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## The results of treatment with radioactive iodine and surgery in patients with toxic multi nodular goiter (tmng) from 1999 to 2005 in Ahvaz

Saeed Saeedinia<sup>1</sup>, Hajieh Shahbazian<sup>2</sup>, Zivar Shirin Pour<sup>3</sup>

1- Medical Doctor, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

2-Professor of Endocrinology, Health Research Institute, Diabetes Research Center, Ahvaz Jundishapur University of Medical Sciences, Golestan Blvd, Ahvaz, Iran.

3- Fellowship of Endocrinology.

### Abstract

**Background:** The aim of this study was the evaluation of the result of two treatment methods (radioactive iodine and surgery), recurrence rate and hypothyroidism after treatment and side effects in Toxic Multi Nodular Goiter

**Material and methods:** In this retrospective study 354 cases of toxic multi nodular toxic goiter patients that referred to endocrine clinic and treated with one of the above-mentioned treatment method were evaluated. Demographic data, thyroid examination, recurrence of hyperthyroidism, incidence of hypothyroidism after treatment and side effects of treatment were collected.

**Results:** From 326 cases, 20% were male and 80% were female. Mean age was 48±14. From 326 patients treated with radioactive iodine, only 34 cases (10%) relapsed after treatment and 186 patients (57%) showed hypothyroidism after treatment. From 28 patients underwent surgery, only 2 patients (7%) had recurrence of hyperthyroidism, but hypothyroidism after surgery was seen in half of patients and in 10 patients (36%) long-term surgical complications such as laryngeal nerve damage and hypoparathyroidism were seen. Euthyroid cases without permanent side effects had not significant difference in these two treatment methods (33% in surgery versus 29% in radioactive iodine (P>0.05).

**Conclusion:** surgery in patients with TMNG does not have any advantage on radioactive iodine. Surgery can lead to lifelong complications in patient.

**Keywords:** nodular goiter, hyperthyroidism, hypothyroidism, iodine therapy, thyroid surgery

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Corresponding author:  
Hajieh Shahbazian; Health research  
Institute, Diabetes Research Center,,  
Ahvaz Jundishapur University of  
Medical Sciences, Golestan Blvd,  
Ahvaz, Iran.  
Tel: 09166131706  
Email: hjb\_shahbazian@yahoo.com

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## Introduction

Toxic Multinodular goiter is one of the most prevalent causes for thyrotoxicosis and occurs mostly in old patients who have had multinodular goiter for times and it is more prevalent in women (14). The thyroid size is more in patients with TMNG compared to other reasons for hyperthyroidism and can cause pressure on the adjacent organs. However, signs such as dysphagia, respiratory distress, or venous congestion are not prevalent in these patients. Besides goiter, these patients may have the presentations of subclinical hyperthyroidism or mild thyrotoxicosis. As these patients are mostly old, they may refer having atrial fibrillation, pulmonary edema, tachycardia, irritability, tremor, or weight loss, the definite treatment for preventing the incidence of cardiovascular complications is necessary in these patients (1, 2). Control and treatment of TMNG are more difficult compared to other reasons of thyrotoxicosis (goiter and toxic adenoma). Anti-thyroid drugs, which are mostly prescribed by  $\beta$ -blocker, can make the function of the thyroid gland normal and control the clinical signs of thyrotoxicosis; yet, this therapy mostly stimulates the growth of goiter and simultaneous remission does not happen against Graves' disease. Therefore, ablation therapy using radioactive iodine or surgical treatment has priority for the treatment of these patients (1, 3). Many studies have been conducted about choosing the best therapeutic method for patients with TMNG, up to now (4, 13). However, considering the inconsistent results of these studies, complete agreement about the kind of therapy for these patients has not been achieved, yet.

In the United States and Europe, the selective therapy for this disease is radioactive iodine, which does not have any contraindications except pregnancy (15, 16). In this study, it is tried to survey the

relapsing rates of hyperthyroidism, hypothyroidism and other side effects of the therapy in these two therapeutic methods and in addition, to compare the rates of thyroid after treatment in these two methods.

## Material and methods

For conducting this descriptive cross-sectional study, all the patients with toxic multinodular goiter who referred to endocrinology clinic and were treated by one of the two methods of radioactive iodine therapy or surgical therapy were evaluated. No restriction of age and sex interfered determining the samples. The patients who did not refer completely in follow-up period nor had imperfect results of therapy or laboratory tests did not enter the study. Age, age for the onset of the disease, sex, the thyroid gland weight before and after therapy, relapsing incidence after treatment, the clinical and laboratory diagnosis time of the relapsing incidence, incidence of hypothyroidism after therapy and time of the clinical and laboratory diagnosis of hypothyroidism, and the presence of permanent side effects caused by therapy were extracted from the medical history of these patients and were included in the information collecting form. The collected data were analyzed using SPSS 17 software. Data description was performed as mean $\pm$ SD. The Kolmogorov - Smirnov test was used for analyzing the normality of variables. Chi-Square and ANOVA tests were used and P value $<$  0.05 was considered significant.

