

## ORIGINAL ARTICLE

# Treatment of Graves' disease in children: The Portuguese experience



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### KEYWORDS

Graves' disease;  
Pediatric;  
Hyperthyroidism;  
Antithyroid drugs;  
Survey

### Abstract

**Introduction:** Graves' disease (GD) is an autoimmune thyroid disease, common in adults but rare in children. The best therapeutic approach remains controversial.

**Objectives:** To ascertain the current treatment of pediatric GD in Portugal and to assess the clinical and biochemical factors that determine definitive/long-term remission after treatment with antithyroid drugs (ATDs).

**Patients and methods:** A retrospective analysis of data about pediatric GD treatment collected from a nationwide survey conducted by the Portuguese Society of Pediatric Endocrinology and Diabetology from May to August 2013. Population was categorized based on sex, age, use of ATDs, dosage, treatment duration, adverse reactions, thyrotropin receptor-stimulating antibody (TRAB) titer, remission and remission/relapse rates, and definitive treatment, and divided into group A (with ongoing treatment) and group B (with treatment stopped). Group B was subdivided into 'Remission', 'Remission + relapse' and 'No remission' subgroups based on the course of disease. The same parameters were compared between both groups.

**Results:** Survey response rate was 77%; 152 subjects, 116 female, mean age at diagnosis  $11.23 \pm 3.46$  years. They all started treatment with ATDs, 70.4% with thiamazole, with a mean treatment duration of  $32.38 \pm 28.29$  months, and 5.9% had adverse effects. Remission rate was 32.6%. Lower age at diagnosis correlated with higher remission rates. Treatment duration was longer when propylthiouracil was used. Initial TRAB titer was significantly higher in the 'No remission' group. Surgery and radioiodine were used as second-line treatments.

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**PALABRAS CLAVE**

Enfermedad de Graves;  
Pediátrico;  
Hipertiroidismo;  
Fármaco antitiroideo;  
Encuesta

**Conclusion:** Our study results were similar to those reported in the literature. Age and TRAB titer were identified as potential clinical and laboratory determinants of remission. Based on risk/benefit analysis, it was concluded that treatment should be individualized based on age, accessibility to treatments, and physician's experience.

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**Tratamiento de la enfermedad de Graves en niños: la experiencia portuguesa****Resumen**

**Introducción:** La enfermedad de Graves (EG) es una enfermedad tiroidea autoinmune frecuente en el adulto pero rara en edad pediátrica. La mejor opción terapéutica sigue siendo controvertida.

**Objetivos:** Conocer su tratamiento en Portugal, y evaluar factores clínicos y bioquímicos determinantes de la remisión definitiva/prolongada con fármacos antitiroideos (AT).

**Pacientes y métodos:** Análisis retrospectivo de los datos obtenidos mediante un cuestionario nacional realizado por la Sociedad Portuguesa de Endocrinología Pediátrica y Diabetología entre mayo y agosto de 2013. Caracterizamos la población por sexo, edad, uso de AT, dosis, duración del tratamiento, reacciones adversas, *thyrotropin receptor-stimulating antibody* (TRABs), tasas de remisión y remisión/recaída, y tratamiento definitivo. Se definieron los siguientes grupos: grupo A (mantiene tratamiento) y grupo B (tratamiento detenido), el cual se subdividió en «remisión», «remisión + recaída» y «no remisión»; se compararon los parámetros entre los diferentes grupos.

**Resultados:** La tasa de respuesta al cuestionario fue del 77%: 152 sujetos, 116 de ellos mujeres, con un promedio de edad al diagnóstico de  $11,23 \pm 3,46$  años. Todos iniciaron tratamiento con AT (70,4% con tiamazol), con una duración media del tratamiento de  $32,38 \pm 28,29$  meses; un 5,9% presentaron efectos adversos y la tasa de remisión fue del 32,6%. Las edades menores al diagnóstico se correlacionaron con mayor índice de remisión. La duración del tratamiento fue mayor con propiltiouracilo. El título inicial de TRABs fue significativamente mayor en el grupo sin remisión. Cirugía y yodo radioactivo se utilizaron en segunda línea.

**Conclusión:** Se obtuvieron resultados similares a los de la literatura. Como posibles determinantes de la remisión, se identificaron la edad y el título de TRABs. Considerando los riesgos/beneficios, se concluye que la terapéutica debe ser individualizada, teniendo en cuenta la edad, la accesibilidad a las terapias y la experiencia del médico.

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**Introduction**

Graves' disease (GD) is an autoimmune disease that causes hyperthyroidism through the stimulation of TRABs (thyrotropin receptor-stimulating antibody). The estimated incidence in the adult population is 1–2 cases per 1000 people per year<sup>1</sup> and in the pediatric population 0.1 cases/100,000 children before puberty and 3 cases/100,000 children during adolescence.<sup>2</sup>

There are three therapeutic options for GD: medical treatment with antithyroid drugs (ATD), radioactive iodine (131-I) and surgery. However, the most efficient therapy remains controversial as pediatric age is a restrictive factor in this decision.

ATD is universally recommended as the first-line treatment. Nevertheless, the relapse rate remains high as only 30% of children achieve prolonged remission after 2 years of treatment.<sup>3,4</sup> Some authors advocate for longer treatment as first course intending to increase definitive remission rates or more prolonged remission.<sup>5</sup>

It is difficult to anticipate the disease course and there is no certainty about the clinical or biochemical factors that predict remission with ATD. Some studies point to older age, lower thyroid hormone concentrations at diagnosis and a faster response to ATD as predictive factors to an early remission.<sup>6</sup> Others highlight the initial titer of TRABs.<sup>7</sup> There is no evidence-based consensus on the clinical utility of these factors as remission determinants.

The present study was designed to assess how pediatric GD is treated in Portugal, investigating the biochemical and clinical factors associated with prolonged or definitive remission after ATD treatment.

**Material and methods**

The Portuguese Society of Pediatric Endocrinology and Diabetology (SPEDP) conducted a national data survey on pediatric GD. It was a retrospective study, between May and August 2013, including all the national public hospitals with Pediatric and/or Endocrinology departments.

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