

# Long term monitoring of graves disease in children and adolescents: a single center experience

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## Introduction

- Graves disease (GD) is more severe requires amore complex treatment and is lover probability of achieving remission in children than adults. (1).
- F/M = 5/1, and peaks in the adolescents age group (11-15 ages) (1).
- The first choice in initial therapy is usually antithyroid drugs (ATD) (propylthiouracil, methimazole) and there is no consensus on the duration of treatment (2).
- Surgical or radioactive iodine (RAI) treatments are not definitive and generally result in permanent hypothyroidism (2).

## Patients and Methods

- This retrospective study included 45 cases, median age 12.5 years) between 4-18 years diagnosed with GD during 2003-2017. (F/M=36/9)
- fT3, fT4, fT3 / fT4 ratio, TRAb, anti TPO, anti T, AST, ALT and leukocyte counts, thyroid gland volume-parenchyma echogenicity and blood supply status were recorded.
- The diagnosis of Graves' disease was made in the presence of elevated fT3 and ft4, suppressed TSH and / or TRAb positivity.
- All cases initially treated with an ATD and beta blocker (propranolol) treatment was started for cases with tachycardia.
- Remission was defined as the sustainment of clinical and biochemical state of euthyroidism for at least 1 year following the termination of ATD treatment and no relapse in follow-up.
- Relapse was defined as increased fT4 or fT3 levels in addition to suppressed serum TSH level following dose reduction or termination of ATD, in patients who receive at least 12 months of proper treatment.
- Accordingly, the cases were classified into two groups as 'relapse' and 'remission'.

## Discussion

- Long term remission is observed at lower rates for GD in children in comparison with adults. While remission rate in children and adolescents in response to ATD treatment varies 29-49%, the declared rate in adults is between 39.5-85% (1). In this study, remission and relapse rates in our study were determined 53.4% and 46% respectively.
- With long-term AED treatment, the remission rate is higher in children than in adults. For this reason, at least 2 years of ATD treatment should be given to children. However, if an improvement is not achieved at the end of this period, radical treatment options should not be considered immediately (2). In our study The duration of ATD treatment before radical treatment was mean 3.5 years.
- Factors predicting remission and relapse for children with GD have been studied in many retrospective and prospective studies (3). However no stable predicting factors have been determined as of yet. In this study, "initial ATD treatment duration" and "total ATD treatment duration" parameters were statistically proved to be predictors of long term remission.

## Statistical Analysis

SPSS 24.0 for Windows package software was used for statistical analyses. Descriptive statistics; number and percentage for categorical variables; average  $\pm$  standard deviation for numeric variables have been provided. Student's t-test was applied for continuous variables during the comparison of two independent groups, while chi square test was used for categorical variables. P<0,05 was accepted as significant.

## Results

	Remission (n= 24)	Relapse (n= 21)	p
Age at diagnosis (years)	10.96 $\pm$ 3.24	12,01 $\pm$ 3.22	0.246
Sex (F/M)	18/6	18/3	0.370
Weight SDS at diagnosis	0.01 $\pm$ 0.87	-0.24 $\pm$ 1.03	0.375
Height SDS at diagnosis	0.39 $\pm$ 1	0.42 $\pm$ 0.77	0.911
Family history of AITD (n)	15	17	0.173
Graves' ophthalmopathy (n)	7	4	0.431
Initial fT4 (0.7-2 ng/dl)	3.66 $\pm$ 1.69	4.20 $\pm$ 1.73	0.302
Initial fT3 (2.6- 4.8 pg/ml)	13.32 $\pm$ 6.64	14.86 $\pm$ 5.61	0.410
Initial fT3/fT4 ratio	3.66 $\pm$ 0.76	3.63 $\pm$ 0.70	0.892
Initial positive TRab (n)	10	16	0.064
Initial thyroid US volume (ml)	16.46 $\pm$ 6.62	12.82 $\pm$ 9.98	0.142
Initial PTU (n)	16	7	0.080
MMI (n)	8	14	0.186
Na- L thyroxine (n)	21	15	0.179
Positive TRab at end of ATD Rx (n)	2	3	0.602
fT4 normalization time (week)	6.45 $\pm$ 3.89	6.85 $\pm$ 4.36	0.731
TRab normalization time (month)	22.28 $\pm$ 13.02	28.85 $\pm$ 11.00	0.267
<b>Initial ATD treatment duration (month)</b>	<b>26.91 <math>\pm</math> 5,17</b>	<b>19.09 <math>\pm</math> 7.14</b>	<b>0.01</b>
<b>Total ATD treatment duration (month)</b>	<b>42.14 <math>\pm</math> 14.35</b>	<b>26.95 <math>\pm</math> 16.13</b>	<b>0.03</b>

## In conclusion

ATD treatment for long-term remission in children and adolescent is effective and reliable. Because of chance of long-term remission, children and adolescent with Graves disease should be treated with long-term ATD before radical treatment.

Radical treatment (RAI and surgery) should be considered as the last option and in selected cases. In children and adolescents chance of long-term remission increases in proportion with "initial ATD treatment duration" and "total ATD treatment duration". There is a need for further prospective randomized studies for evaluating the optimal treatment duration

## Kaynaklar

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