Percutaneous Ethanol Injection for Benign Cystic and Mixed Thyroid Nodules

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Abstract and Introduction

Abstract

Objective: We aimed to determine the effect of percutaneous ethanol injection (PEI) on volume of cystic and mixed thyroid nodules, thyroid function tests (TFTs), antibody titers, and cytologic changes for 1 year.

Methods: Fifty-five nodules from 53 patients with cystic and mixed properties treated with PEI were included. Nodule volumes, TFTs, and thyroid autoantibodies were analyzed at baseline, 6 months, and 12 months. Fine-needle aspiration biopsy (FNAB) was performed to PEI-treated nodules in the 12th month. Thyroid nodules were classified into three groups by structural properties (purely cystic, predominantly cystic, predominantly solid).

Results: PEI caused a volume reduction of 80.7% at 6 months and 82.1% at 12 months, without any serious complications. PEI was repeated 1.4 ± 0.4 times with a mean total ethanol amount of 3.6 ± 3.1 mL. Volume reduction in the purely cystic nodules in the 6th and 12th months after PEI was greater than the volume reductions in predominantly cystic and predominantly solid nodules. We found that smaller nodules had greater volume reductions after PEI in the 12th month. During the study, patients remained euthyroid. Antithyroglobulin levels were decreased at 12 months. None of the FNAB results were compatible with a malignant or suspicious for malignancy cytology at the 12th month.

Conclusion: PEI is an effective means of treatment for benign cystic and mixed thyroid nodules, without any serious side effects. We can also assume that PEI is not a trigger for autoimmunity and malignancy development over the short term.

Introduction

Evaluation by ultrasonography (US) reveals that 15 to 25% of thyroid nodules are cystic or predominantly cystic.[1] Simple aspiration is the treatment of choice for diagnostic and therapeutic aims in symptomatic patients.[2] However, simple aspiration is usually not successful in thyroid cysts, with recurrence rates between 58 and 80%, depending on the size, volume, and number of previous aspirations.[3] Although surgical treatment is curative, especially in large-sized nodules, it has disadvantages, including general anesthesia, postoperative scar formation, increased cost due to thyroid surgery, risk of temporary or permanent complications, and iatrogenic hypothyroidism.[4] Therefore, attempts have been made during the past 2 decades to develop minimally invasive treatment methods.[2] Percutaneous ethanol injection (PEI), radiofrequency ablation, and polidocanol injection therapies are among these treatment methods.[5,6]

PEI is an increasingly common therapeutic alternative for benign thyroid nodules, with positive results confirmed by several groups within the last decade.[7–11] Intranodular injection of ethanol leads to a complex and irreversible local injury associated with hemorrhagic infarction, thrombus formation, coagulative necrosis, and fibrosis, sparing areas outside the nodule.[12] Therapeutic success has been defined as a reduction in cyst volume of more than 50% or complete disappearance of the fluid component and no recurrence of the cyst.[13,14] PEI is a safe and effective outpatient therapy for thyroid cysts and complex nodules with a large fluid component. Currently, PEI is the recommended first-line treatment for predominantly cystic nodules because it is easier to perform and less expensive than other minimally invasive treatments.[15] However, there are some concerns about side effects, mostly linked to seepage of ethanol along the needle tract and effects of ethanol causing tumorigenesis in the long term.[2] Moreover, data are scarce about the effect of PEI on thyroid function in euthyroid patients and on thyroid autoantibodies.

In the present study, we primarily aimed to analyze the effects of PEI on volume of cystic and mixed thyroid nodules, with regard to minimizing ethanol leakage and symptoms. We also investigated the changes in thyroid function tests (TFTs), thyroid autoantibodies, and cytology after PEI.

