Capsular Thyroid Injection Therapy Under Ultrasound Guidance for the Treatment of Subacute Thyroiditis

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Abstract

Purpose

The present study aimed to evaluate the efficacy and safety of capsular thyroid injection therapy under ultrasound guidance for treating subacute thyroiditis.

Methods

Seventy-three patients with subacute thyroiditis were divided into groups A (n=48) and B (n=25). Group A was treated with ultrasound-guided capsular injection consisting of a mixture of dexamethasone (DEX) and lidocaine in the thyroid lesion area, while patients in group B received oral prednisolone (PSL). The duration of pain relief, duration of treatment, time of thyroid function recovery, recurrence rates, hypothyroidism, and side effects between the two groups were compared.

Results

After 12 months of follow-up, the duration of pain relief, duration of treatment and thyroid function recovery in group A were significantly shorter than those in group B ($P<0.05$), except for the recurrence rate and hypothyroidism ($P>0.05$). Weight gain in patients was significantly higher in group A than in group B at the end of treatment ($P<0.001$).

Conclusion

Ultrasound-guided local injection of DEX and lidocaine combination can rapidly relieve pain, shorten the duration of treatment, and reduce adverse effects when compared with oral PSL treatment.

Introduction

Subacute thyroiditis (SAT) is a widespread inflammatory thyroid condition that is generally considered an outcome of a viral infection of the upper respiratory tract, including non-autoimmune painful SAT (pSAT; also known as de Quervain's or granulomatous thyroiditis) and autoimmune painless SAT (silent SAT).[1-3] The incidence of SAT is reported to be12.1 cases per 100,000 population and it is more prevalent in females (19.1 per 100,000) than in males (4.4 per 100,000), with the highest incidence observed in young adults(24 per 100,000).[4-6] Patients with classical pSAT usually experience neck pain, enlarged and swollen thyroid, mild to moderate fever, and occasionally transient vocal cord paralysis.[7, 8] The neck pain associated with pSAT is confined to the affected thyroid lobe during the early stages but subsequently spreads rapidly to the rest of the gland, and may radiate to the jaws or ears.[2] Although pSAT is self-limiting, the painful symptoms are occasionally severe and could last weeks to a few months. Thus, active treatment is usually required to control pain and inflammation.

Oral corticosteroid therapy with prednisolone (PSL) remains the most commonly used approach for treating pSAT because of its effectiveness in relieving pain and distress symptoms.[9-13] However, the

treatment duration of PSL for pSAT is relatively long. Specifically, PSL is administered with an initial dosage of 20–40 mg per day for 1–2 weeks, followed by a gradual dosage tapering over 4–6 weeks.[10-13] The long-term treatment duration is usually associated with poor patient compliance, leading to unsatisfactory overall cure rates and high recurrence rates. Moreover, adverse events associated with the long-term use of PSL, including but not limited to hypertension, bone fractures, cataracts, gastrointestinal conditions, and metabolic complications should be taken into consideration. To date, there are no safe and fast-acting therapeutic approaches for pSAT.

Local injection of dexamethasone (DEX) in combination with lidocaine is widely used in clinical practice due to its well-established anti-inflammatory, anti-hyperalgesic, and analgesic effects.[14-16] Several previous studies have demonstrated that intrathyroidal injection of the DEX-lidocaine combination is an effective and safe therapeutic approach for patients with pSAT.[17, 18] However, performing the procedure successfully is usually a challenge because the texture of thyroid lesions in patients with pSATis coarse. In this study, we improved the technique by injecting DEX-lidocaine combination into the envelope membrane of the thyroid under ultrasound guidance and compared its therapeutic effects with those of oral PSL in 73 patients with pSAT.

Methods

Patients

This study included 96 consecutive patients with untreated pSAT who visited the Department of Thyroid Surgery at the First People's Hospital of Zunyi (The Third Affiliated Hospital of Zunyi Medical University) between June 2016 and December 2017. pSAT was diagnosed based on the following criteria: 1) history of a viral respiratory infection 2–8 weeks prior to onset; 2) pain, tenderness, and enlargement of the thyroid gland; 3) elevated erythrocyte sedimentation rate (ESR), high serum free triiodothyronine(FT3) and free thyroxine (FT4), and low-serum thyrotropin (TSH); 4) diffuse or focal hypoechoic lesions located within the painful thyroid region as determined by ultrasonography. Data for a total of 73 patients who met the inclusion criteria were finally analyzed, and 23 patients with pSAT were excluded because they had received previous treatment for pSAT (n=13) or were lost to follow-up (n=10).

