

Results of treatment of 696 cases of Graves'disease in Sawanpracharuk Hospital

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- Problem/background** : *Graves'disease is common and may have serious complications. Current treatments have their own advantage and disadvantage. The choices in its initial treatment are still controversial.*
- Objective** : *To study the results of treatment of cases of Graves'disease who were either treated with antithyroid drug or radioactive iodine.*
- Design** : *Descriptive study*
- Setting** : *Department of Medicine, Sawanpracharuk Hospital*
- Materials and Methods** : *Results of treatment of patients with Graves'disease from July 1991 to May 2006 were reviewed. Four hundred and eleven patients were treated with antithyroid drug and 385 patients received radioactive iodine.*
- Results** : *In the group of drug therapy, the relapse rate was 64.3 percent (245 patients, 299 relapses). 64.8 percent occurred within 1 yr and 86.2 percent occur within 2 yr after drug withdrawal. In the group treated with radioactive iodine, 9 percent still had hyperthyroid, 36 percent had euthyroid and 55 percent developed hypothyroidism. Hypothyroid occurred in 40 percent within 6 mo, 61 percent within 1yr and nearly all developed hypothyroid within 5 yr.*

Conclusion : *Relapse rate after antithyroid drug therapy was very high. Radioactive iodine therapy as first line treatment in selected cases may improve the outcome and prevent serious complications of Graves' disease.*

Keywords : *Hyperthyroidism, Graves' disease, Antithyroid drug, Radioactive iodine.*

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- เหตุผลของการทำวิจัย** : เนื่องจาก Graves'disease เป็นโรคที่พบบ่อย และอาจทำให้เกิดโรคแทรกซ้อนรุนแรง การรักษาในปัจจุบันแต่ละวิธีมีข้อดี ข้อด้อย ยังไม่มีข้อยุติว่าควรเลือกการรักษาใดเป็นวิธีแรก
- วัตถุประสงค์** : ศึกษาผลการรักษาผู้ป่วย Graves'disease ที่ได้รับการรักษาด้วยยา และ radioactive iodine
- รูปแบบการวิจัย** : การศึกษาเชิงพรรณนา
- สถานที่ทำการวิจัย** : กลุ่มงานอายุรกรรม โรงพยาบาลสวรรค์ประชารักษ์
- ตัวอย่างและวิธีการรักษา** : ติดตามผลการรักษาผู้ป่วย Graves'disease ระหว่างกรกฎาคม 2534 - พฤษภาคม 2549 จำนวนผู้ป่วยที่ได้รับการรักษาด้วยยา 411 ราย ได้รับ radioactive iodine 385 ราย
- ผลการศึกษา** ผู้ป่วยกลุ่มที่ได้รับการรักษาด้วยยา เกิดภาวะธัยรอยด์เป็นพิษซ้ำ 245 ราย (299 ครั้ง) คิด เป็นร้อยละ 64.3 (โดยร้อยละ 64.8 เกิดภายใน 1 ปี และร้อยละ 86.2 เกิดภายใน 2 ปี หลังหยุดยา) ผู้ป่วยกลุ่มที่ได้รับ radioactive iodine ร้อยละ 9 ยังพบภาวะธัยรอยด์เป็นพิษ ร้อยละ 36 ฮอร์โมนธัยรอยด์ปกติ ร้อยละ 55 เกิดภาวะต่อมธัยรอยด์ทำงานน้อย (ร้อยละ 40 เกิดภายใน 6 เดือน ร้อยละ 61 เกิดภายใน 1 ปี และเกือบ ทั้งหมดเกิดภายใน 5 ปี หลังได้รับการรักษา)
- สรุป** : การรักษา Graves'disease ด้วยยา มีอุบัติการณ์ของการเกิดโรคซ้ำสูงมาก การพิจารณาคัดเลือกผู้ป่วยเพื่อให้การรักษาด้วย radioactive iodine ตั้งแต่แรก จะช่วยให้การรักษาได้ผลดีและอาจช่วยลดโรคแทรกซ้อน
- คำสำคัญ** : ต่อมธัยรอยด์เป็นพิษ, ยาด้านธัยรอยด์, radioactive iodine

Graves' disease is an autoimmune disorder characterized by antibodies that are directed against the thyrotropin receptors on thyroid cells. ⁽¹⁾ The hallmarks are a diffuse goiter associated with thyrotoxicosis, commonly the typical ophthalmopathy. ⁽²⁾ Current treatments consist of antithyroid drugs, radioactive iodine and surgery.

The remission rate from antithyroid drug therapy are variable and relapses rate are between 25 -77 percent. ^(3,4) Half of the patients treated with radioactive iodine became hypothyroid within 5 years. ⁽⁵⁾

This study shows the results of treatment of Graves' disease treated with antithyroid drugs and radioactive iodine at the Thyroid Clinic of Sawanpracharuk Hospital and the results may suggest clinicians for early thyroid ablation in patient with Graves' disease.

Material and Method

Patients with Graves' disease at the Thyroid Clinic of Sawanpracharuk Hospital between July 1991 and May 2006 were evaluated on their thyroid function after treatment.

They were divided into 3 groups, namely:

Group 1 included 411 patients (359 females, 52males, age 14 -73 years) who were treated with antithyroid drug for at 18 - 24 months and followed up for more than 1 year after drug withdrawal. Nearly all the patients were received methimazole 15mg daily then titrated to the lowest dose to keep their thyroid hormone normally. In some cases who had pregnancy or could not tolerate methimazole were received propylthiouracil 150 mg daily then titrated the dose by the same regimen.

