Efficacy of Ultrasound-Guided Polidocanol Sclerotherapy for Benign Thyroid Cysts and Analysis of Related Factors (Postprint)

Authors: Chen Zhijiang, Wang Long, Huang Yijing, Lai Shuiqing, Chen Hongmei, Pei Jianhao, Cong Shuzhen, Jian Kuang

Date: 2017-12-21T00:00:00+00:00

Abstract

Objective To analyze the therapeutic efficacy of ultrasound-guided lauromacrogol sclerotherapy for benign thyroid cysts and its main influencing factors, and to investigate the types of thyroid cysts suitable for lauromacrogol sclerotherapy. Methods Ninety-seven patients with a total of 99 cysts with volume 2 cm 3 and cytopathologically diagnosed as benign thyroid cysts underwent ultrasound-guided lauromacrogol sclerotherapy, with follow-up conducted at 1, 3, 6, and 12 months postoperatively. Cysts were classified according to disease course, cyst fluid composition, cyst fluid viscosity, cystic-solid ratio, cyst wall thickness, and septations. Treatment efficacy was evaluated as ineffective for <50% volume reduction, effective for 50% reduction, and cured for 90% reduction. Results The cyst volumes at baseline and at 1, 3, 6, and 12 months after treatment were 12.08±11.56cm 3, 5.63±8.51 cm 3, 5.96±8.42 cm 3, 3.80±5.50 cm 3, and 2.85±3.98 cm 3, respectively; the mean cyst volume reduction was (70.0±33.7)%; the cumulative effective rate was 82.8% (82/99), and the cure rate was 63.6% (63/99); 13.1% (13/99) of cysts required repeat sclerotherapy due to enlargement or no reduction compared with baseline after 1-3 months, and cysts with disease course >1 year was an independent factor for multiple sclerotherapy [23.7% (9/38) vs 6.6% (4/61), OR=4.473 (1.238~16.169), P=0.022]; treatment efficacy was correlated with cyst septations, cyst fluid viscosity, cystic-solid ratio, and cyst wall thickness; COX multivariate regression analysis showed that the main factors affecting final cyst efficacy (<90% reduction) were cyst septations (HR=2.25, 95% CI 1.19~4.25) and viscous cyst fluid (HR=2.02, 95% CI 1.19~3.43). Conclusion Ultrasound-guided puncture lauromacrogol sclerotherapy is an effective and safe treatment for benign thyroid cysts, with maximum therapeutic efficacy achieved at 6 months, and shows optimal treatment outcomes for simple cysts with disease course <1 year, thin cyst fluid, and no septations.

Full Text

Preamble

Efficacy of Ultrasound-Guided Lauromacrogol Sclerotherapy for Benign Thyroid Cysts and Factors Affecting the Therapeutic Effect

CHEN Zhijiang[1], WANG Long[1], HUANG Yijing[1], LAI Shuiqing[1], CHEN Hongmei[1], PEI Jianhao[1], CONG Shuzhen[2], KUANG Jian[1]

[1]Department of Endocrinology, [2]Department of Ultrasound, Guangdong General Hospital/Guangdong Academy of Medical Sciences, Guangzhou 510080, China

