Effect of Post-Operative Thyroid Hormone Therapy on the Recurrence of Benign Thyroid Nodules. A Study in Thai Patients

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Abstract

The efficacy of postoperative thyroid hormone treatment in prevention of recurrent thyroid nodule is still controversial. In order to investigate this effect in Thai patients, a retrospective study was performed on files of 321 post-operative patients with benign thyroid nodules, who were either on thyroid hormone treatment or not after surgery, and were followed-up for at least 1 year. The longest follow-up period was 15 years after surgery. The recurrence of nodules was determined by palpation. It was found that the recurrent rate in patients with adenoma who did not receive post-operative thyroid hormone treatment was 20 per cent (16/82 cases) while there was no recurrence at all (0/25 cases) in the treatment group ($p<0.05$). The recurrent rate was 22 per cent (31/141 cases) in patients with nodular goitre who did not receive post-operative thyroid hormone treatment and 7 per cent (5/73 cases) in those with treatment ($p<0.001$). In the group of patients without post-operative thyroid hormone treatment, for both the group of patients with adenoma and that with nodular goitres, the recurrence was found to occur as late as more than 10 years after surgery.

Thyroid nodule is a common disorder among thyroid diseases. As they are believed to be caused by TSH stimulation, the thyroid hormone suppression therapy for thyroid nodular diseases has been practiced by endocrinologists for decades, although the discordant results of this treatment efficacy have been reported(1).

The question of post-operative thyroid hormone therapy after partial thyroidectomy also arises frequently, as found with the non-operative cases of solitary thyroid nodules and multinodular goitre(1). Its efficacy as well as duration, for preventing the recurrence of thyroid nodules, are still controversial; although such a treatment has been standard practice during the early years(1-10).

Since there has been no previous report of the study on the effect of post-operative thyroid hormone treatment in Thai patients, we performed a retrospective study of operative cases of benign thyroid nodules among Thai patients, during the

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period of 15 years, in order to evaluate whether postoperative thyroid hormone therapy has been beneficial for preventing the recurrence of the disease in this population of subjects.

PATIENTS AND METHOD

A retrospective study was performed on files of 343 patients with benign thyroid nodules, who were subjected to surgery at the Deparment of Surgery, Rajavithi Hospital, Bangkok, Thailand, during the period of 15 years. These patients were the ones who had nodular goitre (adenomatous goitre and colloid goitre) and adenoma (follicular adenoma and cystadenoma). Files of these patients were reviewed for characteristics of patients, postoperative treatment, as well as the time of recurrence after surgery.

Only 321 patients had been followed-up for the period of at least 1 year after surgery by the time the files were reviewed. Ninety eight patients had been regularly followed-up and had constantly taken the thyroid hormones. Two hundred and twenty three patients had refused the treatment. The first group of patients was regarded as the thyroid hormones treatment group while the second group of patients was regarded as the non-treatment group. The daily doses of drugs used in the thyroid hormones treatment group was either 1 to 3 grains of thyroid extract or 0.1 to 0.3 mg of levo - thyroxine tablets.

The recurrence of nodules in the treatment and non - treatmentgroups of patients were determined by palpation. The recurrent rates in these 2 groups were compared by Chi-square test. Probability values < 0.05 are regarded as statistical significance.

RESULTS

Characteristics of 343 patients studied are shown in Table 1. The majority of the patients were female (330/343 cases). This disease could be found in a wide range of ages (10-78 years) and nodular goitre was found more often than adenoma (67% *vs* 33%). Although the nodule was found to be confined in either lobe (54.2% in right lobe and 35.9% in left lobe), it could be found in both lobes of thyroid gland (5.8%) as well as in the middle site (4.1%). The operative procedures commonly performed were lobectomy and isthmusectomy (73.8%). Only a minority of cases were subjected to either excision of the gland (17.8%) or subtotal thyroidectomy (8.4%).

Table 1. Characteristics of patients and operative procedures performed in 343 patients with thyroid nodules.