Patients included in this study (n=73) were randomly divided into two cohorts: group A, which had 48 (65.8%) patients who received ultrasound-guided local DEX-lidocaine injection every other day for three sessions, and group B, which had 25 (34.2%) patients who received oral PSL. The present study was approved by the ethics committee of the First People's Hospital of Zunyi. Written informed consent was obtained from all patients included in the study.

Pain assessment and treatment duration

Pain was assessed using an 11-point numeric rating scale, which was used to score the pain experienced by patients. Pain scores were evaluated based on symptoms during swallowing, which was scored from 0 ("painless") to 10 ("excruciating pain").[19, 20] Patients in each group (n=73) were subjected to pain

score tests before treatment, after 2.5 h, and 2,4, and 6 days of treatment. A patient was considered clinically cured if pain did not recur 72 h after discontinuation of treatment. After three sessions of ultrasound-guided local DEX-lidocaine injections, a few patients with mild pain (pain score ≤3points)received PSL at a dose of 5–10 mg/d for remission for 1–2 weeks, or follow-up without other special treatments.(Fig 1) The number of treatments was increased if necessary (pain score > 3 points).

Measurement of serological markers

Peripheral venous blood samples were collected for the measurement of SAT-associated serological markers every four weeks, including FT3, FT4, TSH, and ESR. Specifically, FT3, FT4, and TSH were measured using a commercial electro-chemiluminescence immunoassay (Roche Diagnostics, Mannheim, Germany). The normal reference ranges were 3.28–6.47 pmol/L for FT3, 7.64–16.03 pmol/L for FT4, and 0.34–5.6 μIU/mL for TSH.ESR was tested using the Westergren method (Roche Diagnostics/Cosmic Corp, Mannheim, Germany), and its normal value was 15 mm/h or lower.

Ultrasonography

Ultrasound-guided injection and post-treatment follow-up were performed using a trolley colour doppler ultrasound scanner (P37, SonoScape Medical Corp, Shenzhen, China) by two qualified and experienced doctors. A standard 10 MHz linear ultrasound probe was used.

Estimated lobe volumes for lobe lesions of all patients were determined using the formula for calculating the volume of a rectangle (longitudinal diameter×width×depth cm3). The demarcation was thyroid isthmus located close to the trachea and the summation of the lobe volumes yielded the lesion volume. The remission of pain symptoms and reduction of lesion volumes indicated that the treatment was effective.

Weight assessment

The weights of patients in each group were measured and recorded before and after the treatment for the evaluation of the changes in body weight.

Assessment of patients during follow-up

The follow-up period was 12 months after the end of treatment. During the follow-up period, we compared the recurrence rates and the incidence of hypothyroidism between the two groups.

Treatment

Ultrasound-guided injection group

The main steps of ultrasound-guided injection are summarized as follows. (Fig .2) First, patients were maintained in a supine position, with the neck slightly extended and the head turned contralaterally. Second, an ultrasound examination of the lesion was performed. (Fig .3A) The region of the lesion and a

suitable injection point on the body surface was marked. Third, the injection area was sterilized with iodophor and a disposable protective sleeve placed on the ultrasonic probe. Fourth, a mixture of 2% lidocaine (1ml) and 0.5% DEX(1ml) for injection was prepared in the ratio of 1:1 using a 2.5-ml syringe. Fifth, the covered ultrasonic probe was held in one hand and the filled syringe held in the other, with the operator standing at the head end of the patient. Sixth, the probe was placed on the marked area and the needle inserted through the injection point. The injection button was not pushed until the margin of the lesion had been reached. (Fig .3B) Afterwards, the solution was slowly injected for at least 30 s and the needle was removed gently. (Fig .3C, Fig .3D) Finally, a patient was instructed to compress the puncture region with sterilized gauze for 20 min to prevent haemorrhage.

Oral drug group

Oral PSL was administered to 25 (34.2%) patients in group B at an initial dosage of 20 mg per day for two weeks, followed by a gradual tapering of 5 mg every 7–14 days.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics (version 26.0; IBM Corp., Armonk, NY, USA). Data were presented as means± standard error of the mean (SEM). Categorical data were analyzed using Chi-square test. Student's *t*-test was performed to determine statistical differences between the two groups. A p-value of 0.05 or less was considered statistically significant.

