

## Ethanol Ablation Safe, Effective for Thyroid Cystic Nodules

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June 20, 2003 — Ultrasound-guided percutaneous ethanol injection (PEI) is safe and effective for the treatment of thyroid cystic nodules, according to two presentations on June 19 at the 85th annual meeting of The Endocrine Society (Endo 2003) held in Philadelphia, Pennsylvania.

"Simple aspiration of the fluid content of thyroid cysts is ineffective as thyroid cysts usually recur," coauthor Michele Zini, MD, an endocrinologist from Arcispedale Santa Maria Nuova in Reggio Emilia, Italy, told Medscape. "Our study provides evidence that PEI is a safe, effective, and curative treatment for benign cystic thyroid nodules."

This technique is a simple interventional procedure performed under ultrasound guidance by inserting a special needle inside the thyroid cyst. After aspirating the fluid content of the cyst, the physician injects a small amount of 95% ethanol. Compared with the traditional surgical treatment of large thyroid cysts, the advantages of PEI include avoidance of surgical risks, outpatient setting, no need for general or local anesthesia, brevity of the procedure (which can be completed in a few minutes), reduced cost, and preservation of normal thyroid tissue.

"Ethanol administration causes the formation of scar tissue and therefore it is usually a definitive cure, while simple cyst evacuation is not," Dr. Zini said.

This prospective controlled study enrolled 281 consecutive patients (221 women and 60 men), aged 18 to 83 years, with benign thyroid cystic nodules. Inclusion criteria were local discomfort or cosmetic damage, volume greater than 2 mL, at least 50% fluid component demonstrated on ultrasound, benign cytology on fine needle aspiration biopsy (FNAB), and euthyroidism. Exclusion criteria were inadequate, suspicious, or positive FNAB cytology; elevated serum calcitonin; and laryngeal cord palsy.

Subjects were randomized to receive either simple cyst evacuation or evacuation plus ethanol injection by an experienced clinician using ultrasound guidance. Age, sex, nodule volume and characteristics, discomfort score, thyroid hormone and thyroid-stimulating hormone (TSH) levels, anti-thyroglobulin and anti-thyroid peroxidase antibodies were similar in both groups.

The amount of ethanol injected was approximately equal to 50% to 70% of cystic fluid extracted. If necessary, patients received a second and a third ethanol injection at follow-up examination, which took place after 1, 3, 6, and 12 months. Seventy-five patients received one PEI treatment, 37 received two treatments, and 23 patients received three treatments. Of 266 subjects who completed the study, 135 received PEI and 131 received simple evacuation.

Before treatment, mean nodule volume was  $19.0 \pm 19.0$  in the PEI group and  $20.0 \pm 13.4$  in the simple evacuation group ( $P = \text{N.S.}$ ). After one year, mean nodule volume was  $5.5 \pm 11.75$  vs.  $16.4 \pm 13.7$  ( $P < .001$ ), and median reduction of the initial volume was 85.6% vs. 7.3% ( $P < .001$ ).

Median nodule volume reduction after PEI was 88.8% in 86 unicamered lesions with greater than 80% fluid component, and it was 65.8% in 49 mixed lesions with 50% to 80% fluid component.

Compressive symptoms improved or disappeared in 74.8% of patients treated with PEI and in 24.4% of patients treated with simple evacuation ( $P < .001$ ). Cosmetic appearance improved in 80.0% and 37.4%, respectively. No patients had permanent vocal cord palsy or other major adverse effects, other than transient laryngeal dysfunction in one patient, which subsided after two months.

"Our study demonstrates that the clinical management of thyroid cystic nodules could change in the future," Dr. Zini said. "PEI may become the first therapeutic option, thus avoiding unnecessary surgery."

No external funding was provided for this study, and none of the authors have financial disclosures.

A separate study compared recurrence of benign thyroid cysts after instillation of ethanol or isotonic saline and subsequent complete emptying.

"Previous studies suggest that alcohol sclerotherapy may improve the effect of cyst aspiration alone, but these studies

were uncontrolled and nonrandomized with short follow-up," senior author Lazlo Hegedus, MD, an endocrinologist at Odense University in Denmark, told Medscape. "We know that as the number of aspirations increases, the number of remissions also increases, so it's important to do a controlled, double-blind study like this one."

Solitary thyroid nodules evaluated by ultrasonography are mostly benign, and 15% to 25% are cystic or predominantly cystic, the authors note. Although simple aspiration is the treatment of choice, the recurrence rate is 10% to 80% depending on the number of aspirations and the cyst volume.

In this study, 66 consecutive patients with recurrent benign thyroid cysts, based on ultrasound-guided biopsy, were randomized to (1) subtotal cyst aspiration under ultrasound guidance, flushing with 99% ethanol and subsequent complete fluid aspiration or to (2) the same procedure but with isotonic saline instead of ethanol. The two groups were similar in terms of age, sex, number of previous aspirations, pretreatment cyst volume, and serum TSH.

For recurrences with cyst volume greater than 1 mL, patients had repeat treatment, limited to a maximum of three treatments. Monthly follow-up took place for six months.

At completion of follow-up, 27 (82%) of 33 patients treated with ethanol were cured, defined as a cyst volume of 1 mL or less (confidence interval [CI], 65% - 93%). In the saline group, 16 (48%) of 33 patients were cured (CI, 31% - 66%;  $P = .006$ ). One treatment was sufficient for cure in 21 patients (64%) treated with ethanol and in six (18%) treated with saline ( $P = .002$ ).

Multiple logistic regression revealed that higher number of previous aspirations or higher cyst volume at baseline was associated with decreased chance of cure ( $P = .005$  for each).

In the ethanol group, seven patients (21%) had moderate to severe pain associated with the procedure. Median duration of the pain was 5 minutes (CI, 2 - 10 minutes). One patient treated with ethanol had transient dysphonia that resolved before ENT evaluation could be completed. Indirect laryngoscopy was normal before and after the last treatment in all patients in both groups.

"A few patients treated with alcohol had a mild degree of transient pain lasting a few minutes, but nothing that would be prohibitive," Dr. Hegedus said. "This is now the standard treatment in our department, and it should be anywhere that has the capability to perform this procedure under ultrasound guidance."

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*Reviewed by Gary D. Vogin, MD*

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