Methods

In the current study, we enrolled 53 patients with cystic/mixed thyroid nodules who were admitted to a tertiary medical center between January 2014 and January 2016. Patients were complaining about either cosmetic or pressure symptoms. In total, 55 nodules in 53 patients were treated with PEI. For 2 patients who had PEI applied to two different nodules, the procedure was performed at different sessions and time periods. Three of the patients had previous subtotal thyroidectomy, and PEI was performed for recurrent nodules in the residual thyroid tissue. None of the remaining patients had any thyroid surgery or radioactive iodine therapy. All patients were euthyroid, except for 1 patient who had subclinical hyperthyroidism on admission. Thyroid sintigraphy of the patient with subclinical hyperthyroidism was not compatible with a toxic nodule or diffuse radioactive ioidine uptake. One of the patients was euthyroid on levothyroxine. The other patients were not on any drug therapy that would effect thyroid functions.

All of the patients underwent a detailed thyroid US exam before the procedure. Thyroid nodules larger than 1 cm in diameter, and thyroid nodules having suspicious ultrasonographic features such as microcalcifications, hyphoechogenicity, irregular margins, or tall

shape were subjected to fine-needle aspiration biopsy (FNAB) in accordance with the American Thyroid Association guidelines.[16] Whenever FNAB revealed cancer, suspicious for cancer, or undetermined sigificance result, the patient was not included. Thyroid nodules with a cystic component of <10% were also excluded. Other exclusion criteria were pregnancy, being under 18 years old, use of any medication that would affect thyroid function, and history of neck radiation.

As mentioned above, we included patients with thyroid nodules in cases in which the cystic component was >10%. Thyroid nodules were divided into three groups according to the cystic component: cystic component ≤50%, cystic component between 50 and 90%, and cystic component ≥90% were categorized as predominantly solid, predominantly cystic, and purely cystic, respectively. Volume of the thyroid nodules was calculated using the ellipsoid formula: (length × width × depth × 0.52), as previously reported.[17]

PEI

The procedure was performed by an endocrinologist (A.O.) having 5 years of experience in PEI using a 'free-hand technique.' In the freehand technique, the operator performs the procedure without a guiding device mounted on the US probe, allowing the probe and the operator the possibility to move freely. The neck of the patient was in hyperextension while in the supine position. During PEI, the physician stands on the left side of the patient, holds the US probe with the left hand, and performs the procedure with the right hand. PEI was performed under continuous, real-time US visualization with use of a 7.5-MHz linear transducer (Toshiba Aplio 300, Otowara, Japan). The volume of the thyroid nodule was calculated. After cleaning the skin with 50% alcohol, the thyroid cyst was aspirated with a 10-mL, 21-gauge injector. The amount of ethanol injected was calculated as not exceeding 20% of the aspirated cyst fluid or 20% of the nodule volume (we selected the lowest volume between these) in every session. No sedatives or local anesthesia were applied before the procedure. The nodule was injected with 96% sterile ethanol with a 27-gauge dental needle moving upward-downward and side to side. During the movements of the needle, ethanol was slowly injected with small pulses. The hyperechoic flushing of the ethanol injection in real-time observation by thyroid US was remarkable during the procedure, and the tip of the needle was continously visualized. In case the aspiration fluid of the cyst was dense, we irrigated the cystic space with 96% alcohol, and after irrigation, the planned amount of alcohol was injected. A 27-gauge dental needle was preferred due to flexibility of the needle, easier intracystic movements, less leakage of ethanol from the needle tract, and therefore, less pain caused by ethanol leakage. After completion of the procedure, the needle was withdrawn when the patient was in inspirium, causing a negative pressure to prevent ethanol leakage. Pressue was then applied for a few minutes over the puncture site. The patient was observed for 30 minutes after the procedure before discharge.

When it was planned that more than one nodule was to be treated by PEI, the dominant nodule was treated first. After completion of therapy of the dominant nodule, secondary nodules were treated in a separate session.

The power of the study was calculated to be 99.8% given a type I error of 0.05 based on the sample size of 55 nodules. A reduction in nodule volume of >50% was regarded as therapeutic success.

