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Maternal autoimmune thyroid disease: Relevance for the newborn☆

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ABSTRACT

Background and objective: Autoimmune thyroid disease is amongst the most frequent endocrine disorders during pregnancy. It is associated with an increase in perinatal morbidity, congenital defects, neurological damage, foetal and neonatal thyroid dysfunction. Maternal thyroid hormones play a key role in child neurodevelopment. We aimed to evaluate the thyroid function and the clinical course of neonates born from mothers with autoimmune thyroid disease during the first months of life in order to define the follow-up.
Patients and method: We monitored thyroid function and clinical status during the first months in 81 newborns of mothers with autoimmune thyroid disease; 16 had Graves disease and 65 autoimmune thyroiditis.
Results: A percentage of 4.93 newborns had congenital defects, and 8.64% neonates showed an increase in thyrotropin (TSH) (>9.5 μUI/mL 2 times) and required thyroxin within the first month of life. A 85.7% of these showed a negative newborn screening (due to a later increase of TSH). A higher TSH value in the newborn was related to an older age of the mother, higher levels of thyroid peroxidase (TPO) antibody during pregnancy and lower birth weight. A higher free thyroxine (FT4) value in the newborn was related to fewer days of life and mothers with Graves disease.
Conclusions: We recommend the evaluation of TSH, T4 and TPO antibodies before 10 weeks in all pregnant women with follow-up if maternal thyroid autoimmunity or disorders is detected. It is also recommended to test children's serum TSH and FT4 at 48 h of life in newborns of mothers with autoimmune thyroid disease and repeat them between the 2nd and 4th week in children with TSH > 6 μUI/mL. Careful endocrine follow-up is advised in pregnant women and children if hyperthyroidism is detected.

Enfermedad tiroidea autoinmunitaria materna: repercusión en el recién nacido

Palabras clave:
Hijo de mujer con enfermedad tiroidea autoinmunitaria
Enfermedad de Graves en el embarazo
Autoinmunidad tiroidea materna
Hipotiroidismo

RESUMEN

Fundamento y objetivo: La enfermedad tiroidea autoinmunitaria es uno de los problemas endocrinológicos más frecuentes del embarazo. Se asocia a mayor morbilidad perinatal, malformaciones, daño neurológico y disfunción tiroidea neonatal. Las hormonas tiroideas maternas son claves en el neurodesarrollo fetal. Evaluamos la función tiroidea, en los primeros meses, de los hijos de mujeres con enfermedad tiroidea autoinmunitaria, para intentar establecer el seguimiento óptimo.
Pacientes y método: Se controló la función tiroidea, durante los primeros meses, en 81 hijos de mujeres con enfermedad tiroidea autoinmunitaria (16 casos de hipertiroidismo y 65 de tiroiditis autoinmunitaria).
Resultados: El 4,93% de los neonatos presentaron malformaciones, y el 8,64% recibieron tiroxina por un valor de tirotropina (TSH) comprobada mayor de 9,5 μUI/ml en el primer mes. En el 85,7% de estos, el cribado neonatal fue negativo, por un aumento tardío de la TSH. Se asoció a TSH elevada en el niño: menor peso al nacimiento, mayor edad materna y mayor título de anticuerpos antiperoxidasa tiroidea (anti-TPO) en la gestación. Se asoció a una tiroxina libre (T4L) más alta en el niño: tener menos edad y que la madre tuviera hipertiroidismo.

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Conclusiones: Se recomienda determinar en todas las gestantes los valores de TSH, T4 y anticuerpos anti-TPO antes de la semana 10, y seguimiento o tratamiento si hubiera alteraciones. Asimismo, se recomienda controlar a las 48 h de vida la TSH y la T4L en hijos de mujeres con enfermedad tiroidea autoinmunitaria y, si la TSH fuera mayor de 6 μUI/l, repetir el control entre las semanas 2-4. Es recomendable efectuar un control cuidadoso de la gestante con hipertiroidismo y de su hijo.

Introduction

Autoimmune thyroid disease is one of the most frequent endocrine disorders during pregnancy. In 2.5% of women, in apparent good health, there is an increase of thyroid-stimulating hormone (TSH) at the beginning of pregnancy, in addition to the 1–2% who already had a hypothyroidism under treatment.[1–3] In addition, 6–10% of the pregnant women have antithyroid antibodies and 4–5% of pregnant women have hypothyroxinemia, which in a recent population study has been related to cognitive retardation in the child.[4]

