Treatment of Pediatric Graves Disease: results of a multicenter survey in Portugal

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Background and objective

Pediatric Graves Disease (GD) is a rare disease and there is currently no evidence-based strategy for its management. Therapy choice is determined by individual consideration of the risks and benefits of the three treatment modalities and varies considerably within and between countries, depending on local traditions and resources and on the different clinical conditions of the patients.

In 2011, American Thyroid Association (ATA) and the American Association of Clinical Endocrinologists (AACE) published Guidelines on GD, changing disease`s evaluation. Nevertheless, GD treatment is still a matter of controversy.

The main objective was to know the characteristics of the pediatric Portuguese GD population, how the different therapies were used and their results.

Methods

SPEDP conducted the first nationwide questionnaire survey among all the Endocrinologists and Pediatricians in the Portuguese Public Health System Hospitals about pediatric GD treatment. A questionnaire (Fig. 1) was designed and distributed to all hospitals with pediatric endocrinology, in order to include all GD patients under 18 years at diagnosis and with a minimum of 6 months follow-up. A retrospective assessment of patient`s medical records was performed from May to August 2013.

For the statistical analysis we used Excell® and SPSS®. We used Kruskal-Wallis Test and Spearman's correlation and considered a level of significance of 5%.

Figure 1 – Questionnaire

Results

- 87 hospitals contacted, 67 responders
- 25 hospitals reported patients
- Pediatric clinic – 56%; Endocrinology clinic – 44%
- 152 patients were identified, 76% were females
- Mean age at diagnosis: 11,3 ±3,4 years [3,3-18,3]

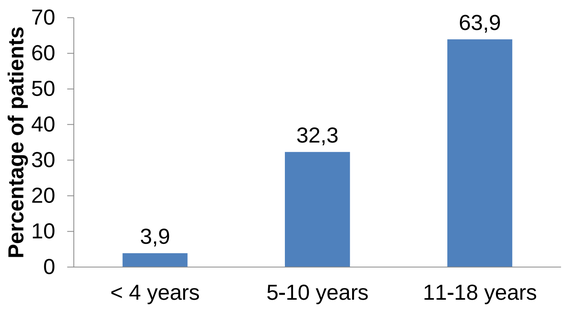

Figure 2 – Age at dianosis

Type of ATD	Total patients (N/%)	Initial dose (mg/Kg)	Initial ATD duration (months)	Adverse effects (all minor) (N/%)
Methimazole (MTZ)	105/69.1	0.38±0.23	28.26±21.27	7/4.6
Propylthiouracil (PTU)	47/30.9	3.74±2.65	41.51±38.55	3/1.9

Table 1 – Initial treatment with ATD and adverse effects

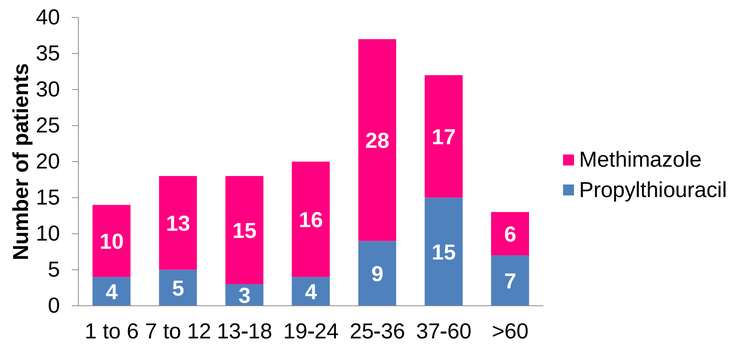

Figure 3 – Duration of firts course of ATD (months)

TRABs evolution (N=152)

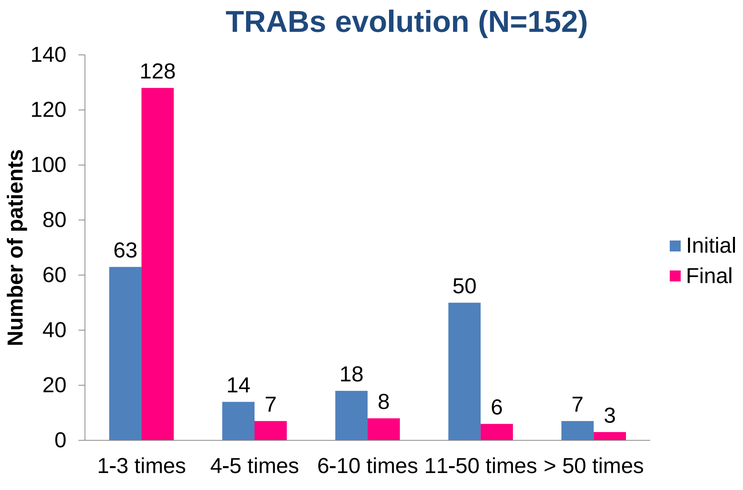

Figure 4 – Comparison of TRABs before and after treatment (increased number of times)