Follow-up

The patients were evaluated 1, 3, 6, and 12 months after the procedure. The data from the 6- and 12-month follow-ups were included in the analysis. Thyroid sonography of the patients was performed by the same operator (A.O.) during follow-up. Complaints, complications related to PEI, and changes in thyroid sonography, especially changes in nodule size, were determined. Volume reduction (%) was calculated according to the formula ([initial volume (mL) – final volume (mL)]/initial volume [mL] × 100). By calculating volume reduction between initial and final volume, we defined response to PEI in three categories, as complete response (≥90%), partial response (<90 to ≥50%), and no response (<50%).

PEI was repeated in 1- to 6-month periods according to the individual response to treatment. TFTs and anti-thyroperoxidase (anti-TPO) and anti-thyroglobulin (anti-TG) antibody measurements were conducted at 6 and 12 months. At the 12th month, FNAB of the detectable nodules >1 cm was repeated in order to evaluate any side effects.

Laboratory Analysis

Blood samples were collected for the analysis of thyroid-stimulating hormone (TSH), free triiodothyronine (fT3), free thyroxine (fT4), and anti-TG and anti-TPO antibodies. TSH was measured by a chemiluminescence immunoanalysis method (third-generation hypersensitive hTSH test; Beckman Coulter Inc, Fullerton, CA). The intra- and interassay coefficients of variation (CVs) were <10%. The reference interval for TSH was 0.34 to 5.6 μIU/mL. fT4 and fT3 were measured by a chemiluminescence immunoanalysis method (Beckman Coulter Inc); for both, the intra- and interassay CVs were <10%. Reference values for fT4 and fT3 were 7.7 to 16 pmol/L and 3.1 to 5.8 pmol/L, respectively. Anti-TPO and anti-TG antibodies were measured by a chemiluminescence immunoanalysis method (Beckman Coulter Inc). For both antibody assays, the intra- and interassay CVs were <10%. Normal ranges for anti-TG and anti-TPO antibodies were 0 to 4 IU/mL and 0 to 9 IU/mL, respectively.

Statistical Analysis

The study protocol was approved by the local ethics committee, and the study was conducted in accordance with the principles of the Declaration of Helsinki. A written informed consent was obtained from each patient.

Statistical analyses were carried out using SPSS, version 17.0 (SPSS Inc, Chicago, IL). Normality of distribution was evaluated by Shapiro-Wilks test. Descriptive analyses are presented using mean and standard deviation and/or median (interquartile range) where appropriate. Comparison of variables between two groups was performed using Mann-Whitney *U* test and/or Student *t* test according to normality of distribution. The Wilcoxon test or paired *t* test was used to compare changes in variables between baseline and 6/12 months. Comparison of variables between more than two groups was performed using the Kruskall-Wallis test. The Mann-Whitney *U* test was performed to test the significance of pairwise differences using Bonferroni correction to adjust for multiple comparisons. $P<.05$ was accepted as statistically significant.

Results

A total of 53 patients (40 women, 13 men) with a mean age of 44.6 ± 13.9 years were included to the study. Fifty-five PEI-treated nodules of these patients were evaluated in the analysis. All nodules were evaluated at the 6-month visit, but 48 nodules were evaluated at the 12-month visit. One of the patients preferred to have total thyroidectomy during the study, which revealed a multinodular goiter. Data for 6 patients were not available due to loss during follow-up. Demographic, clinical, and sonographic features of the patients are presented in . All patients were euthyroid except one, whose TSH level was 0.03 μIU/mL, accompanied by normal fT3 and fT4 levels. This patient's TFTs normalized after the first PEI. Of the nodules treated by PEI, 21.8% were purely cystic (n = 12), 54.6% were predominantly cystic (n = 30), and 23.6% were predominantly solid (n = 13). PEI was performed once for 35 nodules, 2 times for 17 nodules, and 3 times for 3 nodules. Nodule volumes were in the range of 1.7 to 68.1 cm^3. Mean total amount of injected ethanol was 3.6 ± 3.1 mL ().