The pregnant woman with autoimmune thyroid disease presents a greater incidence of infertility, miscarriages and premature labour, which could improve with thyroxine (T4).[2] More frequently, her children present low weight, prematurity, neonatal disease, congenital malformations, developmental delay and thyroid dysfunction.[1,2] Rovelli et al. found a transitory increase in TSH during the first month of life in 28% of these children.[3] In children of pregnant women with active hyperthyroidism, a central hypothyroidism with a hypoplastic thyroid gland produced by the absence of TSH stimulation in the hypothalamic-pituitary-thyroid axis (HPT) development has also been described.[1,5]

Among the different types of antibodies, the anti-thyroid peroxidase (anti-TPO) antibodies are considered to be markers of autoimmune disease and are associated with a greater incidence of miscarriages and premature childbirths, and they could produce transitory hypothyroidism.[6] The anti-TSH receptor antibodies, both stimulating and inhibiting, alter the foetal and neonatal thyroid function for long periods even in women who underwent a thyroidectomy.[6–9] Also, antibodies against the thyroid hormone have been described, although their relevance is unclear.[1]

Thyroid hormones play a key role in the neurodevelopment.[10–13] During the first trimester of pregnancy, the foetal thyroid does not work yet, so the foetus relies only on the hormones that receives from his mother via the placenta. Although as of week 12 the foetus starts its own synthesis, the maternal hormones continue to contribute significantly throughout the pregnancy (30% of hormones in umbilical cord blood are of maternal origin). Therefore, during the first trimester, the development of the foetus brain depends exclusively on the maternal thyroid hormone flow, while in the last trimester, both foetal and maternal hormones are involved.[13]

As the thyroid hormone demands increasingly grow during pregnancy, autoimmunity with normal thyroid function or initial subclinical hypothyroidism can later develop into a symptomatic hypothyroidism.[11,12] Henrichs et al. demonstrated that even a mild maternal hypothyroxinemia in the first trimester produces cognitive retardations in the child.[4] Other authors also found that maternal hypothyroxinemia is related to learning disorders, developmental retardation, encephalopathy and seizures, among other conditions in the child.[1,4,10–13] Also, it was observed that intrauterine exposure to anti-TPO antibodies is related to later autoimmune thyroiditis during childhood.[14,15]

Graves disease (active or past) during pregnancy can produce transitory hyperthyroidism (by stimulating antibodies), foetal or neonatal transitory hypothyroidism (by inhibiting antibodies), or both, aside from central hypothyroidism due to lack of development of the hypothalamic-pituitary-thyroid axis, as well as maternal hypothyroxinemia due to overtreatment with antithyroid drugs.[16–18] Therefore, if the control is inadequate, in addition to the antibodies effects there will be the effects of drugs and the alterations in the maternal thyroid functions, which will increase perinatal risks, congenital malformations, development retardations and central hypothyroidism in the child.[16–20]

One of the major difficulties found in clinical practice is that mild increases in TSH or central hypothyroidism may not be detected during neonatal screening, and TSH level can be normal even until the fourth week of life.[3,21] Moreover, the maternal hypothyroxinemia may go unnoticed during pregnancy.[1,4]

With the objective of clarifying these problems, we started up, in our hospital, a protocol to follow-up the children of women with the autoimmune thyroid disease.

Method

During the 2005–2007 period, we studied 81 children of women with autoimmune thyroid disease, controlled at the Obstetrics Service in the Hospital de Fuenlabrada. The children were selected at birth and were followed up in the consultation of the Paediatric Endocrinology Unit during the first 3 months of life. Those who were younger than 36 weeks of gestational age and those with APGAR test score <7 at min. 5 were excluded.

Data was gathered, after informed consent, during puerperium:

- From the mother history: age, diagnosis, medication prior to pregnancy.
- From the gestation period: medication received, iodine supplements, levels of anti-TPO antibodies and other diseases.
- Type of labour, birth weight, state of newborn and neonatal disease.

Afterwards, a clinical follow-up and a thyroid function follow-up were performed (TSH, free T4 [FT4], anti-TPO-antibodies). Thyroid function was measured in blood collected at 48 h of life and at first, second and third month of life.

At the hospital laboratory, TSH, FT4 and anti-TPO antibodies are determined by chemiluminescence. The normal range at the laboratory is: TSH 0.400–4000 μUI/ml; FT4 0.800–1900 ng/dl; anti-TPO antibodies <35 UI/ml.

Neonatal screening was performed at 48–60 h of life and always before discharge from the maternity ward. The samples were analysed in the Laboratory of Neonatal-Metabolic Screening of the Hospital Universitario Gregorio Marañón, of Madrid. The cut-off point for TSH was 10 μUI/ml.

The statistical study was performed with SPSS® software, using analysis of variance (ANOVA), correlation and multiple regression with variable response turned into logarithms.

Patients

The characteristics of the mothers and their children are detailed in Table 1.