## Results

Overall, 354 patients with toxic multinodular goiter were evaluated. The average age of these patients was 48 $\pm$ 14 and the mean age for the onset of the disease was 42 $\pm$ 15. Seventy-two persons (20%) of

the patients were men and 382 persons (80%) were women. Among these patients, 326 patients (92%) received radioactive iodine and 28 patients (8%) underwent surgery.

Out of 326 persons under treatment with radioactive iodine, a total of 92 patients (28%) had a relapse of hyperthyroidism after receiving the first dose of radioactive iodine which among them, 58 patients referred for receiving the next dosage of radioactive iodine and after receiving the second and third dosages no case of relapse was seen in these patients. Overall, the total relapsing rate after radioactive iodine therapy in patients with TMNG was 34 cases (10%) which this number included patients who did not refer to receive the next dosage following one dose of radioactive iodine after the relapse. The mean duration of the relapse incidence of hyperthyroidism was  $7.3 \pm 4.4$  months after receiving radioactive iodine. The mean dosage of radioactive iodine received in the group who had a relapse of hyperthyroidism was  $15 \pm 7$  millicurie and in the group without the relapse of hyperthyroidism was  $18 \pm 7$  millicurie which this difference was not statistically significant ( $P$  value=0.097).

The mean weight of the thyroid gland before and after the treatment with radioactive iodine was significantly more in the group who had the relapse of hyperthyroidism after treatment compared to the euthyroid group ( $P$  value < 0.001 and  $P$  value < 0.0001, respectively) (Table 1).

The incidence rate of hyperthyroidism after receiving one dosage of radioactive in patients with TMNG was 156 cases from 326 patients (48%), which this rate was 52% after receiving more than one dosage of radioactive iodine (30 persons from 58 patients). Overall, the incidence rate of hypothyroidism after radioactive iodine therapy in patients with TMNG was 186

patients (57%); the mean time of the hypothyroidism incidence rate was  $5.1 \pm 4.9$  months after receiving radioactive iodine. The mean dosage of radioactive iodine received in patients who got hypothyroidism after treatment was  $20 \pm 5$  millicurie and in euthyroid group was  $15 \pm 4$  millicurie which this difference was statistically considerable ( $P$  value < 0.001) (Table 2).

The thyroid gland size before and after radioactive iodine therapy in patients with post-treatment hypothyroidism was considerably less than the euthyroid group ( $P$  value < 0.001 and  $P$  value < 0.001, respectively).

Of the total 28 patients with TMNG who underwent surgery, only two patients had a relapse of hyperthyroidism. The mean duration for the relapsing incidence of hyperthyroidism was 12, 14, 16 months separately in these patients. On the other hand, half of the patients with TMNG who were under surgical treatment got post-surgical hypothyroidism. The mean duration of the hypothyroidism incidence rate after surgery was  $5.9 \pm 8.0$  in these patients. Of the total 28 patients with TMNG who underwent surgery, 10 patients experience the complications induced by surgery (except hypothyroidism). Among these, two patients had the damage of recurrent laryngeal nerve and eight patients got hypoparathyroidism. Permanent side effects were not reported in the group receiving radioactive iodine except hypothyroidism.

Overall, during  $29 \pm 19$  months of follow-up of the patients under radioactive iodine therapy and during  $18 \pm 12$  months of follow-up of the patients after surgery, 33% of the patients and 29% of the patients were respectively with complications induced by therapy and were in euthyroid state, which this difference was not statistically considerable ( $P$  value=0.363) (Table 3).

**Table1: The comparison of the mean weight of thyroid gland before and after the treatment in patients with and without the relapse of hyperthyroidism in the two therapeutic methods**

TMNG	Group with the relapse of hyperthyroidism	Euthyroid group	P value
Thyroid gland size before treatment (gram)	53±28	46±15	P value<0.001
Thyroid gland size after treatment (gram)	41±17	36±13	P value<0.001
The received dosage of radioactive iodine (millicurie)	15±7	18±7	P=0.097

**Table2: The comparison of the mean weight of thyroid before and after the treatment in patients with and without the relapse of hyperthyroidism after treatment with the two therapeutic methods**

TMNG	Group with hyperthyroidism	Euthyroid group	P value
Thyroid size before treatment (gram)	41±13	46±15	P value<0.001
Thyroid size after treatment (gram)	32±11	36±13	P value<0.001
The received dosage of radioactive iodine (millicurie)	20±5	15±4	P value<0.001