Table 1. Clinical Characteristics of the Study Population

Gender (male/female) (n = 53)	13/40
Age (years) (n = 53)	44.6 ± 13.9
Mean basal nodule volume (cm^3) (n = 55)	13.9 ± 12.9
Mean aspirated cyst fluid volume (mL) (n = 55)	11.6 ± 10.7
Mean total ethanol (mL) (n = 55)	3.6 ± 3.1
Nodule characteristics	
Purely cystic (n = 12) (%)	21.8
Predominantly cystic (n = 30) (%)	54.6
Predominantly solid (n = 13) (%)	23.6

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We observed a statistically significant 80.7% mean nodule volume reduction at 6 months and 82.1% at 12 months when compared to initial mean nodule volume (*P*<.001 for both). Mean volumes of the nodules are shown in Figure 1. At 12 months, we observed a complete response in 21 nodules, a partial response in 24 nodules, and no response 3 nodules. As stated above, data for 7 nodules were not avaliable at 12 months. We demonstrated ultrasound views of a purely cystic nodule before and 1 year after PEI that was completely ablated (Figure 2).

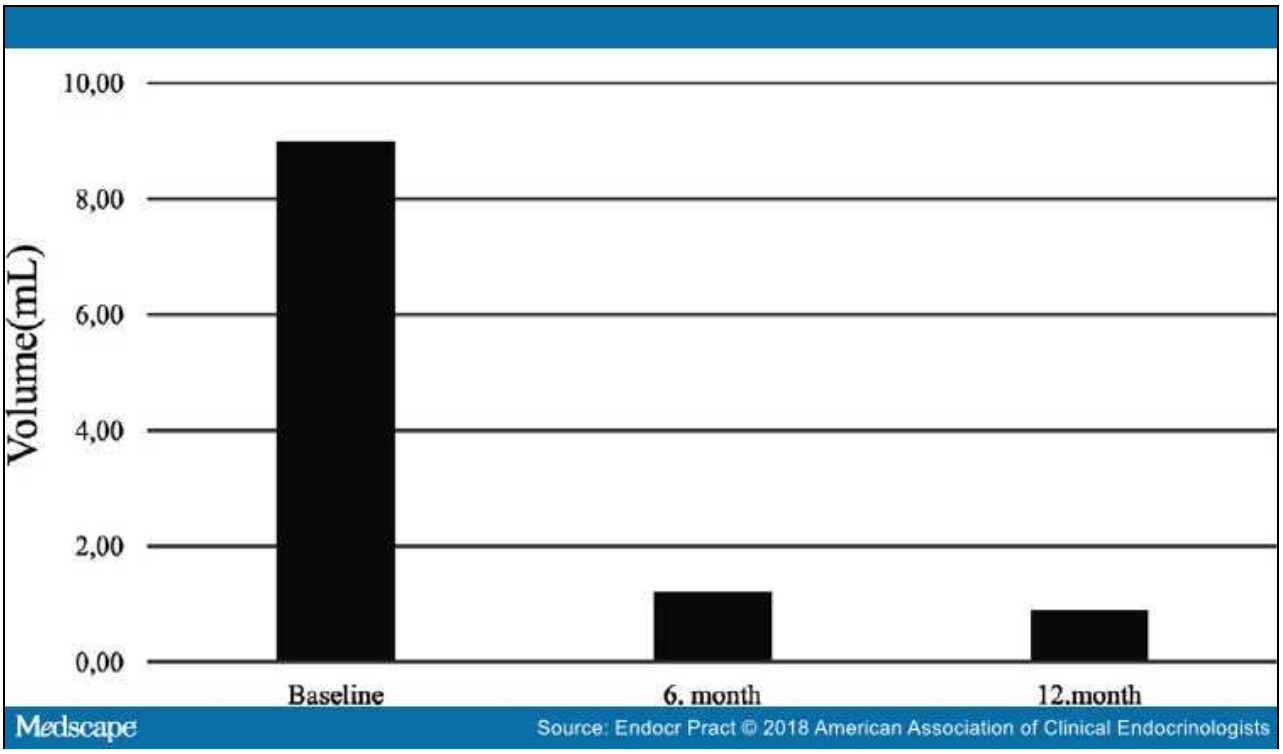

Figure 1.

