Original Article

Study to evaluate the response of ultrasound guided percutaneous ethanol injection in ablation of benign thyroid nodule

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ABSTRACT

Introduction: Benign thyroid nodules not only cause cosmetic disfigurement but also cause pressure effects to the patient. Though surgical excision can be done in the treatment of symptomatic benign thyroid nodules with risk of complications but with the advent of newer minimally invasive modalities like ultrasound guided percutaneous ethanol ablation, surgery can be easily avoided in many patients. Ethanol ablation is an easy and effective procedure which causes atrophy of thyroid nodule. **Methods**: The study was done on seventy four patients with benign solitary thyroid nodule in the department of Radiology in Nil Ratan Sircar medical College & Hospital, Kolkata.

Observations: In the present study, most patients presented with complex solitary nodule (59.46%), followed by solid (24.32%). and then cystic (16.22%).

Results: The remission rate was 100% for cystic nodules after first session, for complex nodules- 65% after first session and another 16.67% after second session and no remission was observed in case of solid nodules even after 2 sessions of percutaneous ethanol injection.

Conclusions: Ultrasound guided percutaneous ethanol injection is a safe, inexpensive and effective method that can be used in the treatment of patients with cystic nodule and complex nodules with predominantly cystic component. It can be used as an alternate to surgery as it can easily be done as an outpatient procedure.

Key words: thyroid nodule, percutaneous ethanol injection, ultrasound guided ablation

Introduction:

The thyroid gland, brownish-red and highly vascular, is placed anteriorly in the lower neck, level with the fifth cervical to the first thoracic vertebrae. It usually weighs 25 g, but this varies. Estimation of the size of the thyroid gland is clinically important in the evaluation and management of thyroid disorders and can be achieved non-invasively by means of diagnostic ultrasound.(1)

Thyroid nodules refer to lesions within the thyroid gland that is either palpable clinically or identified radiologically as a distinct lesion within the thyroid gland. Thyroid nodules are common and seen in about 8.5% population (2). The incidence of thyroid nodules in India is 12.2% according to a recent study (3). If high-resolution ultrasound is used in the evaluation of thyroid, then up to 68% of randomly selected individuals may be found to have thyroid nodules(4). Exposure to ionizing radiation that may occur during childhood, or as a result of occupational exposure, will cause development of thyroid nodules at the rate of 2% per year, reaching a

peak incidence in 15 to 25 years (5). Nodules are mostly benign in nature. The incidence of thyroid cancer is 8.7 per 100000 people per year (6)

Thyroid nodules are clinically significant for several reasons. They may cause thyroid dysfunction, pain and pressure symptoms. However, the most important reason to evaluate them is to exclude malignancy. Initial evaluation of these patients must include a detailed history taking and physical examination.

Although the incidence of malignancy is less it is important to differentiate between benign and malignant nodules. Ultrasound is an inexpensive and easily available modality which allows such differentiation. It identifies the number of nodules, their sizes, shape echogenicity, vascularity and presence of calcification within the nodules. Use of ultrasound does not even expose the patient to harmful radiations and can thus, be used in pregnancy, lactation and in children.

Benign thyroid nodules may cause cosmetic disfigurement to the patient. Large nodules may also cause pressure effects. Surgery may be done in such cases but in the present day surgery can be quite disabling. Surgical excision has been used in the treatment of symptomatic benign thyroid nodules. However, it carries a 2-10% risk of complication, and may also result in hypothyroidism (7).

Percutaneous ultrasound guided ethanol injection of benign thyroid nodule is an easy and effective procedure that can safely be used in such patients. Direct injection of ethanol to cause atrophy of a mass within a solid organ is termed as ethanol ablation, ethanol injection, or ethanol sclerotherapy.

The first interventional attempt that was made to treat thyroid nodule was a simple aspiration of a thyroid cyst in the year 1966 by Crile (8). In 1974, Miller et al, suggested that only a simple aspiration was associated with a high rate of recurrence of about 58%, which was the limitation of this type of procedure (9). Later, various sclerosing agents were used in the treatment of recurrent thyroid cysts (10). In 1985, Rozman et al. first used ethanol to treat thyroid cysts (11). In 1990, Livraghi et al. used ultrasound in EA of functional thyroid nodules (12).

