally, we did not include peripheral thyroid hormones in the analysis.

CONCLUSIONS

LT4 dose necessary to achieve euthyroidism in patients with primary hypothyroidism varies according to its etiology, being higher in patients with hypothyroidism due to radioiodine therapy and thyroid surgery. In addition, patients with hypothyroidism due to Hashimoto's thyroiditis and atrophic thyroiditis require a lower dose than current recommendations.

Limitaciones de responsabilidad:
La responsabilidad del trabajo es exclusivamente de quienes colaboraron en la elaboración del mismo.

Conflicto de interés:
Ninguno.

Fuentes de apoyo:
La presente investigación no contó con fuentes de financiación.

Originalidad:
Este artículo es original y no ha sido enviado para su publicación a otro medio de difusión científica en forma completa ni parcialmente.

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Contribución de los autores:
Quienes participaron en la elaboración de este artículo, han trabajado en la concepción del diseño, recolección de la información y elaboración del manuscrito, haciéndose públicamente responsables de su contenido y aprobando su versión final.

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