doi: 10.3969/j.issn.1673-4254.2016.12.18

Abstract

Objective: To evaluate the clinical efficacy of ultrasound-guided lauromacrogol sclerotherapy for benign thyroid cysts and analyze the factors affecting treatment outcomes. **Methods:** Ultrasound-guided lauromacrogol sclerotherapy was performed in 97 patients with a total of 99 benign thyroid cysts. Changes in cystic volume and other thyroid parameters were evaluated at 1, 3, 6, and 12 months after sclerotherapy. Based on changes in cystic volume, treatment efficacy was defined as therapeutic failure (volume reduction <50%), treatment success (volume reduction 50%), or cure (volume reduction 90%). Factors affecting treatment efficacy were analyzed using COX regression. **Results:** The mean cystic volume at 1, 3, 6, and 12 months after sclerotherapy was reduced from the baseline volume of 12.08±11.56 cm^3 to 5.63±8.51 cm^3, 5.96±8.42 cm^3, 3.80±5.50 cm^3, and 2.85±3.98 cm^3, respectively, with an average cystic volume reduction rate of (70.02±33.72)%. Therapeutic success was achieved in 82 of the 99 cysts (82.83%) and cure was achieved in 63 cysts (63.64%) at 12 months after the procedure. A second sclerotherapy was performed for 13 cysts which did not show volume reduction at 1-3 months after the initial procedure. A disease course of over 12 months was an independent risk factor for requiring repeat sclerotherapy (23.7% [9/38] vs 6.6% [4/61], OR=4.473 [1.238-16.169], P=0.022). The efficacy of sclerotherapy was related to cystic cavity separation, cystic fluid viscosity, cystic/solid ratio, and cystic wall thickness. COX regression analysis revealed that cystic cavity separation (HR=2.25, 95% CI: 1.19-4.25) and cystic fluid viscosity (HR=2.02, 95% CI: 1.19-3.43) were the major factors affecting treatment efficacy. **Conclusion:** Ultrasound-guided lauromacrogol sclerotherapy is effective and safe for treatment of benign thyroid cysts, with maximal treatment effect achieved at 6 months after sclerotherapy. The best outcomes are observed in cases of uncomplicated cysts with non-viscous cystic fluid, no solid cystic cavity separation, and a disease course of less than 12 months.

Key words: cystic thyroid nodule; sclerotherapy; lauromacrogol

Author Information

Corresponding Authors:
KUANG Jian, MD, PhD, Professor, Tel: 020-83827812-61917, E-mail: endometa@126.com
CONG Shuzhen, MD, PhD, Professor, E-mail: shzhcong@163.com

First Authors: CHEN Zhijiang, E-mail: nfm_czj@163.com; WANG Long, E-mail: rulebreaker@126.com

Funding: Guangdong Medical Science and Technology Research Fund (A2016332)

Received: 2016-09-21

Introduction

Thyroid nodules are common clinical findings with a prevalence of only 4-7% on palpation [1-2], but approximately 20-76% in adults when diagnosed by ultrasound [2-3]. Thyroid cysts account for about 15-30% of thyroid nodules, and although the vast majority are benign [4], they often require clinical treatment due to cosmetic concerns and local compression symptoms. Simple fluid aspiration is simple and economical but associated with high recurrence rates. Surgical resection can cure cysts but carries certain surgical risks and high costs. Sclerotherapy is a simple and effective clinical treatment method. While anhydrous ethanol is the main sclerosing agent used abroad [5-7], it has not been routinely implemented in China for various reasons. Lauromacrogol, a vascular sclerosing agent, has been gradually applied to thyroid cyst sclerotherapy in recent years. Domestic and international studies [9-13] have reported that lauromacrogol sclerotherapy has good efficacy and safety for thyroid cysts, but there are differences in treatment protocols and outcomes. Furthermore, thyroid cysts have various clinical types and characteristics. This study aimed to analyze the treatment efficacy of ultrasound-guided lauromacrogol sclerotherapy for benign thyroid cysts and its main influencing factors.

Methods

Patient Characteristics

A total of 97 patients with 99 benign thyroid cysts (volume >2 cm^3 and confirmed by cytopathology) were enrolled. The baseline characteristics are shown in Table 1 . The mean age was 46.48±12.85 years, with male patients being significantly older than female patients (56.92±8.12 vs 42.77±12.19 years,

P<0.006). The mean initial cyst volume was 12.08±11.56 cm³, with male patients having significantly larger cysts than female patients (17.38±16.87 vs 10.19±8.33 cm³, P<0.006). All thyroid-related indices were within normal ranges.

