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ORIGINAL ARTICLE

Treatment of subclinical hypothyroidism in pregnancy using fixed thyroxine daily doses of 75 μg☆

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KEYWORDS
Hypothyroidism;
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Abstract
Background and objectives: Treatment of hypothyroid pregnant women is usually calculated based on weight (1 μg/kg/day) and TSH levels. This study assessed the usefulness of treating these women with a fixed dose of 75 μg/day.
Patients and methods: All women with pregnancy diagnosed from January to August 2012 in the Vigo Health Area (Spain) without previous diagnosis of thyroid disease or thyroxine treatment and with TSH levels over 4.5 mUI/mL were enrolled by consecutive sampling. All 116 women in the sample were treated with a fixed daily dose of thyroxine 75 μg-thyroxine levels were measured at two, four, and six months, and thyroxine dose was modified if TSH level was lower than 0.3 or higher than 4.5 mUI/mL.
Results: A woman had a TSH level less than 0.3 mUI/mL in a test; reduction of thyroxine dose to 50 μg/day allowed for maintaining TSH level within the desired range until delivery. Six women had TSH levels over 4.5 mUI/mL in one test; in all of them, increase in thyroxine dose to 100 μg/day allowed for maintaining the level within the desired range until delivery.
Conclusions: Fixed daily doses of thyroxine 75 μg allowed for achieving goal TSH levels in most of our pregnant women with subclinical hypothyroidism, irrespective of their weight and baseline TSH level.

PALABRAS CLAVE
Hipotiroidismo;
Gestación;
Dosis;
Tratamiento;
Tiroxina

Tratamiento del hipotiroidismo subclínico en gestantes con una dosis fija diaria de 75 μg de tiroxina

Resumen
Antecedentes y objetivos: Los métodos habituales de cálculo de la dosis inicial de tiroxina en el tratamiento de gestantes hipotiroideas usan el peso de las pacientes (1 μg/kg/día) o la concentración plasmática de TSH. Este estudio analiza la idoneidad de tratar a estas mujeres con una dosis fija de 75 μg/día de la hormona.

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Pacientes y métodos: Se seleccionaron mediante un muestreo consecutivo a todas aquellas mujeres diagnosticadas de gestación en el área sanitaria de Vigo entre enero y agosto de 2012, sin antecedentes de tiroidopatía y con una concentración de TSH superior a 4,5 mUI/ml y T4L normal. Las 116 gestantes de la muestra resultante recibieron tratamiento con 75 μg/día de tiroxina, y se les hizo un análisis a los 2, 4 y 6 meses tras la instauración del tratamiento, modificándose la dosis de la hormona si la concentración de TSH era inferior a 0,3 o superior a 4,5 mUI/ml.

Resultados: Una de las pacientes tuvo, en un análisis, una concentración de TSH inferior a 0,3 mUI/ml; el descenso de la dosis de tiroxina a 50 μg/día permitió mantener dicha concentración en el rango deseado hasta el parto. Seis tuvieron en un análisis una concentración de TSH superior a 4,5 mUI/ml; en todas ellas el aumento de la dosis de tiroxina a 100 μg/día permitió mantener dicha concentración en el rango deseado hasta el parto.

Conclusiones: Una dosis de tiroxina 75 μg/día permitió conseguir los objetivos de concentración de TSH de nuestro estudio en la mayoría de las gestantes con hipotiroidismo subclínico, independientemente de su peso y de su concentración inicial de TSH.

Introduction

Diagnosis and treatment of hypothyroidism in pregnant women are frequently controversial.[1] Most, but not all,[2] studies show decreased plasma levels of thyroid-stimulating hormone (TSH) during pregnancy,[3–7] and both the American thyroid Association (ATA) and the American Association of Clinical Endocrinologists (AACE) recommend use of the following specific normal ranges for pregnant women: first trimester, 0.1–2.5 mIU/mL; second trimester, 0.2–3.0 mIU/mL; and third trimester, 0.3–3 mIU/mL, instead of the standard range used in non-pregnant women (0.3–4.5 mIU/mL).

Unlike in frank hypothyroidism, there is no agreement on the indications for treatment in pregnant women with subclinical hypothyroidism (increased TSH levels with normal FT4). The ATA and AACE recommend that only patients with peroxidase antibodies (anti-TPO) or thyroglobulin antibodies (anti-TG) are treated, based on a study which showed increased complications of pregnancy in these patients.[3] By contrast, other guidelines advocate treatment of all pregnant women with subclinical hypothyroidism, regardless of plasma levels of thyroid antibodies.[4] The goal of treatment, if administered, is to achieve normal TSH levels for each trimester of pregnancy.

There is no agreement either on how to calculate the starting thyroxine dose. Some authors suggest that dose is calculated based on patient weight (1 μg/day),[5] while others recommend that dosage is based on TSH levels at diagnosis: 25 μg/day if TSH level is 4–8 mIU/mL; 50 μg/day if TSH level is 8–12 mIU/mL; 75 μg/day if TSH level is greater than 12 mIU/mL.[6] A recent report by our group showed that a fixed dose of 50 μg thyroxine in pregnant women with subclinical hypothyroidism allowed for maintaining TSH levels ranging from 3.0 to 4.5 mIU/mL in approximately 80% of women, regardless of weight and baseline TSH level.[7] This study subsequently analyzed the convenience of treating subclinical hypothyroidism in pregnant women with a daily dose of 75 μg of thyroxine.

Subjects and methods

A consecutive sample of women with plasma TSH levels higher than 4.5 mIU/L was obtained from all women diagnosed with pregnancy in the Vigo health area between January and August 2012. Women with plasma FT4 levels less than 0.93 ng/100 mL (frank hypothyroidism), those who had ever been treated with thyroxine, and those previously diagnosed with any thyroid disease (including hypothyroidism, hyperthyroidism, goiter, and thyroid nodule) were excluded.

The resulting cohort consisted of 116 pregnant women, all of whom received (as usual in our health area) 200 μg/day of potassium iodide at least from the time pregnancy was diagnosed. One of the patients moved to another town in the second trimester of pregnancy, and pregnancy did not reach its term in another four patients.

All pregnant women were informed of diagnosis of subclinical hypothyroidism and the need for treatment with thyroxine. The thyroxine dose of 75 μg/day has become our standard since we found in a pregnant cohort that doses of 50 μg/day is often inadequate and never excessive in this population.[7] All pregnant women signed an informed consent.

All women were prescribed since diagnosis of hypothyroidism a daily dose of 75 μg of thyroxine (Eutirox® 75) administered 30 min before breakfast, regardless of weight, height, presence of thyroid antibodies, or plasma TSH levels. TSH and FT4 levels were tested in all pregnant women 2, 4, and 6 months after diagnosis. When TSH levels in any test were higher than 4.5 mIU/mL, thyroxine dose was increased by 25 μg/day, and when levels were less than 0.3 mIU/mL, thyroxine dose was reduced in the same amount.

Plasma levels of thyroid peroxidase and thyroglobulin antibodies were tested in all pregnant women in the first trimester.

Plasma TSH levels (normal range in our laboratory: 0.3–4.5 mcU/mL) were tested using a chemiluminescent immunometric assay (Cobas 6000®, Roche, Mannheim, Germany), FT4 levels (0.9–2 ng/100 mL) and TPO antibodies