

THE INCIDENCE OF POST-OPERATIVE GOITER RECURRENCE

ERKAN IBIS*
RADIFE AKCURA*
GÜNER ERBAY*
GÜLSEREN ARAS*
ASIM AKIN*

SUMMARY: A study was conducted on the incidence of post-operative non-toxic goiter in 206 cases. The average duration of post-operative observation was 7.8 years. The incidence of recurrence was 30.7% in the 26 cases where thyroxine was used in sufficient doses (0.15 mg/day or over) and regularly in the post-operative period; and 46.9% in the 32 cases where thyroxine was used in insufficient doses (0.10 mg/day) and regularly. Whereas it was found 71.4% in the 49 cases where thyroxine usage was irregular and in insufficient doses; and 81.8% in the 99 cases where there was no use of drugs. It was observed that the incidence of recurrence was perceptively reduced in the patients who used thyroxine regularly and in sufficient doses as compared to those who use irregularly or not at all. It was concluded that in Turkey, where iodine deficiency is a major contributory factor to the prevalence of goiter, post-operative usage of thyroxine is necessary in reducing the incidence of post-operative goiter.

Key Words: Nodular goiter, thyroid resection, recurrence.

INTRODUCTION

In Turkey, endemic goiter connected to iodine deficiency continues to be one of the major health issue despite combatting it with iodine salts (19, 31, 32). When there is iodine deficiency, the amount of thyroid hormones drops, and as a result, the increase in the amount of TSH produced through a feed-back mechanism leads to growth and structural change of the thyroid gland (2,3,6, 19,32,33). Among other causes of goiter, some substances and genetic defects in hormone synthesis can be counted (3). On the other hand, it has been claimed that thyroidal growth could turn into nodular goiter and could be a symptom of latent hypothyroidism (3).

Thyroid hormone treatment can either be with the aim to remove thyroid hormone deficiency or to prevent goiter growth by suppressing TSH release through pituitary-thyroid negative feed-back mechanism (1,4,7,13,14, 22,23). Thyroxine is also widely used to prevent recurrence in the post-operative period in non-toxic goiter cases (1,3,4,7, 10,11,12,20,22,23).

The joint use of physical examination, scintigraphy, and ultrasonography in detecting thyroid nodules proves

highly accurate in the search for post-operative recurrence (12, 15,17,21,21,26,28,30,35).

In this study, we tried to determine the incidence of post-operative goiter recurrence by physical examination, scintigraphy and ultrasonography, and the effect of thyroxine on those determinations.

MATERIALS AND METHODS

A total of 206 patients who had had operations due to benign nodular goiter, and who reported to the Nuclear Medicine Department of Ankara University Medical School during 1988-1989 were investigated. The ages of the patients varied between 20 to 67. Of the 206 cases, there were 176 women, with average age of 32.8, and 30 men with average age 41.6.

The patients were divided into four groups according to their usage of thyroxine in the post-operative period;

Group 1: Patients taking regularly 0.15 mg or more thyroxine daily. A total of 26 cases.

Group 2: Patients taking regularly thyroxine at low doses (0.1 mg per day). A total of 32 cases.

Group 3: Patients who used irregularly doses of insufficient doses of thyroxine. A total of 49 cases.

Group 4: Patient who did not use any thyroxine. A total of 99 cases.

*From Department of Nuclear Medicine, Medical School, Ankara University, Ankara, Turkiye.

The types of operative procedures were hemithyroidectomy in 29 cases, bilateral partial in 94 cases and unilateral partial in 83 cases. Each was physically examined by an experienced physician and then admitted first for scintigraphy and finally for ultrasonography. In scintigraphic examination, the patient was given an intravenous of 2mCi of Tc-99m pertechnetate, followed by 15 minutes of 150.000 counts at the neck area, using a Pin-holl detector a Siemens Searle camera, with the patient in the supine position. Then, the patient was examined ultrasonographically, using a Toshiba 32B instrument with a 5 MHz linear transducer. Sonographic pillow was used to increase the resolution. The three examinations taken together decided the incidence of recurrence in the patients.

RESULTS

Any growth or nodular change in the residual thyroid tissue was interpreted as an evidence of recurrence.

Of the 139 patients with recurrence, 84 (60.4%) had multi-nodular, 36 (25.9%) had solitary nodular and 19 (13.7%) had diffuse growth. The cases were appraised by

age groups, post-operative periods and thyroxine usage (Table 1). Recurrence was detected in 21 (65.6%) of the 32 patients in the 20-30 year age group, in 49 (62.0%) of the 79 patients in 31-40 year age group, and 69 (72.6%) of the 95 patients of over 40 years of age.