Treatment Protocol

All patients underwent ultrasound-guided lauromacrogol sclerotherapy. Follow-up was conducted at 1, 3, 6, and 12 months after the procedure. Cysts were classified according to disease course, cyst fluid composition, viscosity, cystic-solid ratio, wall thickness, and presence of septations. Treatment efficacy was evaluated based on volume reduction: <50% reduction was considered ineffective, while 90% reduction was considered cured.

Results

Treatment Frequency and Follow-up

Among the 99 cysts, 86 required only a single sclerotherapy session, while 13 cysts (13.1%) required repeat sclerotherapy due to enlargement or no reduction at 1-3 months (9 cysts required 2 sessions, 4 cysts required 3 sessions). A total of 116 sclerotherapy procedures were performed. The mean follow-up duration was 6.47±3.64 months.

Efficacy Analysis

The mean cyst volumes at baseline and at 1, 3, 6, and 12 months after treatment were 12.08±11.56 cm³, 5.63±8.51 cm³, 5.96±8.42 cm³, 3.80±5.50 cm³, and 2.85±3.98 cm³, respectively. Each follow-up measurement showed statistically significant differences compared to baseline (P<0.001), with volume reductions of 59.5-68.6%. The cumulative volume reduction rate was (70.0±33.7)%.

Paired t-tests comparing pre- and post-treatment volumes showed reductions of -6.30±8.79 cm³, -7.72±10.74 cm³, -7.75±8.76 cm³, and -7.03±6.38 cm³ at 1, 3, 6, and 12 months, respectively (all P<0.001). Comparison between months 6 and 3 showed continued significant volume reduction (V_{-V} = 2.08±5.73 cm³, t=2.06, P=0.045), but no significant difference between months 12 and 6 (V_{-V} = 0.34±2.55 cm³, t=0.59, P=0.56), indicating that maximal therapeutic effect was achieved by 6 months after sclerotherapy.

The success rate after a single sclerotherapy session was 82.6% (71/86), with a cure rate of 66.3% (57/86). For cysts requiring two sessions, the success rate was 77.8% (7/9) and cure rate 33.3% (3/9). For cysts requiring three sessions, the success rate was 100% (4/4) and cure rate 50.0% (2/4). The final overall success rate was 82.8% (82/99) and cure rate was 63.6% (63/99), with no significant difference in efficacy between male and female patients.

Cysts requiring multiple sclerotherapy sessions were characterized by a disease course exceeding 1 year (23.7% [9/38] vs 6.6% [4/61], t=6.021, P=0.029) and thick cyst walls (17.6% [12/68] vs 3.2% [1/31], t=3.882, P=0.058). Logistic regression analysis identified a disease course >1 year as the main independent risk factor for requiring repeat sclerotherapy (OR=4.473 [1.238-16.169], P=0.022).

Factors Associated with Treatment Efficacy

Baseline cyst volume did not affect treatment outcomes (cured vs not cured: 10.71±10.94 vs 14.37±12.35 cm^3, F=2.354, P=0.128; effective vs ineffective: 12.14±11.92 vs 11.79±9.96 cm^3, F=0.013, P=0.909).

Univariate chi-square analysis showed that the success rate was primarily affected by cyst cavity septations (P<0.001) and marginally by cyst wall thickness (P=0.056). The cure rate was significantly influenced by multiple factors including cyst fluid viscosity, cystic-solid composition, cyst wall thickness, and cavity septations (Table 2).

In COX regression analysis for success rate, univariate analysis showed no significant effects for any factors. Multivariate backward conditional regression included cyst fluid viscosity and cavity septations, but neither reached statistical significance (viscous fluid: HR=1.465, P=0.093; septations: HR=1.613, P=0.066). For cure rate, univariate analysis showed significant effects for cyst fluid viscosity, cystic-solid composition, and cavity septations. Multivariate analysis identified cyst fluid viscosity (HR=2.066, 95% CI 1.221-3.497, P=0.007) and cavity septations (HR=2.298, 95% CI 1.220-4.330, P=0.010) as major independent influencing factors (Table 2).