Results

Clinical characteristics of patients

A total of 89 consecutive patients were diagnosed with SAT, of which 73 patients with complete clinical data were included in the present study. Among them, 48 patients were treated with injection therapy (group A) and 25 patients received PSL (group B)on their first visit to the clinic. No statistically significant differences(P>0.05)were observed in the male-to-female ratio, onset time, and age between the two groups. In addition, no significant difference was observed in symptoms between the two groups (P>0.05, Table 1). Remarkably, the mean time between onset and first visit to the clinic was shorter in the injection group (6.19±4.95 days) than in the PSL group (7.80±3.78 days, P= 0.0737), although the difference was not statistically significant.(Table 1)

Comparison of the durations of pain relief and treatment

The time taken for painful symptoms to disappear was significantly shorter in the injection group than in the PSL group (Fig. 4). A highly significant difference was observed in the duration of pain relief between the injection and PSL groups. In particular, the mean duration of the treatment cycle was significantly lower in group A(6,2–32 days) than in group B(20,5–190days, P>0.05).

Comparison of laboratory parameters between groups

No statistically significant differences were observed in FT3, FT4, TSH, and ESR levels at admission between the two groups(P>0.05).ESR and thyroid function were significantly lower in group A than in group B after four weeks of treatment(P□0.05), while recovery times of thyroid function in the two groups were similar(P>0.05). (Table 2)

Comparison of recurrence rates and hypothyroidism between groups

Two patients were treated with DEX-lidocaine combination and one patient who received oral PSL treatment exhibited recurrence of SAT within two months after discontinuation of the treatment. However, there was no significant difference in the recurrence rates between the two groups (P>0.05). The occurrence rates of hypothyroidism were higher in the injection group than in the PSL group. However, the differences were not statistically significant (P>0.05).

Comparison of side effects

Regarding the side effects of the two treatments (DEX-lidocaine combination and PSL), two patients in the PSL group with type 2 diabetes mellitus showed clinically significant deterioration in blood glucose control during the treatment. Three patients who received the injection treatment and four patients who received PSL treatment exhibited recurrence of SAT within two months after discontinuation of the drugs. However, there was no significant difference in recurrence rates between the two groups (P= 0.635).In addition, weight gain was significantly higher in the PSL group (1.56±2.55 kg) than in the injection group after the end of treatment (0.42±1.26 kg, P< 0.001).

Discussion

pSAT is a rare disease but its prevalence has been increasing over the last few years.[8] The pathogenesis of pSAT remains unknown, and the potential mechanisms associated with the condition include viral infections, immune disorders, and genetic factors.[1-3] Among them, viral infection is the most frequent trigger.[21, 22] High-dose glucocorticoid therapy is relatively effective but often requires prolonged use, and many patients are unable to discontinue glucocorticoid use even after months or years of treatment. Furthermore, the possible drawbacks of using glucocorticoid drugs are immune suppression and other side effects. To avoid such problems, we employed ultrasound-guided subcutaneous injection of pSAT instead of a systemic high dose of hormone therapy in the present study. The results revealed that injection treatment in patients with pSAT decreased the duration and the side effects associated with hormone therapy.

pSAT is a self-limited thyroid disorder that presents with localized neck pain, low-grade fever, and/or temporal and ear pain. Systemic inflammation is induced by the local inflammatory process in the thyroid. Based on their anatomical auriculotemporal nerve region has been demonstrated to be caused by conduction through the ansacervicalis nerve. Treating pain is the priority during the treatment course.[11, 23] DEX is a highly effective anti-inflammatory drug with a long half-life in the tissue compared with oral gavage.[24, 25] Lidocaine is a local anaesthetic belonging to the amide local aesthetics category and is

