

«Letter to Editor»

Long-term follow-up for the results of the treatment with Anti-Thyroid Drugs, Radioactive iodine and surgery in patients with Graves' disease

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Abstract

This study aimed to evaluate factors that influence in: relapse of hyperthyroidism, the incidence of hypothyroidism and long-term treatment with different methods (e.g.: surgery, iodine therapy, anti-thyroid drugs) in Graves' disease.

In a retrospective study, 580 patients with Graves' disease were evaluated. They were treated with one of the treatment methods from October 1999 until September 2005. Using a questionnaire that related data were collected: demographic information, onset of disease, the recurrence rate incidence of hyperthyroidism and side effects of treatment were collected. Out of 580 patients enrolled the study, 268 (46%) were treated with anti-thyroid drugs (for 18 months at least), 284 (49%) with radioactive iodine and 28 (5%) underwent the surgery. Recurrence rates of hyperthyroidism after treatment with anti-thyroid drugs, iodine therapy and surgery were recorded at 53%, 8%, 14%, respectively ($P < 0.001$). Hypothyroidism occurrence after three methods was 6%, 74% and 71%, respectively. Overall, 6.39% of patients with Graves' disease were treated with anti-thyroid drugs in 16 ± 31 months follow-up remained euthyroid without side effects. This figure was 18% in patients treated with radioactive iodine on 11 ± 30 months and 7% in surgical patients in 13 months follow up. The differences between the three groups were statistically significant ($P < 0.001$).

The result showed that the long term with anti-thyroid drugs was superior to surgery or radioactive iodine long-term euthyroidism with the study complication.

Keywords: thyrotoxicosis, thyroid Gland, hyperthyroidism, Iodine therapy, surgery

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Graves' disease or diffuse toxic goiter, which is an autoimmune disease, is determined by the excess secretion of thyroid hormones (1). The most prevalent cause of hyperthyroidism in the United States of America is Graves' disease caused by anti-thyroid antibodies (2). Besides great improvement in the treatment of Graves' disease, choosing the best therapeutic method has been yet controversial. Decreasing the synthesis of thyroid hormones using anti-thyroid drugs (3) and minimizing thyroid tissue by radioactive iodine therapy (4) or subtotal thyroidectomy (5) are two main methods to cure hyperthyroidism caused by Graves' disease. In this study, it was tried to choose the best therapy for the patients with Graves' disease. And also find the best therapeutic results for these patients, the relapse rates of hyperthyroidism and hypothyroidism after treatment, in each of the three therapeutic methods (surgery, radioactive iodine, and anti-thyroid drugs). In a descriptive cross-sectional study, the records of all the patients with Graves' disease who referred to endocrine clinic and were under treatment by one of the three methods therapy: long-term use of anti-thyroid drugs (at least for 18 months), radioactive iodine, or surgery were surveyed between October 1999 and September 2005. Diagnosis of the Graves' disease was based on the presence of thyrotoxicosis signs, patients' tests (high level of thyroid hormones with suppressed TSH), and the presence of diffuse goiter (in physical exam, sonography or thyroid scans) with or without ophthalmic symptoms of Graves' disease. All the patients were visited, followed-up and treated by an endocrinologist. No limitations of age and sex interfered determining the sample. The patients who did not complete the follow-up period, or

had imperfect therapy results or laboratory tests did not enter the study. For collecting the samples, the medical history of all the patients was considered. The questionnaire filled for each patients included age, age for the disease onset, sex, treatment state before referral, the kind of used therapy, presence or absence of relapsing hyperthyroidism after finishing the treatment, the time of clinical or laboratory diagnosis for relapsing incidence, presence or absence of hypothyroidism after treatment, the time of clinical or laboratory diagnosis for the incidence of hypothyroidism, and the presence or the absence of side effects caused by treatment. Finally, the collected data were analyzed using the SPSS version 14. The chi-square and ANOVA tests were used to compare and describe the findings and P value <0.05 was considered as significant.

Overall, 580 patients with Graves' disease entered this study. The mean age of the patients was 36 ± 27 years and the mean age for the onset of the disease was 33 ± 13 years. Of these patients, 206 persons (36%) were male and 374 persons (64%) were female women. The kind of the therapy and long-term follow-up of the studied patients are present in the table 1. The relapse rates of hyperthyroidism in Graves' patients treated by the three studied therapeutic methods are produced in the table 2.

The above results showed that the relapse rate in Graves' patients after long-term treatment with antithyroid drugs was highly more than the other two therapeutic methods (P value < 0.001) and by prescribing more than one dosage of radioactive iodine in these patients, the relapse rate in Graves' patients was lower, compared to the group treated by surgery (P value = 0.036). The incidence rate of hypothyroidism after treatment of the

Graves' patients was significantly more in the groups treated with radioactive iodine and surgery compared to the group treated with anti-thyroid drugs (P value < 0.001). However, this rate did not have a significant difference in the groups treated by radioactive iodine and surgery (P value > 0.05) (Table 3).