Group 2 included 285 patients (233 females, 52 males, age 17-76 years) who were treated with radioactive iodine as first treatment due to their severe symptoms(history of thyroid storm, congestive heart failure, hypokalemia), large gland size, uncontrolled hyperthyroidism or history of relapsed Graves' disease.

Group 3 included 100 patients (90 females, 10males, age 19-75 years) who were treated with radioactive iodine after relapse from group 1.

Most of the patients in group 2 and 3 were referred to be treated with radioactive iodine at King Chulalongkorn Memorial Hospital and the rest at Rajavithi Hospital.

The result of treatment of each patient was reported in 3 categories by using the following criteria:

Remission : patient who still had normal thyroid hormone level after drug withdrawal

Relapse : patient who had high thyroid hormone level after drug withdrawal

Hypothyroid : patient who had low free thyroxin and high thyroid stimulating hormone level.

Results

Table 1 shows the overall results of treatments: 411patient (59 %) were treated with antithyroid drug (Group 1) : 285 (41 %) with radioactive iodine as there initial treatment (Group 2) : total number of patients who received radioactive iodine is 385 (Group 2 and 3).

In group 1,245 patients (205 females, 40 males, age 14 - 73 years) had a relapse (299 relapses): 166 (154 females, 12males, age 14 - 67 years) had remission. The relapse rate is 64.3 percent. 64.8 percent of the relapses occurred within 1 year and 86.2 percent occurred within 2 years after drug

withdrawal (Table 2). Our data seem similar to other studies (Table 3).

In patient who received radioactive iodine, 36 (9 %) were still hyperthyroid, 139 (36 %) were euthyroid and 210 (55 %) developed hypothyroid (Table 1).

Forty percent of hypothyroid cases occurred within 6 months : 61 percent within 1 year : and nearly all cases developed hypothyroid within 5 years (Table 4).

Table 1. The overall results of treatment.

1. Total case	696 cases
2. Antithyroid drug treatment	411 cases
2.1 relapse	245 cases
2.2 remission	166 cases
3. Radioactive iodine treatment	385 cases
: initial	285 cases
: post relapse	100 cases
3.1 hyperthyroid	36 cases (9 %)
3.2 euthyroid	139 cases (36 %)
3.3 hypothyroid	210 cases (55 %)

Table 2. Percent relapse of patients in group 1 after drug withdrawal.

Duration	Number	Percent	Cumulative percent
Within 3 Mo	52	17.4	17.4
3-6 Mo	60	20	37.4
7-12 Mo	82	27.4	64.8
13-24 Mo	64	21.4	86.2
25-36 Mo	16	5.4	91.6
37-60 Mo	19	6.4	98
more than 60 Mo	6	2	100

Table 3. Relapse rate compare to other studies.

	Sawanpracharuk Hospital	Taiwan ⁽¹³⁾	UK ⁽¹⁴⁾	Ireland ⁽¹⁵⁾
1. Patient (case)	411	210	434	272
2. Remission	35.7 %	40 %	43 %	38 %
3. Relapse	64.3 %	60 %	57 %	62 %

Table 4. Percent hypothyroid after radioactive iodine therapy.

Duration	Case	Percent	Cumulative percent
Within 3 mo	30	14.3	14.3
Within 6 mo	55	26.2	40.5
Within 1 yr	43	20.5	61
Within 2 yr	24	11.4	72.4
Within 5 yr	49	23.3	95.7
More than 5 yr	9	4.3	100

Discussion

Graves' disease is a common endocrine disease. Current treatments have both advantages and also disadvantages. Long-term antithyroid drug is usually used as primary treatment.

This study shows that the relapse rate of drug therapy is very high (64.3%). And if we include patients who were initially treated with radioiodine (Group 2) as drug failure, the relapse rate will be as high as 76 percent.

Because Graves' disease has serious and maybe irreversible complications such as thyroid storm, heart failure, atrial fibrillation, hypokalemic paralysis and osteoporosis⁽¹⁾, the aim of initial treatment should be considered of the possibility of long-term disease remission and early thyroid ablation for patients with severe disease or high risk of relapse.⁽⁶⁾

Data from previous studies⁽⁷⁻⁹⁾, patients who had poor remission were: having large goiter size (more than 40 gm), young age (less than 40 yr), high pretreatment hormone level (FT₄ higher than 61-64 pmol/L, FT₃ higher than 21-24 pmol/L), and those who were in need of high doses of antithyroid drug to maintain euthyroidism. I, hereby, suggest that these

group of patients or those who have associated comorbid diseases should be treated with radioactive iodine as first-line therapy.

For any clinician who is considering the drug therapy, the treatment should start with a low dose of antithyroid drug (methimazole 7.5-10 mg/d^(10,11) or P.T.U 150 mg/d⁽¹²⁾) for 18-24 months. Our data showed that the relapse rates are higher in the first and second years after drug withdrawal (64.8% and 86.2%). Therefore, after drug withdrawal, the patient should be re-evaluated for thyroid function test every 3-4 months during the first year and every 6 months during the second year and then once yearly.

After radioactive iodine therapy, most patients developed hypothyroidism within two years. Clinician should therefore follow-up for freeT₄ and TSH every 3-6 months in the first year and every 6 months in the second year, then once yearly.

There are some limitations in this study. First, we do not include patients who were lost to follow up from the clinic. Second, we did not analyze the data yearly, so the incidence of thyroid status in each group of patients is present at the end point of each treatment instead of being shown as longitudinal data.

Conclusion

We can improve outcome and prevention of serious complications of Graves'disease by carefully evaluation of patients from there first visits. In most cases, radioactive iodine should be used as first line treatment. However, every patients with Graves'disease should receive a life-long follow- up of thyroid function after each kind of treatment they receive, i.e., antithyroid drugs, radioactive iodine and thyroid surgery.

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