Figure 1 [Figure 1: see original paper] shows ultrasound imaging characteristics of thyroid cysts related to treatment efficacy.

Safety Profile

Among the 97 patients, only 2 (2.0%) reported mild local burning sensation during sclerotherapy, which resolved spontaneously within 10 minutes. No patients experienced voice changes, hoarseness, or facial flushing. Two patients developed low-grade fever on the day after treatment, which resolved without special intervention, likely related to the medication.

Discussion

Thyroid cysts are common thyroid lesions, most resulting from degenerative changes, hemorrhage, or ischemic necrosis and liquefaction of nodular goiter or thyroid adenoma. Some form from fusion of adenoma follicles, and 极少数 originate from thyroglossal duct or ultimobranchial body remnants, or from

hemorrhage and necrosis of thyroid carcinoma. The vast majority are benign, with a malignancy rate of approximately 0.5-3% [14].

The decision to treat and the choice of treatment method depend on the nature and size of the cyst. For benign thyroid cysts, treatment is generally indicated only when local compression symptoms or cosmetic concerns are present. Guidelines recommend ultrasound-guided fine-needle aspiration (US-FNA) or treatment when cysts reach 1.5-2.0 cm [14]. Current treatment options include simple aspiration, sclerotherapy, surgical resection, and chemical or physical ablation. Simple aspiration has high recurrence rates (60-90%), particularly in repeatedly aspirated and large-volume cysts [5]. Surgical resection and physical ablation (radiofrequency, microwave, laser) are suitable for significantly enlarged complex or recurrent cysts but involve higher costs and surgical risks. Chemical ablation (anhydrous ethanol) and sclerotherapy are simple, inexpensive, and effective, gaining increasing clinical application. Anhydrous ethanol is most widely used abroad [7,19] but has not been routinely implemented in China. Other reported sclerosing agents include dexamethasone, sodium morrhuate, hypertonic glucose, arginine hydrochloride, OK-432, tetracycline, lauromacrogol, and anhydrous ethanol.

Lauromacrogol (polidocanol) is a vascular sclerosing agent that directly damages vascular endothelium, promotes thrombosis, and obstructs blood vessels, subsequently inducing local inflammatory reactions and fibrosis for permanent occlusion. After intracavitary injection, it cleanses and destroys the cyst lining cells, reducing fluid exudation and promoting adhesion, followed by fibrotic obliteration of the cyst cavity. It has been used for years in sclerotherapy of hemangiomas, internal hemorrhoids, varicose veins, ganglion cysts, and hepatic and renal cysts [8,20-21]. Recent animal studies show that lauromacrogol-induced local thyroid tissue fibrosis does not affect thyroid function or cause adhesion to surrounding tissues [15]. Clinical studies demonstrate that lauromacrogol has good safety and efficacy for thyroid cyst sclerotherapy [9-13]. Additionally, lauromacrogol is a mild local anesthetic with analgesic effects, offering advantages of less local irritation and fewer adverse reactions compared to anhydrous ethanol [8].

In this follow-up study, ultrasound-guided lauromacrogol sclerotherapy demonstrated good efficacy for benign thyroid cysts: single-session treatment achieved an 82.6% success rate and 66.3% cure rate, with only about 13% of cysts requiring repeat treatment. These results are similar to previous domestic studies reporting success rates of 84.6-95.5% and cure rates of 52.6-89.1%. However, the retreatment rate in our study (13.1%) was significantly lower than reported rates of 24.1-64.1% in other studies, possibly due to differences in treatment protocols, cyst types, and clinical practice. Some studies used weekly review and treatment [10], while others focused on simple cysts with review at 3 months before considering retreatment.