No. of patients	343	cases	
- Male	13	cases	(4%)
- Female	330	cases	(96%)
Age	10-78	years	(median = 37 years)
Diagnosis			
- nodular goitre (adenomatous, colloid)	230	cases	(67%)
- adenoma (follicular, cystadenoma)	113	cases	(33%)
Site of nodule			
- right lobe	186	cases	(54.2%)
- left lobe	123	cases	(35.9%)
- both lobes	20	cases	(5.8%)
- middle site	14	cases	(4.1%)
Operative procedures			
- lobectomy and isthmusectomy	253	cases	(73.8%)
- excision	61	cases	(17.8%)
- subtotal thyroidectomy	29	cases	(8.4%)

Recurrent rate of thyroid nodules in these patients was reviewed in relation to sex of patients, post-operative procedures and pathological diagnosis. The data are shown in Table 2. It can be seen that the recurrence appeared in males more often than females (30.8% *vs* 14.6%). The recurrence occurred as early as within 5 years and as late as more than 10 years after surgery, for both adenoma and nodular goitre.

Table 2. Recurrent rate of thyroid nodules after surgery in a total of 343 patients studied, relating to various parameters.

Parameters	Recurrent rate (%)
Sex	
- Male	30.8
- Female	14.6
Operative procedures	
- lobectomy and isthmusectomy	13.4
- excision	21.3
- subtotal thyroidectomy	17.2
Pathological diagnosis	
- adenoma	15
- nodular goitre	17

Only 321 out of 343 patients described above were the ones who had been followed-up for the period of at least one year. Ninety - eight patients were regarded as the thyroid hormones treatment group while 223 of them were regarded as the non - treatment groups. The recurrent rates of the nodules in these 2 groups were compared, in order to evaluate the efficacy of postoperative thyroid hormone therapy in prevention of the nodule recurrence. The results are shown in Tables 3 and 4. It can be seen that, among 107 patients with adenoma (Table 3), there was no recurrence of nodules in any of 25 patients with post-operative thyroid hormone treatment, while 16/82 (20%) patients without such treatment had recurrence of the nodules. By using statistical analysis, the difference of the recurrent rate between these 2 groups of patients was also found to be significant ($p < 0.05$). The recurrence in the group of patients without thyroid hormone therapy appeared to be more common (30% of cases) during 1-5 years. However, it can be found to occur during the longer period of time after surgery, i.e. 15 per cent during >5-10 years and 19 per cent during >10-15 years.

Table 3. Recurrence of thyroid nodule in patients with adenoma who were either treated or not treated with thyroid hormone after surgery and had been followed-up for at least 1 year.

	Treated			Not treated		
Follow-up perior (years)	Total cases	Recurrent cases	Recurrent rate (%)	Total cases	Recurrent cases	Recurrent rate (%)
1-5	13	0	0	20	6	30
>5-10	10	0	0	46	7	15
>10-15	2	0	0	16	3	19
Total	25	0	0	82	16	20

Table 4 Recurrence of thyroid nodule in patients with nodular goitre who were either treated or not treated with thyroid hormone after surgery and had been followed up for at least 1 year.

	Treated			Not treated		
Follow-up perior (years)	Total cases	Recurrent cases	Recurrent rate (%)	Total cases	Recurrent cases	Recurrent rate (%)
1-5	38	4	10	34	9	26
>5-10	31	1	3	79	15	19
>10-15	4	0	0	28	7	25
Total	73	5	7	141	31	22

Among 214 patients with nodular goitre, the recurrent rate in the group of patients with post-operative thyroid hormone treatment was 5/73 cases (7%) while it was 31/141 cases (20%) in the non-treatment group (Table 3). Nevertheless, the difference of the recurrent rate between these 2 groups of patients was still found to be statistically significant ($p<0.001$).

In the group of patients with postoperative thyroid hormone treatment, the recurrent rate was found to be highest (10%) during 1-5 years after surgery, while it was 3 per cent during >5-10 years and none was found during >10-15 years period. However, in the group of patients without such a treatment, 9/34 (26%), 15/79 (19%) and 7/28 (25%) cases of patients had recurrent disease during the period of 1-5, >5-10 and >10-15 years after surgery respectively.