Median nodule volumes at baseline, 6 months, and 12 months. Volume reductions at 6 and 12 months were statistically significant compared to baseline volume (*P*<.001 for both).

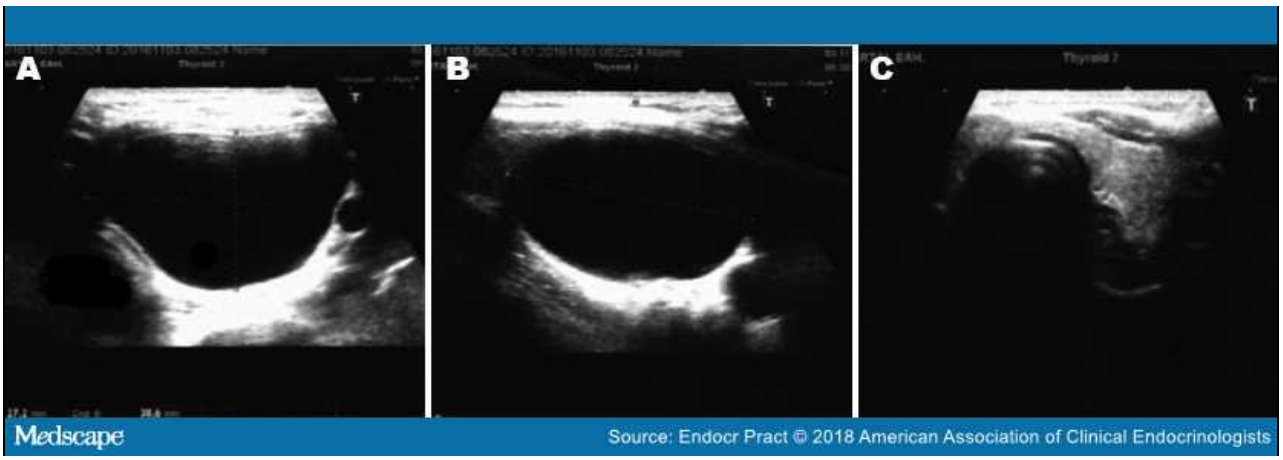

Figure 2.

A 24-year-old female patient. (*A*, *B*) Anechoic mass lesion compatible with a purely cystic nodule in the left thyroid lobe, with dimensions of 3.86 × 2.72 × 3.89 cm (21.24 mL), before percutaneous ethanol injection (PEI). (*C*) The cystic nodule was completely ablated 1 year after PEI (volume reduction, 100%).

During the study, none of the patients had any serious complications, such as dysphonia or hemorrhage. Some of the patients complained of mild and transient pain at the injection site, however.

TSH levels remained unchanged during the study. We observed a statistically significant decrease in fT4 levels both at 6 and 12 months (*P* = .003 and *P* = .036, respectively) and statistically significant increase in fT3 levels only at 12 months (*P* = .008). Despite the statistically significant changes in thyroid hormone levels, all fT3 and fT4 levels were in the normal range. While anti-TPO antibodies remained unchanged during the study, anti-TG antibody levels decreased significantly at 12 months. Data related to the changes in TFTs, thyroid autoantibodies, and nodule volumes during the study are presented in

Table 2. Thyroid Function Tests, Thyroid Autoantibodies, and Nodule Volumes During the Study