The variation of recurrence with post-operative period is summarized in Table 2. Recurrence was observed in 58 (55.8%) of the 104 patients whose post-operative period was in the range 1-5 years, in 39 (79.6%) of the 49 patients whose post-operative period ranged 6-10 years, and in 42 (87.5%) of the 48 patients who were operated on 11 years ago or earlier.

The variation of the incidence of recurrence with thyroxine usage is given under Table 3. Group 1 consisted of 26 patients, 21 women and 5 men, who used thyroxine in sufficient doses and regularly. The average post-operative period for this group was 6.8 years, and the average age was 40.1 years. Recurrence was detected in 8 (30.7%) patients of whom 7 were women. In this group, one patient was taking 0.25 mg/day, 5 patients were taking 0.20 mg/day and 20 were taking 0.15 mg/day. Recurrence was observed after 1.5 years in the patient who was taking 0.25 mg/day. Of the 5 patients taking 0.20 mg/day, one had recurrence 12 years after the operation; whereas, six of the patients taking 0.15 mg/day showed recurrence after an average of 5.2 years following the operation.

Group 2 consisted of 32 patients, 27 women and 5 men, who used insufficient doses of thyroxine regularly. The post-operative period averaged 6.4 years. Recurrence was observed in 15 (46.9%) cases, 14 women and 1 man, and average post-operative period before recurrence was 6.7 years.

Group 3 consisted of 49 patients, 39 women and 10 men, who used insufficient doses of thyroxine irregularly. Averages for age and post-operative period were 40.4 and 7.1 years, respectively. Recurrence was detected in 35 (71.4%) cases, of whom 26 were women and 9 were men. The average post-operative period before recurrence was 6.7 years.

Table 1: The variation of the incidence of post-operative recurrence with age.

| Age groups | Number of all cases | Number of cases with recurrence |
|------------|---------------------|---------------------------------|
| 20 - 30 | 32 | 21 (65.6%) |
| 31 - 40 | 79 | 49 (62.0%) |
| 40 < | 95 | 69 (72.6%) |

Table 2: The variation of the incidence of post-operative recurrence with post-operative period.

| Post-op. period | Number of all cases | Number of cases with recurrence |
|-------------------|---------------------|---------------------------------|
| 1 - 5 years | 104 | 58 (55.8%) |
| 6 - 10 years | 49 | 39 (79.6%) |
| 11 or above years | 48 | 42 (87.5%) |

Table 3: The variation of the incidence of post-operative recurrence with thyroxine usage.

| Groups | Number of all cases | Mean years old | Mean post-operative period (year) | Normal cases | Recurrence |
|---------|---------------------|----------------|-----------------------------------|--------------|-------------|
| Group 1 | 26 | 40.1 | 6.8 | 18 | 8 (30.7%) |
| Group 2 | 32 | 36.7 | 6.4 | 17 | 15 (46.9%) |
| Group 3 | 49 | 40.4 | 7.1 | 14 | 35 (71.4%) |
| Group 4 | 99 | 42.5 | 10.9 | 18 | 81 (81.8%) |
| Total | 206 | 37.7 | 7.8 | 67 | 139 (67.5%) |

Group 4 consisted of age of 99 patients who did not use thyroxine, 89 women and 10 men. Averages for age and post-operative period were 42.5 and 10.9 years respectively. Recurrence was detected in 81 (81.8%) cases, of whom 75 were women and 6 were men. The average post-operative period before recurrence was 10.1 years.

We observed that, overall 139 (67.5%) cases out of a total of 206, had recurrence and that the average post-operative before recurrence was 7.8 years.

DISCUSSION

Recurrence is an important issue following the surgical treatment of nodular goiter. It is known that inadequacy of surgical technique, as well as patho-genetic factors play a role in recurrence (9). The objective of the wide usage of thyroxine and preventive medication in the post-operative period is the suppression of TSH (4,7,9,20,22,23,26,29). It has been pointed out that 0.15 to 0.20 mg of thyroxine can be sufficient to suppress the pituitary-thyroid mechanism (13,14,18,20,23).

Different views have been expressed on the use of thyroxine in the prevention of recurrence. A large number of researchers support the incidence of recurrence in thyroxine users; during the post-operative period is less than that in the non-users (3,5,7,20,22,23,29,34). On the other hand, Geerdson, *et al.* claimed that incidence of recurrence was not significantly affected by the use of thyroxine (10). Their conclusion was based on study of 175 patients who had been operated on due to non-toxic goiter, and who had an average of 8.8 years of post-operative monitoring and an incidence of 10-11 percent.

Watt-Boolsen, *et al.* also reported that there is no need to use thyroxine to prevent post-operative recurrence as none of their 22 patients developed recurrent growths during a 2-28 year period (34). Their patients were operated on due to benign intra-thoracic goiter.