**Table 3: The comparison of the treatment results in two groups of surgery and radioactive iodine**

TMNG	Relapse of hyperthyroidism	Hypothyroidism after treatment	Complications	Euthyroid Cases without complications
Radioactive iodine (326)	34 (10%)	186 (57%)	-	106(33%)
Surgery (28)	2 (7%)	14 (50%)	10 (36%)	8(29%)
P value	P value=0.75	P value=0.26	P value=0.0001)	P value=0.66

### Discussion

The results of this study show that radioactive iodine therapy can remove hyperthyroidism in most patients as the remission rate after receiving one dosage of radioactive iodine and after receiving the next dosages are 72% and approximately 90%, respectively. In an average follow-up period of 29±19 months, these results are closely the same as the results of other studies. In Leary *et al.*'s study, only 5% of the patients with TMNG treated with

radioactive iodine still remained hypothyroidism (4) and in Nygaard *et al.*'s study, this rate was reported eight percentages (5). In our study, the relapsing cases of hyperthyroidism after radioactive iodine was mainly due to no further referral of the patients for receiving the next dosages. Considering that all the 58 patients receiving more than one dosage of radioactive iodine remitted, it seems that if the residual patients had referred for

receiving the next dosages, the relapsing rate of hyperthyroidism would have been less than 10%. It is not easy to predict which patients will have relapses of hyperthyroidism after radioactive iodine therapy. Nevertheless, considering the results, the patients who have bigger thyroid before and after receiving radioactive iodine, more probably will have the relapse of hyperthyroidism after radioactive iodine therapy. Beside the desirable effects of radioactive iodine in removing the hyperthyroidism signs in patients with TMNG, the incidence of hypothyroidism which is in about 57% of the patients receiving it, affect the desirable results of this therapeutic method as only 33% of the patients were in the euthyroid state during follow-up period (29±19 months). The incidence rate of hypothyroidism also depends on the thyroid gland size before and after the radioactive iodine therapy, as those patients who have smaller thyroid before and after treatment, more probably will have hypothyroidism following the use of radioactive iodine. In different studies, the incidence rate of hypothyroidism in one to eight years of follow-up was reported 11-58 % (19). In the present study, the incidence rate of hypothyroidism was 57%, which was among the highest rates reported (The rate in Nygaard *et al.*'s study (5), Leary *et al.*'s study (4), Heidari *et al.*'s study (6) and Davis *et al.*'s study (16) was reported 14%, 32%, 27%, and 10-20%, respectively). This difference may be due to receiving more amount of radioactive iodine in the studied patients; or genetical and continental differences; amount of received iodine, and the duration of follow-up the patients. Surgery is done in cases of big goiters with pressure signs for cosmetic reasons and probability of malignancy, which is better to be performed by an expert surgeon using total or near total thyroidectomy (17). In the present study, the relapse of

hyperthyroidism following the surgery was low (7%). The results of Medeiros *et al.*'s study were consonant with our results (9%) (18). But in Leary *et al.*'s study the relapsing rate after surgery was reported 19 % (4). Hypothyroidism incidence rate followed by surgery was 50% in the present study that shows a considerable raise (15 to 20%) comparing other studies (4, 16, and 18). The incidence rate of the complications of the surgery in the present study was very high comparing other studies (7% paralysis of the recurrent nerve and 29% hypoparathyroidism) which shows considerable raise comparing other studies (the paralysis of the recurrent nerve and hypoparathyroidism were reported 0.6 to 1% and 1 to 4%, respectively) (16, 20, 21). The high rate of these complications in the present study may be due to the lack of efficient skill of the surgeon. The incidence of the mentioned complications make the incidence of euthyroid without side effects after surgery to not have significant difference with the rate of euthyroidism after radioactive iodine therapy (29% versus 33%, respectively, P value>0.050). Nevertheless, if the surgery is done by expert surgeons of thyroid surgery, the rate of the complications will be highly lower (22, 23, 24). Because our patients underwent surgery by different surgeons, the complication rate was more. So if thyroid surgery is needed for any reason in toxic multi nodular goiter, it is better to be done by expert surgeons in order to reduce the complication rate.

The present study was a retrospective study and some of the patients did not enter the study because of no follow-up which this issue can affect the results. In addition, the number of patients who underwent surgery was low. Moreover, patients who underwent surgery mostly had bigger goiters so this issue makes the judgment more difficult. So, it is suggested to perform a prospective

study with more number of patients for follow-up. In Conclusion Although no significant difference was found between surgical treatment and radioactive iodine therapy in patients with TMNG from the viewpoints of the relapsing rate after treatment, the incidence of hypothyroidism, and the rate of euthyroid, considering the very higher rate of permanent complications of surgery in patients with TMNG, radioactive iodine therapy is suggested as the selective therapy.

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