International Surgery Journal
Madathil JP et al. Int Surg J. 2021 Sep;8(9):2707-2710
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20213600

Original Research Article

Role of thyroxine in reducing the size of benign thyroid swellings and pre-treatment thyroid stimulating hormone as a predictor of response to therapy

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Received: 27 June 2021
Accepted: 11 August 2021

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ABSTRACT

Background: Conservative management for benign thyroid swellings which do not require surgery is a matter of controversy. There has been studies and trials on the role TSH suppression in reducing thyroid volume, but low dose thyroxine was never been properly studied. Being such a common disorder, more studies have to be undertaken to have an idea on managing the goitres conservatively.
Methods: Patients with benign thyroid goitres without indications for surgery and who were on 50-100 µg of thyroxine per day was included in the study. Their initial thyroid hormone levels, volume on ultrasonogram, and fine needle aspiration cytology were collected along with biodata. They were reassessed after 6 months and 1 year for change in volume of thyroid.
Results: Majority of patients showed a decreasing trend in volume of thyroid after 1 year of thyroxine therapy, even though the amount of reduction was not statistically significant. Rate of decrease in thyroid volume was significantly higher in patients with higher TSH values.
Conclusions: Thyroxine therapy has got a role in reducing and arresting further growth of benign thyroid swellings which doesn't require surgical management. Pre-treatment TSH can be used a predictor of response to thyroxine therapy.

Keywords: Benign thyroid swellings, Conservative management, Thyroxine therapy, Initial TSH levels

INTRODUCTION

A goitre means an enlarged thyroid. A goitre can either be a simple goitre or a multinodular goitre. they can be either toxic or non-toxic. MNG is the most common endocrine disorder affecting 500 to 600 million people worldwide.[1]

Surgery is the definite management of choice when patient presents with neoplasia, toxic adenoma, pressure symptoms or cosmetic problems. Benign goitres without above mentioned features can be managed conservatively. Efficacy of thyroxine therapy to reduce the nodule size has been a matter of discussion for many years.[2] Although the pathogenesis of thyroid nodules and sporadic non-toxic multinodular goitres is poorly understood, TSH levels have a role in its development, and therefore, suppression of TSH secretion might be expected to result in a decrease in nodule or goitre size or at least prevent further enlargement.[3] The effectiveness of orally administered thyroid substance in the treatment of simple goitre was noted 70 years ago. But its justification awaited the modern discovery of the relation of the thyroid to thyrotropic hormone of the hypophysis.[4] Because thyroid hormone is presumed to reduce goitre size by reducing TSH secretion, suppressive therapy would be expected to be ineffective in patients in whom serum TSH concentrations were already subnormal due to autonomous thyroid hormone production.

Studies are very few on the effectiveness of thyroxine therapy on reducing size of thyroid nodules. this study aims to find out whether thyroxine therapy will reduce the size of nodules and the level of pre-treatment TSH in those who adequately respond to the thyroxine therapy.

METHODS

The study was conducted in 67 patients attending general surgery op at government medical college Thrissur, Kerala, India with benign thyroid swelling. It was a single cohort study conducted during 2018-2019. Patients were followed up for 1 year.

Patients with benign goitres and who were on low dose thyroxine were included in the study. Those with thyroid malignancy, other patients in whom thyroidectomy is indicated as in pressure effects and cosmetic concerns, hyperthyroid individuals and those with reversal of thyroid status after starting on thyroxine were excluded from the study.

Details were explained to the subjects and informed consent obtained. Clinical findings, T3, T4, TSH levels, USG findings and FNAC findings were recorded initially. volume of thyroid was calculated using USG.

They were called after 6 months for review, clinical examination, laboratory testing and imaging as a part of follow up. Those who become hyperthyroid were excluded from the study. All of the clinical and laboratory data were collected and recorded prospectively at the point of routine follow up after 1 year also.