	Basal n = 55	6th month n = 55	12th month n = 48	*P* [a] (basal-6 months)	*P* [b] (basal-12 months)
TSH	1.51 ± 1.39	1.42 ± 0.76	1.45 ± 0.87	.268	.128
fT3	4.80 ± 0.67	5.11 ± 0.97	5.28 ± 0.814	.158	.008
fT4	11.82 ± 2.17	10.88 ± 1.89	11.02 ± 1.85	.003	.036
Total nodule volume (mL)	9.0 (4.4 –20.90)	1.2 (0.3–4.1)	0.9 (0.2–4.0)	<.001	<.001
Percent decrease in nodule volume		80.7 ± 15.9	82.1 ± 12.2		
Anti-TPO antibody	0.4 (0-2.5)	1.4 (0-3.8)	0 (0-3.07)	.357	.822
Anti-TG antibody	0.1 (0-1.62)	0 (0-1.10)	0 (0-0)	.398	.033

Abbreviations: Anti-TG = anti-thyroglobulin; Anti-TPO = anti-thyroperoxidase; fT3 = free triiodothyronine; fT4 = free thyroxine; TSH = thyroid-stimulating hormone.
[a]For assessment of basal and 6 months.
[b]For assessment of basal and 12 months.

In order to understand whether PEI was effective in thyroid nodules with different structural properties, we compared the changes in purely cystic, predominantly cystic, and predominantly solid nodules after PEI (). We observed that decreases in nodule volumes at 6 and 12 months were statistically significant among the three groups, despite the similar basal nodule volumes. To determine the cause of this difference, we further analyzed the changes between the two groups using the Mann-Whitney *U* test. We found that the volume reduction in the purely cystic nodules at 6 and 12 months after PEI was greater than the volume reduction in predominantly cystic and predominantly solid nodules (all *P*<.05 in comparisons between purely cystic nodules and the others at 6 and 12 months).

Table 3. Comparison of Changes in Purely Cystic, Predominantly Cystic, and Predominantly Solid Nodules After Percutaneous Ethanol Injection Therapy

	Purely cystic n = 12	Predominantly cystic n = 30	Predominantly solid n = 13	*P* value
Basal volume (mL)	13.8 ± 12.3	15.9 ± 14.8	9.8 ± 7.8	.563
Decrease in nodule volume at 6 months (%)	91.0 ± 8.8	78.6 ± 17.6	76.0 ± 13.6	.009
Decrease in nodule volume at 12 months (%)	96.8 ± 5.4	77.3 ± 21.8	79.0 ± 13.3	.001
Number of procedures	1.3 ± 0.5	1.4 ± 0.6	1.5 ± 0.7	.693
Total ethanol (mL)	2.5 ± 2.2	4.0 ± 3.6	11.0 ± 1.9	.367

We further grouped the thyroid nodules into two according to the median thyroid volume, which was found to be 9.0 mL. Thyroid nodules with volumes ≤9.0 mL were categorized into group 1, and thyroid nodules with volumes >9.0 mL were categorized into group 2. We compared the changes between group 1 and group 2 (). We found that smaller nodules had greater volume reductions after PEI. But this was statistically significant only at 12 months. The number of repeated PEI treatments and total amount of ethanol given were higher in the larger nodules (*P* = .003 and *P*<.001, respectively).

Table 4. Comparison of the Effects of Percutaneous Ethanol Injection Therapy on Thyroid Nodules Grouped According to Median Nodule Volume

	Group 1 (volume ≤9.0 mL) n = 28	Group 2 (volume >9.0 mL) n = 27	*P* value
Basal volume	4.9 ± 2.5	23.4 ± 12.7	<.001
Decrease in nodule volume at 6 months (%)	83.8 ± 12.6	77.5 ± 18.5	.239
Decrease in nodule volume at 12 months (%)	87.9 ± 14.4	76.8 ± 21.7	.037
Number of procedures	1.2 ± 0.4	1.7 ± 0.7	.003
Total ethanol (mL)	1.6 ± 1.0	5.5 ± 3.4	<.001

At the end of the study period, 46 nodules were evaluated by FNAB. Nine patients had nodule volumes <0.2 cm^3, so FNAB was not performed. FNAB of 37 nodules was benign for 16, atypia of unknown significance (AUS) for 13, and nondiagnostic for 8. None of the FNAB results was compatible with a malignant or suspicious for malignancy cytology. After volume reduction of a nodule treated with PEI, an extra nodule became apparent on the ultra-sonographic examination. The FNAB of this nodule was suspicious for medullary

thyroid carcinoma. The patient underwent total thyroidectomy after the study period, and the diagnosis was confirmed to be medullary thyroid carcinoma in the pathologic examination.