DISCUSSION

Although post-operative thyroid hormone treatment has become standard practice during the early years, it is still debated for its efficacy as well as duration for preventing the recurrence of thyroid nodules[1-10].

In our present study, we found that the proportion of male to female patients with thyroid nodules was approximately 1:25, which is lower than that reported by other investigators (around 1:10)[5,6,10]. However, while most investigators [1,4-6,8-10] did not observe any effect in prevention of recurrence using post-operative thyroid hormone therapy, we did observe a significant difference in the recurrent rate between the groups of patients who received post-operative thyroid hormone treatment and those who did not ($p<0.05$ in patients with adenoma and $p<0.001$ in those with nodular goitre).

We have to admit that, as our study was a retrospective study, the number of patients in the treatment and non - treatment groups could not be designed to be comparable as well as the characteristics of the patients in these 2 groups which could be much different; and these parameters could possibly bias the evaluation of these rerults.

Nevertheless, our findings are in agreement with those reported by other investigators, using non-operated patients[11,14], and at least one of the studies using operated patients[7], for the supressive effect of thyroid hormone treatment. The discrepancy of our results from those of others, using operated patients, could be due to the shorter follow-up period in other studies. None of those studies had followed-up patients up to 10 years after surgery, while we did up to 15 years and found that 19 per cent of patients with adenoma and 25 per cent of those with nodular goitre who did not receive post-operative thyroid hormone treatment did have recurrence at the period of > 10 years after surgery. The recurrence of disease at this period of time was not found in any patients with either adenoma or nodular goitre who received post-operative thyroid hormone treatment.

In conclusion, the results of our study indicate that post-operative thyroid hormone treatment significantly reduces the recurrent rate of thyroid nodule, at least in Thai patients, and lifelong administration is beneficial as the recurrence can occur as late as longer than 10 years after surgery without such treatment.

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REFERENCES

1. Cooper DS. Clinical Review 66. Thyroxine suppression therapy for benign nodular disease. J Clin Endocrinol Metab 1995; 80: 331-4.
2. Bergfelt G, Risholm L. Postoperative thyroid hormone therapy in nontoxic goitre. Acta Chir Scand 1963; 26: 531-7.
3. Bernstein RS, Robbins J. Intermittent therapy with L-thyroxine.N Engl J Med 1969; 281: 1444-8.
4. Persson CP, Johansson H, Westermark K, Karlsson FA. Nodular Goiter-is thyroxine medication of any value? World J Surg 1982; 6: 391-6.
5. Geerdsen JP, Frolund L. Thyroid function after surgical treatment of nontoxic goitre. A randomized study of postoperative thyroxine administration. Acta Med Scand 1986; 220: 341-5.
6. Hegedus L, Hansen JM, Veiergang D, Kastrup S. Does prophylactic thyroxine treatment after operation for non-toxic goiter influence thyroid size? Br Med J 1987; 294: 801-3.
7. Anderson PE, Hurley PR, Rosswick P. Conservative treatment and long term prophylactic thyroxine in the prevention of recurrence of multino dular goiter. Surg Gynecol Obstet 1990; 171: 309-14.
8. Berglund J, Bondesson L, Christensen SB, Larsson AS, Tibblin S. Indications for thyroxine therapy after surgery for nontoxic benign goitre. Acta Med Scand 1990; 156: 433-8.
9. Mandel SJ, Brent G, Larsen PR. Levothyroxine therapy in patients with thyroid disease. Ann Intern Med 1993; 119: 492-502.
10. Bistrup C, Nielsen JD, Gregersen G, Franch P. Preventive effect of levothyoxine in patients operated for non-toxic goitre : a randomized trial of one hundred patients with nine years of follow-up. Clin Endocrinol (Oxf) 1994; 40: 323-7.
11. Nilsson G, Pettersson U, Levin K, Hughes R. Studies on replacement and suppressive dosage of L-thyroxine. Acta Med Scand 1977; 202: 257-60.
12. Perrild H, Hansen JM, Hegedus L. Triiodothyronine and thyroxine treatment of diffuse non-toxic goitre evaluated by ultrasonic scanning. Acta Endocrinol 1982; 100: 382-7.
13. Berghout A, Wiersinga WM, Drexhage HA, Smits NJ, Touber JL. Comparison of placebo with L-thyroxine alone or with carbimazole for treatment of sporadic non-toxic goitre. Lancet 1990; 336: 193-7.
14. La Rosa GL, Lupo L, Giuffrida D, Gullo D, Vigneri R, Belfiore A. Levothyroxine and potassium iodide are both effective in treating benign solitary solid cold nodules of the thyroid. Ann Intern Med 1995; 122: 1-8.