The total incidence rate for the side effects except hypothyroidism caused by long-term use of anti-thyroid drugs was 10 % (26 cases). Of these, 10 patients (4%) had pruritus and dermal reactions, eight patients (3%) had a mild decrease of WBC, four patients (1.5%) were with arthralgia and four patients (1.5%) had hepatitis, but no case of agranulocytosis was seen. Among the above complications, only hepatitis caused dissection and fail of the long-term therapy with anti-thyroid drugs and other complications were removed by changing the dosage, kind of the drug and supportive therapies and they did not fail the drug therapy. In relation use of about using radioactive iodine except hypothyroidism, no side effect affecting the therapy was seen during the follow-up period. Among the patients under surgery, four patients (14%) had hypothyroidism after surgery but no case of the injury of the recurrent laryngeal nerve and other long-term complications caused by surgery except hypothyroidism was seen. Overall, the rate of euthyroid without the incidence of side effects after treatment of the patients in patients with Graves' disease, treated with antithyroid drugs was significantly more than the patients treated with radioactive iodine and it was more in the two mentioned groups compared to the group of surgical treatment (P value < 0.00) (Table 4).

Long-term treatment with anti-thyroid drugs is usually the first therapeutic method in patients who have been diagnosed with Graves' disease lately (6,

7). The relapse rate after the above treatment in the studied patients was 53% during 31 ± 16 months of follow-up. In a similar study by Muller *et al.* on patients with Graves' disease, treated with anti-thyroid drugs, from 76 patients who were followed-up for 99 ± 22 months, totally 42 patients (70%) had relapsing hypothyroidism (6, 8).

In general, the relapse rate was equivalent in the current study and other similar studies as well as the present difference are mainly due to the different duration for following-up the patients and the number of studied patients, considering that the remission rate is not the same in different geographical zones (9). These results showed that more than half of the patients did not have permanent remission after a long-term treatment with anti-thyroid drugs. In Muller *et al.*'s study the incidence of hypothyroidism after long term treatment with anti-thyroid drugs was 1.7 % (8), which this rate in the present study was also relatively low about 6%. Which this rate was also relatively low and about 6% in our study. In addition, in Leary *et al.*'s study, the rate of hypothyroidism after this therapeutic method was reported 4% (10). The incidence rate for serious complications after long-term treatment with anti-thyroid drugs was is very low (hepatitis 1.5%), no case of agranulocytosis was seen and the mild pharmaceutical complications were seen in 8.5% of the patients, which was not clinically so worthy and they could be removed by switching the drug or the supportive therapies. The incidence rate of the side effects was documented was 1-5% in other studies (8, 9).

Iodine therapy is known as the prior treatment in America (11). The capability of the radioactive iodine in removing the hyperthyroidism signs and remitting the disease in patients with Graves' disease is

very desirable. From this viewpoint, it has priority to anti-thyroid drugs; as in 92% of the patients treated by this therapeutic method, hypothyroidism remitted and only in 23% of the patients after one dosage and in eight percent of the patients after two to three dosages, hypothyroidism relapsed. Most of the relapsing cases in the current our study were because the patients did not referred to receive the next dosage of the radioactive iodine it seems that if all the patients have referred the relapse rate after taking the next dosages of the radioactive iodine would have been very lower. In addition, the relapse rate was also low (between 0 and 11.5%) in other similar studies (10, 12, 13).

The surgery of the thyroid gland was performed rarely and was used for cases such as very large goiter, relapse of the disease, in children (14), and in patients

who want quick therapy or have the complications of antithyroid drugs or in pregnant women needing high dosage of the drug (5). According to the present study, surgery can remove the hyperthyroidism in 86% of the patients, which this rate was lower than radioactive iodine therapy and was more than long-term use of anti-thyroid drugs. This rate was 80% in other studies (6, 10). In addition, the rate of hypothyroidism cases after surgery in patients with Graves' disease was about 71% which was more than other studies (59% in Leary *et al.*'s study and 58% in Hadj Ali *et al.*'s study) (6,10). The above results showed that long-term use of anti-thyroid drugs in patients with Graves' disease was prior to radioactive iodine therapy and surgical treatment from the viewpoint of causing euthyroid without side effects.