We analyzed the predictors of response to PEI in a multiple linear regression model. Age, gender, TSH, number of PEI treatments, total ethanol amount, nodule characteristics, and basal nodule volume were analyzed in the model. However, none of the estimated parameters had a direct influence on the volume reduction.

Discussion

In the current study, we showed that PEI is an effective means of treatment for benign cystic and mixed thyroid nodules causing cosmetic or pressure symptoms. The procedure does not produce any serious side effects using 27-gauge dental needles and small ethanol pulses. Most studies in the literature have considered a nodule volume reduction of >50% as therapeutically successful.[13,14] At 12 months, we attained a success rate of >50% in 93.8% of the nodules treated with PEI.

The current success rate of PEI in cystic and mixed nodules (excluding solid nodules and functioning nodules) ranges between 68 and 94% over a wide-ranging follow-up period of 3.5 months to 9 years.[13,18–21] Similar to our study duration, Raggiunti et al[7] observed an 82.6% volume reduction at 12 months in their study analyzing PEI in thyroid cysts and pseudocysts. In our study, we analyzed and compared the changes in cystic thyroid nodules with different degrees of cystic component. We found that volume reduction in purely cystic nodules was more pronounced than in predominantly cystic nodules and predominantly solid nodules. Our results are comparable with the literature in that success rates were even higher in cystic nodules than in mixed nodules.[19,20] Ferreiara et al[11] analyzed the effect of PEI for benign cystic and mixed thyroid nodules. They similarly subgrouped their patients into three, as in our study. However, they did not detect a difference between subgroups based on cystic component. Current literature regards PEI as not as useful for solid nodules as cystic nodules. It was stated that its use in benign solid thyroid tumors is waning due to the availability of alternatives with a better ratio between efficacy and side effects.[22] Even though our study did not include solid nodules, predominantly solid nodules could give some information related to the effect of PEI in solid nodules. We found that the efficacy of PEI was similar at 12 months between predominantly cystic and predominantly solid nodules (77.3% vs. 79.0%, respectively). A number of studies, depending on nodule size, ethanol amount, and length of follow-up, report reductions of up to 80% in nodule size in solid benign thyroid nodules.[23–25] PEI may be an alternative therapy for solid nodules, especially in patients for whom surgery is contra-indicated.

One of the points that we wanted to assess in this study was the effect of PEI on different-sized nodules. We found that nodules smaller than 9 mL had a volume reduction greater than nodules larger than 9 mL. In the study by Guglielmi et al,[26] nodule volume <5 mL was found to be an independent predictor of favorable outcome in both toxic and pretoxic nodules. In a prospective randomized study comparing isotonic saline with PEI, the chance of success decreased with increasing cyst volume.[14] Our results are comparable with the literature. Small thyroid nodules seemed to be more easily handled during PEI.

PEI therapy is reported to be associated with mild to moderate complications, ranging from mild to severe transient pain and low-grade fever to dysphonia, facial dysesthesia, necrosis of the larynx, and impairment of post-PEI surgery due to local fibrosis.[2] In our series, none of the patients had any serious complications other than mild pain. We think that our methodology has an important role in this. We used 27-gauge dental needles, which permitted easier, flexible intranodular movements and less seepage of ethanol from the needle tract. Additionally, withdrawal of the needle while in inspirium caused a negative pressure that minimized pain. In earlier studies, ethanol amounts were higher, and this was believed to increase the pain experienced by the patient. Additionally, the needles used were thicker than dental needles and caused the needle tracts to close later, thus causing more leakage of ethanol from the tract. As in the recent studies, we limited the ethanol amount so as not to exceed 20% of the aspirated cyst fluid or 20% of the nodule volume (we selected the lowest volume between these). Moreover, in our study, we demonstrated that ethanol amount was not a predictor of volume reduction. This low ethanol amount, together with use of small-gauge dental needles, constitutes a complication-free and affective treatment modality for benign cystic thyroid nodules.