ผลของการรักษาด้วยธัยรอยด์ฮอร์โมนหลังผ่าตัดต่อการเกิดใหม่ของก้อนเนื้อธัยรอยด์ชนิดไม่ร้ายในผู้ป่วยไทย

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การใช้ธัยรอยด์ฮอร์โมนเพื่อป้องกันการเกิดก้อนเนื้อต่อมธัยรอยด์ขึ้นใหม่ในผู้ป่วยหลังการผ่าตัดจะมีประสิทธิภาพหรือไม่นั้นยังเป็นเรื่องที่ถกเถียงกันอยู่ และยังไม่มีรายงานผลการวิจัยเรื่องนี้ในผู้ป่วยไทยมาก่อน การศึกษานี้ได้กระทำโดยการศึกษารายงานผู้ป่วย 321 ราย ที่ได้รับการผ่าตัด ก้อนเนื้อธัยรอยด์ชนิดไม่ร้าย ทั้งผู้ที่ได้รับและผู้ที่ไม่ได้รับธัยรอยด์ฮอร์โมนหลังการผ่าตัดและได้มารับการรักษาดูแลต่อเนื่องหลังจากผ่าตัดแล้วเป็นระยะเวลาอย่างน้อย 1 ปี ระยะเวลาที่ศึกษาตามดูแลผู้ป่วยนานที่สุดในการศึกษานี้คือ 15 ปี หลังผ่าตัดใช้การคลำเพื่อตรวจว่าผู้ป่วยเกิดมี ก้อนเนื้อต่อมธัยรอยด์ขึ้นอีกหรือไม่ ในการศึกษานี้พบว่าผู้ป่วยที่เป็นอะดีโนมา และไม่ได้รับธัยรอยด์ฮอร์โมนหลังการผ่าตัดมีอัตราการเกิดมีก้อนเนื้อขึ้นใหม่คิดเป็นร้อยละ 20 (16/82 ราย) ส่วนผู้ที่ได้รับธัยรอยด์ฮอร์โมนหลังผ่าตัดไม่เกิดมีก้อนเนื้อขึ้นใหม่เลย (0/25 ราย) (ค่าพี <0.05) สำหรับผู้ป่วยที่เป็น คอพอกชนิดเป็นก้อน ซึ่งไม่ได้รับธัยรอยด์ฮอร์โมนหลังการผ่าตัดมีอัตราการเกิดก้อนเนื้อ ขึ้นใหม่คิดเป็นร้อยละ 22 (31/141 ราย) ส่วนผู้ที่ได้รับธัยรอยด์ฮอร์โมนหลังการผ่าตัดมีอัตราการเกิดก้อนเนื้อขึ้นใหม่คิดเป็นร้อยละ 7 (5/73 ราย) (ค่าพี <0.001) พบว่าผู้ป่วยที่ไม่ได้รับการรักษาด้วยธัยรอยด์ฮอร์โมนหลังการผ่าตัดเกิดมีก้อนเนื้อขึ้นใหม่ได้หลังจากผ่าตัดไปแล้วนานมากกว่า 10 ปีทั้งในกลุ่มผู้ที่เป็น อะดีโนมา และคอพอกชนิดเป็นก้อน

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