There are many sclerosing agents like sodium tetradocyl sulphate, hydroxypolyethoxydodecan, tetracycline and ethanol. But ethanol is the most commonly used sclerosing agent that gives the best results. (13)

Mechanism of action of percutaneous ethanol injection (PEI) is coagulative necrosis with local partial or complete thrombosis of small vessels. In contrast to surgery PEI is less time consuming, inexpensive, causes less discomfort to patients and can be performed on outpatient basis. They can easily resume their duties post ablation. It does not cause any hindrance to their day to day activities.

AIMS & OBJECTIVE:

In my study I have used absolute ethanol (99.99%) to cause reduction in size of benign thyroid nodules- cystic, solid and complex nodules.

The objective of this study to find out remission rate after PEI with absolute ethanol in patients with benign thyroid nodules.

MATERIALS AND METHODS:

The study was undertaken on 74 patients who presented with solitary thyroid nodule to the department of Radiology during January 2018 to June 2019 in Nil Ratan Sircar medical College & Hospital, Kolkata.

Patients who had a malignant nodule, pregnancy, multinodular lesions of thyroid, patients with other malignancies were excluded from this study. With the help of department of pathology, FNAC is conducted on these patients. Study tools used to do this study were-

- Thyroid function test
- Ultrasonography machine: Philips HD7/ Alpinion E cube 8 machine with 3-12 MHz linear probe mainly and 3.5-5 MHz curvilinear probe
- FNAC report from dept. of Pathology
- A proforma was designed for recording the details of the patient including history, ultrasound finding, FNAC report, response to treatment with absolute ethanol at 2, 5 and 7 months. If the regression in size was inadequate (<50%) a second session of ablation was done with absolute ethanol. The response at 2, 5 and 7 months was mentioned. Consent forms were also signed by patient.

The volume of the entire nodule was calculated and under aseptic precautions the cystic part was aspirated by using a 10 cc syringe under ultrasound guidance. Another 10 cc syringe was loaded with half the volume of nodule with absolute ethanol. This was injected within the nodule under ultrasound guidance. The ethanol is not re aspirated and is left within the nodule.

RESULTS:

The study included 74 patients who presented with solitary thyroid nodules referred from the department of Endocrinology to the Department of Radiology, Nil Ratan Sircar Medical College and Hospital.

	Number	Percentage
Cystic	12	16.22
Solid	18	24.32
Complex	44	59.46
Total	74	100

Table 1: Types of solitary thyroid nodule

Most patients had a complex solitary nodule – both solid and cystic components (59.46%), followed by solid (24.32%). and then cystic (16.22%).

Table 2: FNAC Findings

FNAC	Number	Percentage
Colloid nodule	54	73
Adenomatoid nodule	20	27
Total	74	100

Among the 74 patients who were initially evaluated, 73% had colloid nodule while 27% had adenomatoid nodule. Both are types of benign follicular nodule.

Table 3: Remission rate after percutaneous ethanol injection

Types of nodule	1 st Ablation	2 nd Ablation
Cystic	100 %	NA %
Complex	65 %	16.67 %
Solid	0 %	0 %

(Remission criteria - more than 50 percent reduction in size)

		1 st session of	Reduction in	2 nd session of	Reduction in
		PEI	size	PEI	size
	Mean volume SD	Mean volume at	Mean %	Mean volume at	Mean %
		$7^{\text{th}} \text{ month}(\text{cm}^3) \pm$	reduction \pm SD	$7^{\text{th}} \text{ month}(\text{cm}^3) \pm$	reduction \pm SD
		SD		SD	
Cystic	15.42±13.66	3.98±4.73	74.34±12.40	0±0	NA
Complex	9.53±5.72	5.03±4.48	49.19±25.66	2.32±4.83	34.92±25.05
Solid	10.43±4.11	9.14±3.7	12.35±6.48	8.18±3.77	19.30±10.14

Table 4: Percentage reduction in size of nodules in both sessions

All patients with Cystic lesions had a favourable response of more than 50 % reduction in the first session after 7 months. Solid and complex nodules were subjected to second session of ethanol ablation. Out of 74 patients 6 were lost to follow up in the first session. Data was calculated for the rest of 68 patients. 10 patients with cystic nodules had an average initial size of 15.42 cm^3 (± 13.66), 18 patients with solid nodules had an initial average size of 10.43 cm³ (± 4.11) and 40 patients with complex nodules had an initial average size of 9.53 cm³ (± 5.72). The average size of the nodules after first injection at 7 months was: 3.98 cm^3 (± 4.73) for cystic nodules, 9.14 cm³ (± 3.7) for solid nodules and 5.03 cm^3 (± 4.48) for complex lesions.