Table 1. Treatment and follow-up states in patients with Graves' disease

| Kind of treatment | Number | Percentage | Duration of following- up the patients (month) |
|--|--------|------------|--|
| Long- term treatment with anti-thyroid drugs | 268 | 46 | 31±16 |
| Radioactive iodine therapy | 284 | 49 | 30±11 |
| Surgical treatment | 28 | 5 | 13 |
| Total | 580 | 100 | - |

Table 2. The hyperthyroidism relapse rate in patients with Graves' disease, treated by the three therapeutic methods

| Graves' disease | Long-term treatment by anti-thyroid drugs | One radioactive dosage | More than one dosage of radioactive iodine | Surgery |
|--|---|------------------------|--|---------|
| Relapse of hyperthyroidism | 142(53%) | 66(23%) | 22(8%) | 4(14%) |
| Cases without the relapse of hyperthyroidism | 126 | 218 | 262 | 24 |

Table 3. The hypothyroidism relapse rate of in patients with Graves' disease, treated with the three therapeutic methods

| Graves' disease | Long-term treatment by anti-thyroid drugs | Radioactive iodine | Surgery |
|----------------------------------|---|--------------------|---------|
| The group with hypothyroidism | 16(6%) | 210(74%) | 20(71%) |
| The group without hypothyroidism | 252 | 74 | 8 |

Table 4. The three therapeutic methods comparison for euthyroid cases rate in patients with Graves' disease

| Graves' disease | Number of patients | Relapse of hyperthyroidism | Hypothyroidism after treatment | Side effects | Cases of euthyroid without side effects | One period of follow-up (month) |
|--|--------------------|----------------------------|--------------------------------|-----------------------|---|---------------------------------|
| Long-term treatment with anti-thyroid drug | 268 | 142(53%) | 16(6%) | 26(10%)* 4(1.5%)** | 106(39.6%) | 31±16 |
| Radioactive iodine | 284 | 22(8%) | 210(74%) | - | 52(18%) | 30±11 |
| Surgery | 28 | 4(14%) | 20(71%) | 4(14%) | 2(7%) | 13 |

*The total complications of the therapy

**The complication leading to disruption of the therapy

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References

- 1-Jameson J, De Groot LJ. Thyroid in: Endocrinology adult and Pediatric 6th ed. Philadelphia: Saunders 2010;1342-780.
- 2-Schouten BJ, Brownlie BE, Frampton CM, Turner JG. Subclinical thyrotoxicosis in an outpatient population-predictors of outcome. Clin Endocrinol (Oxf) 2011;74(2):257-61.
- 3-Bahn RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, Klein I, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. Endocr Pract 2011;17(3):456-520.
- 4-Douglas S, Ross MD. Radioiodine therapy for hyperthyroidism. New Engl J Med 2011;364(6):542-50.
- 5-Brent AG. Graves Disease. New Engl J Med 2008;358(24):2594-605.
- 6-Hadj Ali I, Khiari K, Cherif L, Ben Abdallah N, Ben Maiz H, Hajri H, et al. Treatment of Graves' disease: 300 cases. Presse Med 2004;33(1):17-21. (French)
- 7-Bakker SC, Zanin DE, Zweers EJ. [Treatment of hyperthyroidism caused by Graves' disease or toxic multinodular goitre by radioiodine: over 80% cure retrospectively after one calculated dose]. Ned Tijdschr Geneesk. 2002;146(39):1837-41. (Dutch)

- 8-Wille T, Müller B, Noth D, Bürgi U, Diem P. [Long-term follow up after antithyroid drug treatment in Graves' disease]. *Praxis (Bern 1994)* 2006;95(29-30):1121-7. (German)
- 9-Bonert V, Friedman TC. The thyroid gland. In: Andreoli TE, Carpenter CCJ, Gnggs RC, Loscalzo J, eds. *Cecil essentials of medicine*. 6th ed. Philadelphia: Saunders; 2004. P. 593-602.
- 10-Leary AC, Grealay G, Higgins TM, Buckley N, Barry DG, Murphy D, et al. Long-term outcomes of treatment of hyperthyroidism in Ireland. *Ir J Med Sci* 1999;168(1):47-52.
- 11-Levy EG. Treatment of Graves' disease: the American way. *Baillieres Clin Endocrinol Metab* 1997;11(3):585-95.
- 12-Heidari B, Farhangi F, Amiri M. Comparison of radioiodine and antithyroid drugs in the treatment of thyrotoxicosis. *Iran J Endocrinol Metab* 2002;4(13):29-34. (Persian)
- 13-Fard-Esfahani A, Dabbagh Kakhki VR, Eftekhari M, Zarpak B, Saghari M, Aflahi B et al. Comparative evaluation of the two fixed dose methods of Graves' disease. *Tehran Univ Med J* 2003;61(4):300-7.
- 14-Abós D, Ruiz P, Prats E, Razola P, García F, Tardín L, et al. Treatment of Graves-Basedow's disease with ¹³¹I. Assessment of a "modulated fixed activity" protocol. *Rev Esp Med Nucl* 2007;26(1):3-10.