PEI therapy is suspected promoting carcinogenesis. In our study, after 12 months from the first PEI, we did not detect a malignant or suspicious for malignant cytology on FNAB. Zingrillo et al[20] performed FNAB of cystic nodules larger than 1 mL at 6 and 24 months after PEI. Post-PEI FNAB smears did not show a suspicious cytology, but the authors speculated that in most of the specimens, necrotic material could have reduced cytology accuracy. Our post-PEI results were higher for AUS and nondiagnostic cytology; we believe that these high rates might have been the result of both the cystic nature of the nodules and the necrotic changes caused by PEI. Re-biopsy of nodules with AUS and nondiagnostic cytology would be appropriate in follow-up.

There are limited data about changes in thyroid function after PEI in euthyroid nontoxic nodules. In toxic nodules, normalization of thyroid function is one of the success criteria. In our study, we found that TSH levels remained unchanged, while there was an increase in fT3 levels at 12 months, and there was a decrease in fT4 levels at both 6 and 12 months. Despite the statistically significant changes in thyroid hormone levels, all fT3 and fT4 levels were in the normal range. In the study by Del Prete et al,[27] PEI caused an increase in TSH and a decrease in fT4 levels in nontoxic euthyroid solid nodules, whereas there was no change in TSH and fT4 in cystic nodules, before and 1 year after therapy.[28] Since fT4 is the principal hormone secreted by the thyroid gland, the decrease in fT4 might have been a direct and ongoing effect of ethanol. Also, it may be theorized that an increase fT3 level is a compensatory mechanism.

In our study, we detected a significant decrease in anti-TG levels at 12 months, while anti-TPO levels remained unchanged. Contrary to our findings, Del Prete et al[27] observed a transient increase in anti-TPO and anti-TG levels, which returned to basal levels at the end of the study period. In the study by Fronio et al,[29] anti-TG levels increased significantly after 6 months but returned to baseline levels after 12 months, whereas anti-TPO levels remained unchanged during the study. PEI causes release of large amounts of thyroglobulin within the thyroid, which may become an autoantigen. Ongoing necrosis after PEI might have decreased thyroglobulin levels. The decrease in anti-TG levels in our study could be explained in part by this. At least we can reach a point that PEI may not be a trigger for autoimmunity.

One of the limitations of our study could be the study period of only 1 year. In a study with longer-term follow-up, Del Prete et al[19] observed that PEI treatment induced a >50% nodule shrinkage in 92 of 98 patients in the first year of the study, and the decrease in

mean nodule volume was stable after the first year. Only 6 of 92 responder patients had relapsed at a follow-up of 9 years. Another study analyzing the effectiveness of PEI in long-term follow-up by Lee et al[30] reported that in 432 complex thyroid cysts, mean volume reduction was 66% immediately after the first PEI, and the rate only reached 73% at 36 months, despite up to seven PEI sessions. Due to the stable treatment responses to PEI after the first year despite recurrent treatment, we believe that a 1-year study period was acceptable for our study.

Conclusion

In conclusion, PEI is an effective means of treatment for benign cystic and mixed thyroid nodules using dental needles and small ethanol pulses. The procedure does not produce any serious side effects. We can also assume that PEI does not lead to carcinogenesis and is not a trigger for autoimmunity over the short term.

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Abbreviations
anti-TG = anti–thyroglobulin; **anti-TPO** = anti–thyroperoxidase; **AUS** = atypia of unknown significance; **CV** = coefficient of variation; **FNAB** = fine-needle aspiration biopsy; **fT3** = free triiodothyronine; **fT4** = free thyroxine; **PEI** = percutaneous ethanol injection; **TFT** = thyroid function test; **TSH** = thyroid-stimulating hormone; **US** = ultrasonography

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