The average percentage reduction was $(74.34\pm12.40)\%$, $(49.19\pm25.66)\%$ and $(12.35\pm6.48)\%$ for patients with cystic, complex and solid nodules respectively. Complex nodules had a mixed response with 26 of them showing more than 50% reduction in size from baseline and 12 of them had a response of less than 50% from baseline. 2 patient with complex nodule had a reduction of approximately 49% and they refused the second injection .Among the 18 patients with solid nodules 2 was lost to follow up after second session of ethanol ablation. So 16 patients with solid nodules and 12 patients with complex nodules were subjected to a second session of ethanol ablation.

The final average size after second session was (2.32 ± 4.83) cm³ for complex nodules while for solid nodules it was (8.18 ± 3.77) cm³. The average percentage reduction in size for complex and solid nodules after second session of ethanol ablation was (34.92 ± 25.05) %, (19.30 ± 10.14) % respectively

Over all the 10 patients with cystic nodules had a response of more than 50 percent after the first session. 26 out of 40 patients with complex nodules had more than 50 percent reduction in size after first session and none of the patients with solid nodules had a reduction more than 50 percent after 1st session. Of the 14 patients with complex nodules 2 had a response of 49% and did not want another injection and among patients with solid nodules 2 was lost to follow up .After second session of injection at 7months only 2 out of 12 patients with complex nodules had a reduction in size more than 50%. Rest of the 10 patients had a reduction less than 50%. 16 patients with solid nodules had a reduction of less than 50 percent even after second injection.

The remission rate was 100% for cystic nodules, 65% for complex nodules and none for solid nodules after first session of PEI. It was another 16.67% for complex nodules after second session of PEI and no remission was observed in case of solid nodules even after 2 sessions of PEI, where considering the remission criteria being more than 50 percent volume reduction in size. The complications that were encountered in the study was headache, transient pain at the injection site and nausea and vomiting.

DISCUSSION:

The prevalence of clinically palpable goiter is higher in region of eastern India ranging from 9-33% from different studies conducted in the past (14,15) as compared to 9-15% in rest of the country (16,17). A solitary nodule may not only be cosmetically distressing to a patient but may also cause compressive symptoms. Less commonly, an autonomously hyper-functioning nodule may cause hyperthyroidism. Surgery can be done in such cases but with the advent of newer minimally invasive modalities like radiofrequency and percutaneous ethanol ablation, surgery can be easily avoided in many patients.

A study was perfomed by Jin Hyoung Kim, et al to find out the efficacy of absolute ethanol in treatment of thyroid cysts and solid nodules .20 patients with simple or complex cysts and 22 patients with solid thyroid nodules were selected which were benign as proved by FNAC. Absolute (99.9%) ethanol was used in this study. Follow up ultrasound was done 1 to 6 months after the procedure. The study showed that the mean volume reduction rate for cysts (65%) was greater than that for solid nodules (38.3%) (18). In my study I have got similar results that cysts show a greater reduction in size than solids.

A study similar to ours was performed by Nupur Basu, et al. Sixty patients who had both simple cystic (42 cases) and complex cystic (18 cases) nodules with mean follow-up of 12.3 ± 2.88 months were analyzed in this study. Response rate of PEI was 78.33% overall. For simple cystic it was 92.86% and for complex cystic it was 44.44%.(19) In our study we have got similar results for simple cystic and complex nodules. The reduction in size for simple cystic nodules was >50% in all cases whereas the average reduction in size for complex nodules was (49.19 ± 25.66) % after the first session of ethanol ablation and it was (34.92 ± 25.05) %.