Patients with >50% reduction in volume of thyroid after 1 year of thyroxine therapy were defined as responders, 20-50% reduction as partial responders and with <20% as non-responders.[5] TSH more than 2 was taken as high normal and that below 2 was low normal.

Sample size was calculated by using values of a similar study.

Sample size calculation:

Alpha error at 95% confidence interval (ZX) = 1.96

$$N = \frac{(ZX)(ZX) \times p \times q}{d \times d}$$

Sample size = 67, based on study by Lima (Brazil, 1997).[6]

Data was coded and entered in MS excel. Quantitative variables were expressed in terms of mean and standard deviation. Qualitative variables were expressed as proportion.

Association between quantitative variables were analysed using correlation, regression, multiple regression.

Association between qualitative variables were analysed using Chi square or Fischer exact test. Data was presented as mean±SD. P value<0.05 was considered statistically significant. Analysis was done using statistical software SPSS.

RESULTS

In this study total 67 subjects were followed up. Ranging from 17 to 72 years. Mean age was 43 years with a standard deviation of 11.75.

Sex distribution

Study consisted of 85% females and 15% males.

Response to thyroxine therapy

Clinically detectable change in volume was seen in only 7 out of 67 cases, accounting to 10.44%.

Response based on initial TSH levels

On comparing the response to thyroxine therapy based on TSH levels, mean decrease in size for patients with high normal TSH was 14.23% and for low normal it was 3.36%. it was analysed for significance with t test, and found to be statistically significant (p value<0.05).

Table 1: Case distribution.

Diagnosis	Number
Nodular colloid goiter	45
Lymphocytic thyroiditis	20
Hashimoto's thyroiditis	2

Table 2: TSH levels.

TSH level	Number
More than 2	44
Less than 2	23

Table 3: Response to thyroxine therapy.

Percentage of volume reduction after 1 year (%)	Percentage of patients (%)
>20	13.4
10-20	32.8
<10	37.3
No decrease	13.4
Size increased	2.9

Table 4: Response to thyroxine, categorised.

Response to therapy	N	Percentage (%)
Partial responders	9	13.43283582
Non-responders	56	83.58208955
Negative responders	2	2.985074627

Table 5: Response based on initial TSH levels.

Variables	TSH>2	TSH>2 (%)	TSH<2	TSH<2 (%)
Partial responders	9	100	0	0
Non-responders	34	60.7	22	39.3
Negative responders	1	50	1	50

Table 6: Analysis of response to thyroxine based on initial TSH.

Variables	TSH	N	Mean	SD	Std. error mean
Percentage of decrease in volume (%)	1	44	14.232355	9.7664551	1.4723485
	2	23	3.363966	3.7967245	0.7916718

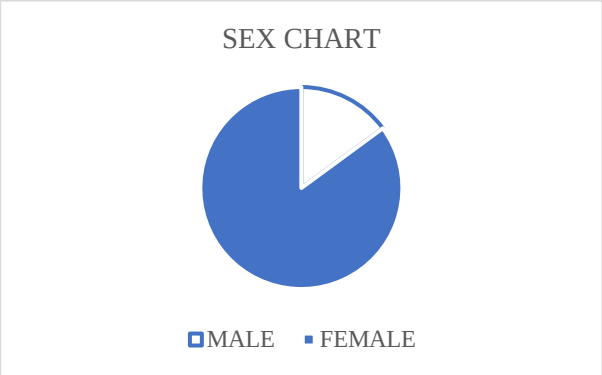

Figure 1: Sex distribution of thyroid swelling.

