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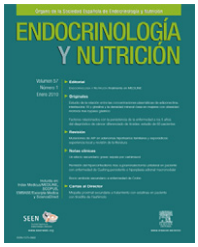

ORIGINAL ARTICLE

Serum free triiodothyronine (T3) to free thyroxine (T4) ratio in treated central hypothyroidism compared with primary hypothyroidism and euthyroidism

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KEYWORDS
Central hypothyroidism;
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T4

Abstract The standard treatment of hypothyroidism (central and primary) consists of thyroxine (T4) administration alone. However, the normal thyroid gland produces a small proportion of triiodothyronine (T3) directly into the circulation.
Aim: We aimed to study the free T3 to free T4 ratio in treated central hypothyroidism compared with euthyroidism and treated primary hypothyroidism.
Methods: Eighty-three subjects were included in this cross-sectional study: 36 with central hypothyroidism, 20 with primary hypothyroidism and 27 healthy controls. A clinical history and a physical examination, including height and weight measurement, were performed and body mass index (BMI) was calculated. Fasting blood was drawn to measure T3, T4, free T3, free T4 and TSH.
Results: The free T3 to free T4 ratio was lower in treated central hypothyroidism than in euthyroidism but was similar to treated primary hypothyroidism. Free T4 was higher in treated central and primary hypothyroidism than in euthyroidism. Age, sex and BMI did not affect the free T3 to free T4 ratio.
Conclusions: Treated patients with central hypothyroidism had a lower free T3 to free T4 ratio, similar free T3 levels and higher free T4 concentrations than euthyroid controls, whereas all these parameters were similar in central and primary hypothyroid patients treated with T4. The question of whether these findings translate into adequate tissue concentrations of free thyroid hormones in all tissues remains to be answered. Further studies should aim to determine whether clinical outcomes could be improved by a treatment achieving more physiological plasma concentrations.

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PALABRAS CLAVE
Hipotiroidismo central;
Razón triyodotironina tiroxina;
T3;
T4

Razón entre la triyodotironina (T3) libre en suero y la tiroxina (T4) circulante en el hipotiroidismo central tratado comparada con el hipotiroidismo primario y el eutiroidismo

Resumen El tratamiento habitual del hipotiroidismo (central y primario) consiste en administrar sólo tiroxina (T4). Sin embargo, la glándula tiroides normal produce una proporción pequeña de triyodotironina (T3) que va directamente a la circulación.
Objetivo: Estudiar la razón entre las concentraciones de T3 /T4 circulantes en el hipotiroidismo central tratado respecto al eutiroidismo y al hipotiroidismo primario también tratado.
Métodos: Se incluyeron 83 sujetos en este estudio transversal: 36 presentaban hipotiroidismo central, 20 hipotiroidismo primario y 27 eran controles sanos. Se realizó una historia clínica y una exploración física que incluía la altura y el peso, y se calculó el índice de masa corporal (IMC). Se extrajo sangre en ayunas para medir T3, T4, T3 libre, T4 libre y TSH.
Resultados: La razón T3/T4 circulantes fue inferior en el hipotiroidismo central que en el eutiroidismo, pero similar a la del hipotiroidismo primario. La T4 libre fue mayor en el hipotiroidismo central y en el primario que en el eutiroidismo. La edad, el sexo y el IMC no afectaron la razón T3 /T4 circulante.
Conclusiones: Los pacientes con hipotiroidismo central tratados presentan una razón T3/T4 circulante más baja, niveles de T3 circulante similares y concentraciones de T4 libre superiores a los controles eutiroideos; sin embargo, todos estos parámetros son similares en los pacientes con hipotiroidismo central y primario tratados con T4. No se sabe si esto se traduce en concentraciones tisulares adecuadas de hormonas tiroideas libres en todos los tejidos. Queda por investigar si un tratamiento que obtenga una concentración plasmática más fisiológica sería mejor desde el punto de vista de los resultados clínicos. Es de esperar que se diseñen estudios en esa dirección.

Introduction

Triiodothyronine (T3) is the active thyroid hormone. Plasma T3 is generated by direct thyroid production (about 20%) and from peripheral conversion of thyroxine (T4) to T3, mainly in liver and kidneys (80%).[1-4] The T3 found in the cell nucleus in distinct tissues is derived in a different proportion either from the plasma pool or from local T4 deiodination within the tissue.[4]

Patients with primary hypothyroidism correctly treated with levothyroxine (LT4) [based on normal thyroid-stimulating hormone (TSH) levels] are known to have a lower plasma T3 to T4 ratio than euthyroid individuals.[5,6]

Central hypothyroidism is usually part of a complex hormonal dysfunction. This disorder is rarely found as an isolated deficiency and is frequently combined with other pituitary deficiencies. Therefore, in addition to the clinical consequences of thyroid hormone deficiency and replacement, other hormone deficiencies and their treatments come into play. Cortisol and growth hormone (GH) play a role in T4 to T3 conversion;[7-9] non-replacement or suboptimal replacement of these hormones affect T4 deiodination[10] and may alter the plasma free T3 to free T4 ratio. In addition, TSH levels are not useful to adjust the LT4 dose in central hypothyroidism and consequently a potential T3 deficiency will be more difficult to detect.[11]

Whether the free T3 to free T4 ratio in patients with stable treated central hypothyroidism is similar to that of euthyroid individuals and to that of primary hypothyroid patients treated with T4 is unknown. Determining this issue would be the first step to evaluate the adequacy of LT4 alone in the treatment of central hypothyroidism and to define optimal thyroid replacement therapy for this disorder.

We aimed to study serum free thyroid hormone concentrations in patients with treated central hypothyroidism in comparison with patients with treated primary hypothyroidism and euthyroid controls.

Methods

Patients

A total of 83 subjects participated in this cross—sectional study. Thirty-six patients with central hypothyroidism who were followed-up in our tertiary referral center were recruited. Patients were included if they were receiving stable treatment for thyroid and other pituitary deficiencies for at least 3 months prior to participating in the study and pituitary disease was inactive. Adequate central thyroid replacement was defined as free T4 levels within the normal range. Twenty patients with primary hypothyroidism were also included. These patients had to show normal TSH levels and have been receiving a stable LT4 dose for at least 3 months prior to entering the study. Twenty-seven control subjects were recruited from the patients' relatives and hospital staff and their relatives. Exclusion criteria for patients and controls consisted of a serious concomitant medical disease, glucocorticoid treatment for reasons other than replacement therapy, and treatment with antiepileptic drugs.