In various publications covering different periods, the incidence of post-operative recurrence has been reported as; without the use of thyroxine 9.1%, 11.3%, 15.0%, and 38.5% (3,9,16,24); while with thyroxine 0.0%, 2.0% and 9.5% (3,9,25). For Turkey, where the incidence of endemic goiter is high, Kologlu, *et al.* examined 237 cases with recurrence and post-operative periods of 0.4-20 years, and found that 178 (75.1%) patient had not used thyroxine, 36 (15.2%) patients had used insufficient doses of thyroxine and 21 (9.7%) patients had used sufficient doses regularly (20).

Saygin, *et al.* studied patients who had undergone operations for benign nodular goiter, and determined recurrence in 39 (40.6%) cases out of 96 patients who had not used thyroxine (27).

Our results, indicates a lower level of incidence of recurrence in patients who use thyroxine, are in line with the results reported in literature. Our findings have been that the incidence of post-operative recurrence was 30.7% for those who use thyroxine in sufficient dose and regularly, and 81.8% for those who did not use thyroxine. We speculate that the higher rates of recurrence found in our study is based on the prevalence goiter due to iodine deficiency in Turkey, as compared to many other countries.

We observed that the incidence of recurrence was higher in those who regularly use thyroxine in low dose or who irregularly use thyroxine in low doses, than those who take thyroxine in sufficient doses regularly.

As regards the higher incidence of recurrence we observed, it is most likely that our corroborative use of the three methods of detection, namely, physical examination, scintigraphy and ultrasonography proved more accurate. Of the 139 cases of recurrence observed, 99 (71.2%) were corroborated by physical examination, 112 (80.6%) by scintigraphy, and 134 (96.4%) by ultrasonography. Sensitivity of detection by physical examination or by scintigraphy is affected by such factors as the increase in the amount of fibrotic tissue, the change of structure in the thyroid gland, the dimensions and localization of the nodules. It is known that ultrasonography can detect those nodules which escape physical examination or scintigraphy (12,21,26,28,30).

It has been stated that the incidence of recurrence increases in direct proportion to the post-operative period, reaching a maximum at 10-15 years (11,16). Our findings also support this conclusion; recurrence was observed in 42 (86.2%) of the 48 cases where the post-operative period was 11 years or above. However, we would like to point out that our findings do not show any perceptible trend between incidence of recurrence and age.

CONCLUSION

We conclude that preventive use of thyroxine, in regular and sufficient doses in the post-operative period, is essential in Turkey where iodine deficiency is a major contributor to the prevalence of goiter. We also submit that the corroborative use of the techniques of physical examination, scintigraphy and ultrasonography can significantly enhance the accuracy of diagnosis.