In our cohort, cysts requiring multiple sclerotherapy sessions were characterized by thick walls, particularly those with a disease course exceeding 1 year. Ad-

ditionally, during sclerotherapy, rich blood flow at the puncture site, multiple needle passes, and excessive negative pressure during fluid aspiration may increase the risk of intracystic hemorrhage and affect treatment outcomes. Our clinical experience shows that selecting puncture sites with less blood flow, minimizing needle passes, avoiding excessive negative pressure, aspirating quickly, and avoiding excessive pressure during irrigation can reduce the risk of intraoperative and postoperative hemorrhage. After treatment, observing for 15-30 minutes to ensure no cyst enlargement allows for review at 1 month. Small amounts of intracystic hemorrhage generally resolve spontaneously within 1-3 months, with most cysts shrinking by nearly 60% after 1 month. Therefore, weekly review and retreatment appear unnecessary, while 3-month review may delay retreatment. Follow-up at 1, 3, 6, and 12 months post-treatment, then annually, is appropriate.

In this and previous studies, the success rate (50% volume reduction) exceeds 80%, but the cure rate (90% reduction or disappearance) ranges from 50-70%. Thyroid cysts have various etiologies and clinical presentations, including hemorrhagic and colloid cysts, simple and cystic-solid cysts, and multiseptated cysts. Our analysis shows that different clinical and ultrasound features affect lauromacrogol sclerotherapy outcomes differently: (1) For achieving 50% volume reduction, lauromacrogol sclerotherapy is highly effective and not significantly affected by these factors; (2) For achieving 90% reduction or disappearance, cyst fluid viscosity, cystic-solid composition, cyst wall thickness, and cavity septations are influencing factors, with cyst fluid viscosity and cavity septations being the most important independent factors.

Cystic-solid cysts, thick-walled cysts, and multiseptated cysts often show rich blood flow in the cyst wall and/or internal septations on ultrasound, and combined with fluid color and characteristics, are mostly caused by nodular hemorrhage. These cysts are prone to intraoperative and postoperative hemorrhage during and after sclerotherapy. Multiseptated cysts often require multi-angle puncture and position adjustment during treatment, which increases bleeding risk and makes complete fluid aspiration and adequate lauromacrogol irrigation difficult, compromising treatment efficacy. Studies on anhydrous ethanol treatment also found that septations affect sclerosant diffusion, preventing complete sclerosis of each cavity and deep solid components, thereby affecting final outcomes [7,16-17,22-23].

Viscous cyst fluid is mostly colloid, old hemorrhage, or both. Due to high viscosity, aspiration often requires high negative pressure or larger needles, and may be slow or incomplete. Domestic researchers have developed an "open-window" needle with a 5 mm × 1 mm side window adjacent to a larger PTCA needle, which effectively addresses viscous fluid aspiration [18]. In our practice, we found that lauromacrogol and 5% sodium bicarbonate have some dissolving effect on viscous fluid. When viscous fluid is encountered, we inject 1-2 mL of lauromacrogol or sodium bicarbonate solution, allow 1-2 minutes for dissolution, then aspirate slowly with 2-4 mL negative pressure while adjusting needle posi-

tion. Repeating this process at multiple sites achieves near-complete aspiration, followed by lauromacrogol irrigation and retention, yielding good results though requiring longer, more patient and meticulous operation. Therefore, mastering appropriate techniques is crucial for efficacy and reducing retreatment.

For benign thyroid cysts with recurrence after multiple lauromacrogol treatments, or those with multiseptations or solid components >50%, we have used radiofrequency ablation directly after fluid aspiration in some cases with significant results. International studies on switching to radiofrequency ablation after unsatisfactory ethanol ablation have also confirmed good efficacy [24].

In summary, ultrasound-guided lauromacrogol sclerotherapy offers good efficacy, minimal side effects, and is economical and simple for benign thyroid cysts. The best outcomes are achieved in simple cysts with thin walls, non-viscous fluid, and no internal septations. Cysts with long disease courses, rich peripheral blood flow, large solid components, or multiple septations have higher retreatment rates, for which radiofrequency/microwave ablation after aspiration or direct surgical resection may be more appropriate.

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Note: Figure translations are in progress. See original paper for figures.