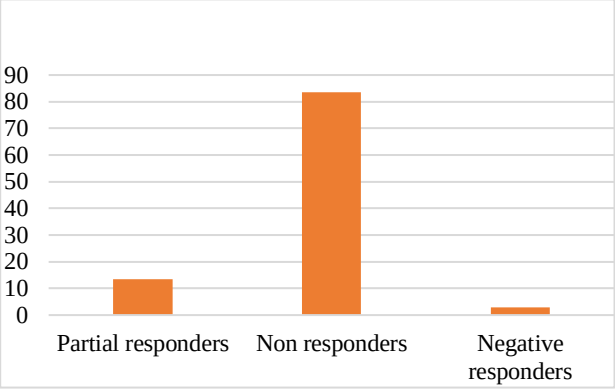

Figure 2: Response to thyroxine, categorised.

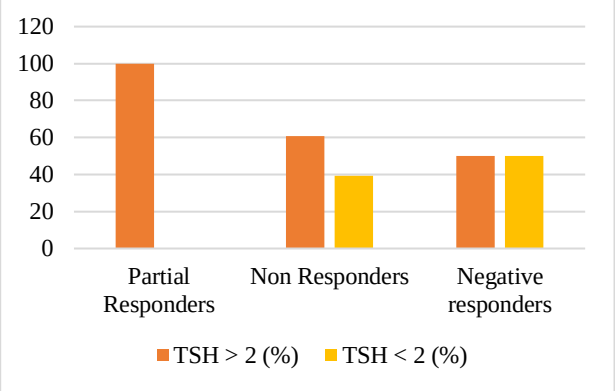

Figure 3: Response based on initial TSH levels.

DISCUSSION

Total number of patients included in the study was 67. Age of study population ranged from 17 to 72. Mean age was 43 years. 85% were females and rest 15% comprised of males. Commonest diagnosis was nodular colloid goitre accounting to 67%, followed by lymphocytic thyroiditis and Hashimoto's thyroiditis.

More than 65% 0f them had a high normal TSH level prior to starting thyroxine therapy. 13.4% of subjects had more than 20% reduction in thyroid volume after 1 year of low dose thyroxine therapy. 83% had shown a decreasing trend of volume of thyroid swelling, whereas there was no increase or decrease in volume for 13.4% of the population. 2.9% showed an increase in size of the thyroid swelling.

Since earlier studies have defined those with 50% volume reduction as responders, 20-50 as partial responders and less than 20 as non-responders, there was no responders in this study. 13.4% had partially responded, while 83.5% are non-responders and 2.9% are negative responders.

Pre-treatment TSH level was high normal (more than 2) for 65.66% of the study population. Mean reduction of volume after 1 year of thyroxine therapy for patients with high normal initial TSH was 14.23% with a standard deviation of 10.97. Those with low normal pre-treatment TSH had a mean volume reduction 3.36% with a standard deviation of 3.79.

Analysis with t test showed that this difference was statistically significant, which points out that there is a significant volume reduction for patients with high normal initial TSH than with low normal and thus pre-treatment TSH is a useful tool to predict the response to thyroxine therapy.

CONCLUSION

This study has shown that treatment with low dose thyroxine for benign thyroid swellings without indications for surgery shows a decreasing trend of the thyroid volume. 83% had shown a decreasing trend even though it was not clinically relevant. Complete regression of thyroid

nodule seems anecdotal, but it may be recommended for reducing the thyroid volume and for preventing further growth. Pre-treatment TSH can be used as a predictor of response to therapy, patients with a high normal pre-treatment TSH reduces the size of thyroid swelling, and the reduction is statistically significant when compared to those with low normal TSH.

Further studies are required to get an answer to many questions as the optimum dose, duration of treatment required for getting clinically relevant size reduction and other factors influencing the growth of thyroid so that we can predict the response of benign goitres to conservative management with thyroxine and plan accordingly.

ACKNOWLEDGEMENTS

Authors would like to thank the department of general surgery, Government medical college, Thrissur for the studentship that allowed us to conduct this thesis.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Madathil JP, Rajesh TR, Babu PJ. Role of thyroxine in reducing the size of benign thyroid swellings and pre-treatment thyroid stimulating hormone as a predictor of response to therapy. Int Surg J 2021;8:2707-10.