REFERENCES

1. Asfwood EB, Cassidy CE, Aurbach ED : *Treatment of goiter and thyroid nodules.* JAMA, 174:459-472, 1960.

2. Beckers C, Cornette C : TSH production rate in nontoxic goiter. *J Clin Endoc Metab*, 32:852-856, 1971.
3. Bergfelt G, Risholm L : Post-operative thyroid hormone therapy in on-toxic goiter. *Acta Chir Scand*, 126:531-537, 1963.
4. Bernshein RS, Robbins J : Intermittent therapy with L-thyroxine. *N Eng J Med*, 281:1444-1448, 1969.
5. Blichert-Taft M, Egedorf J, Christiansen C, et al : Function of pituitary-thyroid axis after surgical treatment of nontoxic goiter. *Acta Med Scand*, 206:15-19, 1979.
6. Buttfield IH, Black ML, Hofman MJ, et al : Studies of the control of thyroid function in endemic goiter in Eastern New Guinea. *J Clin Endoc Metab*, 26:1201-1207, 1966.
7. Clarck HO : Thyroid nodules and thyroid cancer. In Clarck HO (Ed), *Endocrine Surgery of the thyroid and parathyroid gland*, 1st edition, St Louis, CV Mosby Co, p 56-90, 1985.
8. Delange FM, Hershman JM, Erman AM : Relationship between the serum thyrotropin level, the prevalence of goiter and the pattern of iodine metabolism. *J Clin Endoc Metab*, 33:261-268, 1971.
9. Düren E : Residue problem in the surgical treatment of goiter. *Türkiye Endokrinoloji Yilligi*, Ankara, pp 38-42, 1976.µ
10. Geerdson JP, Frolund L : Recurrence of non-toxic goiter with and without post-operative thyroxine medication. *Clin Endoc*, 21:529-533, 1984.
11. Geerdson JP, Frolund L : Thyroid function after surgical treatment of non-toxic goiter. *Acta Med Scand*, 220:341-345, 1986.
12. Gharib H, Goellner JR : Evaluation of nodular thyroid disease. In Young FW, Klee GC (Eds), *Endocrinology and Metabolism Clinics of North America*, Philadelphia, WB Saunders Co, pp 511-526, 1988.
13. Glassford GH, Fowler EF, Cole WH : Treatment of non-toxic nodular goiter with desiccated thyroid. *Results of Evaluation Surgery*, 58:621-626, 1965.
14. Hoffman DP, Surks MI, Oppenheimer JA, et al : Response to thyrotropin releasing hormone: An objective criterion for the adequacy of thyrotropin suppression therapy. *J Clin Endoc Metab*, 44:892-901, 1977.
15. Ikekubo K, Higa T, Hirasa M, et al : Evaluation of radionuclide imaging and echography in the diagnosis of thyroid nodules. *Clin Nucl Med*, 11:145-149, 1986.
16. Jenny H, Block MA, Horn RC, et al : Recurrence following surgery for benign thyroid nodules. *Arch Surg* 92:525-528, 1965.
17. Katz JF, Kane AR, Reyes J, et al : Thyroid nodules; sonographic pathologic correlation. *Radiology*, 151:741-745, 1984.
18. Krugmann LG, Hersmann JM : TRH tests as an index of suppression compared with thyroid radio-iodine uptake in euthyroid goitrous patients treated with thyroxine. *J Clin Endoc Metab*, 47:78-83, 1978.
19. Kologlu S : Euthyroid goiter. *Türkiye Klinikleri*, 4:299, 1984.
20. Kologlu S, Baskal N, Uysal AR, et al : The importance of thyroid suppression treatment in post-operative prevention of post-thyroidectomy residue. *Journal of Ankara Medical School*, 10:467-480, 1988.
21. Mazzaferri EL, Santo ET, Keyhani SR : Solitary thyroid nodule: diagnosis and management. In Geokas MC (Ed), *Medical Clinics of North America*, Philadelphia, WB Saunders Co, pp 1178, 1988.
22. Nilsson G, Petersson U, Levin K, et al : Studies on replacement and suppressive dosages of L-thyroxine. *Acta Med Scand*, 202:257-260, 1977.
23. Perrild H, Hansen JM, Hegedüs L, et al : Tri-iodothyronine and thyroxine treatment of diffuse non-toxic goiter evaluated by ultrasonic scanning. *Acta Endoc*, 100:382, 1982.
24. Piercy JE, Lange MJ : Recurrent goiter. *Lancet* 177:77-81, 1957.
25. Roher HD, Goretiki PE : Management of goiter and thyroid nodules in an area of endemic goiter. In Clarck O, Weber AC (Ed), *Surgical Clinics of North America-Endocrine Surgery*, Philadelphia, WB Saunders Co, pp 233-251, 1987.
26. Rojeski MT, Gharib H : Nodular thyroid disease. *New Eng J Med*, 313:428-436, 1985.
27. Saygin T, Aras N, Söylemez A : Recurrence issue in thyroid surgery. *Buletin of Ankara Numune Hospital*, 3:117-118, 1987.
28. Scheible W, Leopold GR, Woo VL et al : High resolution real-time ultrasonography of thyroid nodules. *Radiology*, 133:413-417, 1979.
29. Sekadde CB, Slaunwhite WR, Aceto T, et al : Administration of thyroxine once a week. *J Clin Endoc Metab*, 39:759-764, 1974.
30. Simeone J, Daniels GH, Mueller RP, et al : High-resolution real-time ultrasonography of thyroid. *Radiology*, 145:431-435, 1982.
31. Urgancioglu I, Hatemi H, Kökçü E, et al : Iodine determination in drinking water samples of Turkey: in relation to the endemic goiter problem. *Istanbul, University of Istanbul*, pp, 1-6, 1982.
32. Urgancioglu I, Hatemi H, Yenici O, et al : Endemic goiter in Turkey. *Istanbul, Ornek Matbaasi*, pp 8-39, 1988.
33. Wahner HW, Mayberry WE, Gaitan E, et al : Endemic goiter in the Cauca Valley. *J Clin Endoc Metab*, 32:491-496, 1971.
34. Watt-Boolsen S, Blichert-Toft M, Folk K, et al : Surgical treatment of benign non-toxic intra-thoracic goiter. *Am J Surg* 141:721-722, 1981.
35. Yokoyama N, Nagayama Y, Kakezono F, et al : Determination of the volume of the thyroid gland by high-resolution ultrasonic scanner. *J Nucl Med*, 27:1475-1479, 1986.

Correspondence:
 Erkan Ibis
 Ankara Üniversitesi Tıp Fakültesi
 Nükleer Tıp Anabilim Dalı
 Cebeci-Ankara
 TÜRKİYE.