Treatment evolution

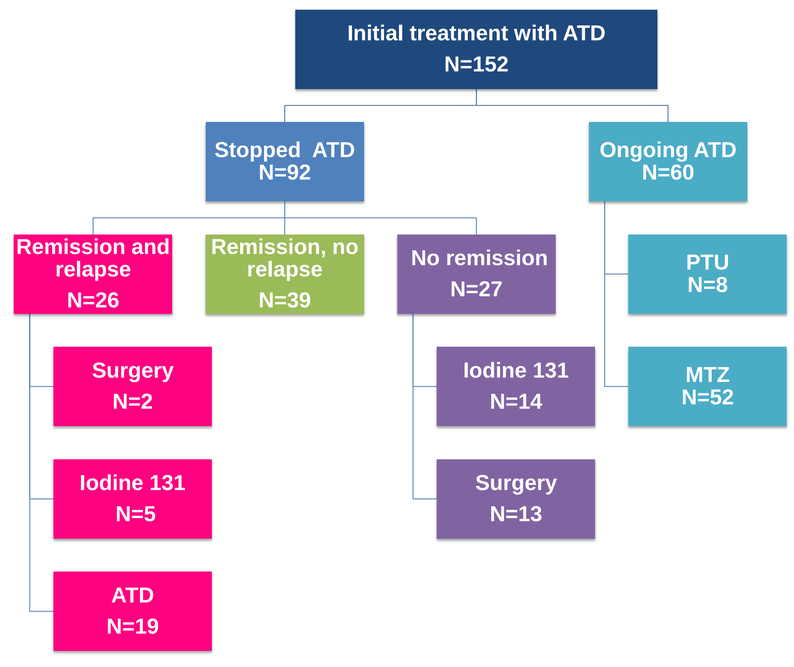

Figure 5 – Treatment evolution

Patients ongoing first course ATD (N=60)

Figure 6 – Duration of treatment in patients ongoing first ATD course (months)

Patients that stopped ATD (N=92)

	Remission, no relapse	Remission and Relapse	No remission	p
Number of patients (%)	39 (42,4%)	26 (28,3%)	27 (29,3%)	NS
Age at diagnosis (years)	10.57±3.36	12.02±3.32	11.46±3.60	NS
Type ATD (PTU/TMZ)	23/16	7/19*	9/18*	0.02*
ATD duration (months)	35.59±22.24	26.85±14.89	41.67±47.61	NS
MTZ dose (mg/Kg)	0.36±0.14	0.42±0.19	0.40±0.18	NS
PTU dose (mg/Kg)	3.96±2.07	2.33±2.46	5.71±3.16**	0.024**
Combination therapy (ATD+LT4) (N/%)	20 (51,3%)	17 (65,4%)	10 (37,0%)	NS

*p<0.05 vs remission, no relapse; **p<0.05 vs remission and relapse

Table 2 – Caracterization of patients that stopped ATD

Initial and final TRABs and remission status (N=92)

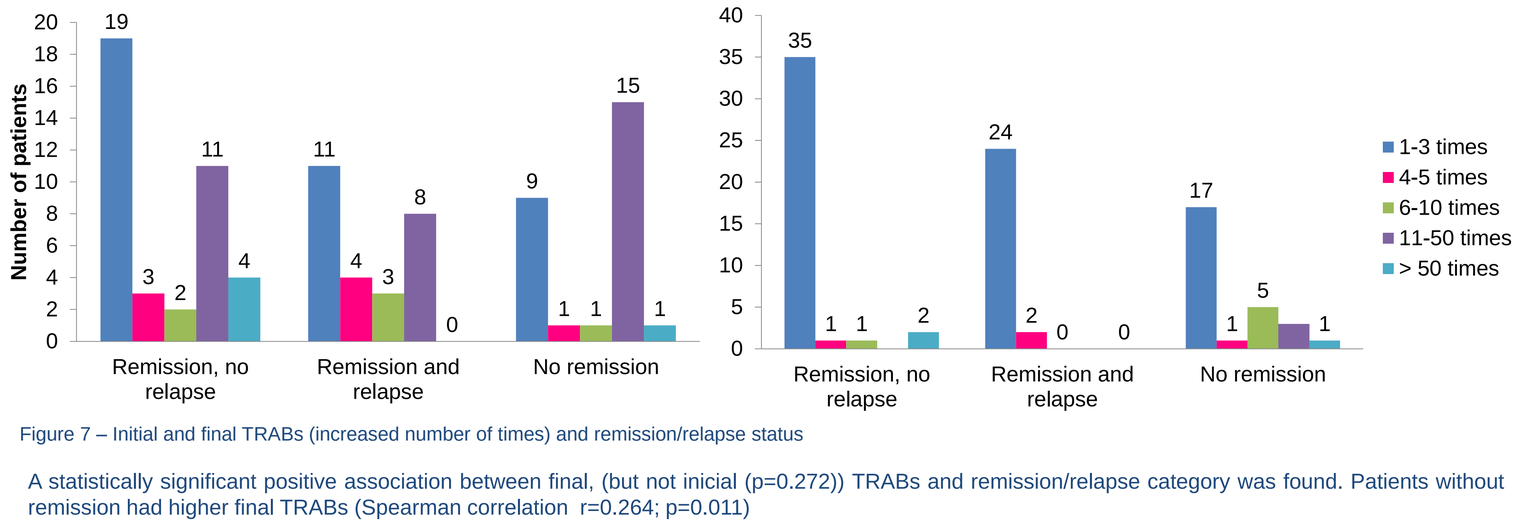

Figure 7 – Initial and final TRABs (increased number of times) and remission/relapse status

A statistically significant positive association between final, (but not inicial (p=0.272)) TRABs and remission/relapse category was found. Patients without remission had higher final TRABs (Spearman correlation r=0.264; p=0.011)

Conclusion

This first multicenter portuguese survey is representative of the national pediatric GD population as it included 77% of all hospitals in our country. ATD therapy was the first choice for all patients, MTZ being preferred. Only minor adverse effects of the drugs were found. Despite a long treatment duration, only 25% patients achieved long term remission. Definitive therapy was a second choice in few patients (22.4%) and more frequent in recent years. Few significant predictive factors of remission were found between groups that finished first course of ATD, namely lower final TRABs and the use of MTZ instead of PTU.

Our population results are conform with literature and reflect a tendency to change GD therapy, introducing definite therapy sooner in the course of treatment.

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