In a study conducted similar to ours by Yotsapon Thewjitcharoen on efficacy of percutaneous ethanol injection of benign thyroid nodules a total of 167 patients were selected. Overall, 80 % of treated nodules achieved more than 50 % volume reduction. The mean volume reduction in this group was 79.61 %. In the subgroup of solid thyroid nodule (65 nodules), the mean volume reduction was 58.73 ± 35.33 %. In the subgroup of cystic thyroid (8 nodules), the mean volume reduction was (92.38 ± 6.57) %. In the subgroup of mixed solid-cystic nodule (44 nodules), the mean volume reduction was 67.35 ± 35.18 %. In the subgroup of multinodular goiters (50 nodules), the mean volume reduction was (72.27 ± 23.76) %. However, in our study there was more than 50 percent reduction of cystic and complex nodules with predominantly cystic component. Solid nodules showed a reduction of less than 50 percent.(20)

A study was conducted by Seong Jin Lee, et al on the efficacy of PEI on solid nodule and complex cysts. In patients with solid nodules, 40 underwent PEI once, 81 twice, 46 patients underwent PEI thrice, 20 underwent PEI 4 times, 7 underwent PEI five times and 4 patients six times. Initial volume was 15.7 ± 12.2 ml and was significantly reduced to post PEI volume 2.4 ± 1.7 ml and the final volume was 1.8 ± 1.1 ml. In patients with complex cysts, 67 patients underwent PEI once, 202 patients twice, 108 patients undwerwent thrice, 36 patients 4 times, 14 patients 5 times, 3 patients 6 times and 2 patients seven times. Baseline volume which was 15.6 ± 12.6 ml was reduced post PEI 2.8 ± 1.9 ml. The final volume being 2.5 ± 1.5 ml. However, in my study solid nodules did not show a significant reduction in volume, the reduction was less than 50 % after both the sessions of PEI (21).

PEI is a safe and effective method that can be used in the treatment of patients with cystic and complex nodules with predominantly cystic component. It can be used as an alternate to surgery as it can easily be done as an outpatient procedure. Admission either before or after the procedure is not required. Patients can easily return to their day to day activities after the procedure. No pre anaesthetic evaluation is required here, thus saving the cost

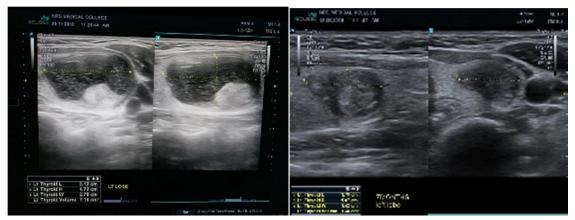
and time of treatment. PEI can effectively reduce the bed occupancy rates in hospital. PEI is a simple and effective procedure at the hands of experienced radiologists.

Not many studies have been conducted in our country on the efficacy and safety of PEI. Through this study I have tried to establish the usefulness of this simple yet effective procedure which can be used as an alternate to surgery.

CONCLUSION:

Percutaneous ethanol injection is a relatively safe and inexpensive procedure that can be given to patients as it is highly efficacious in cystic nodules and complex nodules with predominantly cystic component. The complications are mostly minor and transient and do not lead to any morbidity to the patient. In a country with a huge patient load percutaneous ethanol injection must be given to patients fulfilling the criteria as it is a simple and effective procedure which would reduce the cost and time of treatment.

Case 1: Complex nodule- pre and post ablation



a: Pre ablation

Ultrasound image showing the initial volume of a complex nodule which was 7.16cm3

b: Post ablation

Ultrasound image showing the final volume of the thyroid nodule after 7months of 2nd session following ethanol ablation was

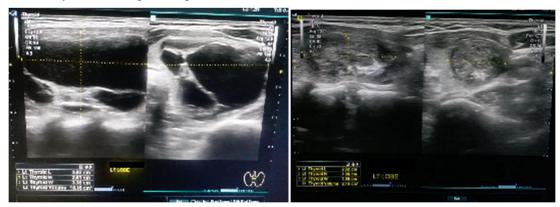


a: Pre ablation Ultrasound image showing the initial volume of the solid thyroid nodule was 12.82cm3

b: Post ablation

Ultrasound image showing the final volume of nodule after 7months of second session of ethanol ablation was 9.97cm3

Case 3: Cystic nodule- pre and post ablation



a: Pre ablation Ultrasound image shows a cystic nodule with an initial volume (pre ablation) of 16.15cm3 b: Post ablation Ultrasound image showing the final volume after 1st session of ethanol ablation was 2.15cm3

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