the most widespread anaesthetic used for local infiltration.[26] Studies have revealed that lidocaine has a certain degree of anti-inflammatory effect in patients with pSAT.[27] PSL influences both acute and chronic inflammation.[28] However, long-term treatment with PSL can lead to severe adverse effects.[12] The injection of patients with pSAT using DEX-lidocaine combination can rapidly prevent local inflammation reactions, in turn, preventing long-term treatment with steroids. By contrast, we speculated that the injection of DEX into the thyroid wound area could sustain enough drug density to inhibit inflammatory response when compared to oral PSL. These could be the possible reasons associated with shortening the treatment period. In the present study, the average duration of pain relief was 2.5 h, and the average treatment period was approximately six days. Injection therapy significantly reduced the treatment period when compared with oral PSL. Similar previous studies have also employed a combination ofDEX and lidocaine as local injection therapy.[17, 18] The volume of lidocaine is gradually increased during the injection until the pain is relieved. Previous studies have reported that the duration of pain relief is approximately 30s, and the average treatment period is four days.[18] The results obtained in the present study could be attributed to the variations in the injected drug dosage, concentration, and injection time interval. Previous studies have also suggested that the DEX-lidocaine combination should be administered once every other day for three sessions, and an additional 600 mg/d oral ibuprofen administered to patients who continue to experience severe pain after three injections. Additionally, the painful lobe is injected with 20 to 80 U at each administration until the pain abates.[18] However, during the actual operation, the operator established that performing the procedure successfully was a challenge because the texture of thyroid lesions was coarse. In this study, we improved this technique according to our experience. We used a single fixed combination of DEX and lidocaine in a dose ratio of 1:1, which was injected into the envelope membrane of the thyroid under ultrasound guidance. We also used a low-dose orally administered PSL. The results of the present study revealed that the treatment duration was similar to that reported in previous studies. Our method is more convenient and accessible because the specific operating steps are more simple. Moreover, our results revealed a better treatment outcome with regard to the injection treatment for SAT-related symptoms, such as fever, muscle soreness, fatigue and so on.

Fine-needle aspiration biopsy of thyroid nodules under ultrasound has been carried out at our department for many years, with rich experience in puncture operations and appropriate postoperative complication management. Ultrasound-guided injection of DEX-lidocaine combination to modulate inflammation is an invasive procedure with specific risks. Bleeding is the most common complication associated with injection therapy. Generally, SAT is also called granulomatous thyroiditis. During inflammation, the glands are coarse in texture and bleeding is infrequent. A little bleeding is mostly caused by needle punctures. We believe that the pressure applied to the puncture area for 20 min after the puncture is sufficient. In this study, the areas of puncture in 48 patients were compressed for 20 min after a puncture. Only one patient experienced increased pain after injection with the DEX-lidocaine combination and ecchymosis of the skin around the puncture area. Ecchymosis disappeared after two weeks. No patient complained of pronounced pain after the puncture and injection process because lidocaine was administered during the injection.

Several observations with regard to the entire injection therapy process are noteworthy. First, the operator must be skilled in thyroid nodule puncture technique. Specifically, the left and right hands can operate flexibly. The anatomy of the neck, such as the sternocleidomastoid muscle, internal jugular vein, common carotid artery, thyroid gland, and trachea must be accurately identified. Second, we recommend the "lateral route" rather than the "vertical route". The "lateral route", that is, through the skin, sternocleidomastoid muscle and gland, facilitates easy operation and patients can conveniently compress the punctured area after the injection. Conversely, if the needle is inserted through the isthmus, it often appears as a vertical needle insertion on the body surface, and postoperative compression may pressure the trachea and cause neck discomfort. Third, transient voice problems, such as hoarseness should be taken into consideration. In this study, three patients complained of transient hoarseness after injection, which was alleviated several hours later. The results suggest that the injection mixture extravasated into the recurrent laryngeal nerve because the lidocaine component in the DEX-lidocaine combination can cause temporary paralysis of the recurrent laryngeal nerve. Therefore, simultaneous bilateral injection should be avoided to prevent bilateral vocal cord paralysis. For patients with bilateral lesions, it is recommended that the combination of DEX and lidocaine should be injected at one-day intervals.

Nonetheless, the present study had the following limitations. First, the sample size was small, and the study was single-centred and retrospective in nature. Second, there might be some selection bias in the recruitment of patients, although no significant differences were observed in the clinical characteristics of patients between the two groups. Therefore, prospective studies using larger sample sizes are required to validate the present findings.

In conclusion, the present study has demonstrated that the performance of capsular thyroid injection therapy in patients with SAT is superior to that of oral PSL with regard to the resolution of initial symptoms. Nevertheless, further research should be conducted using large, multicenter prospective cohort studies to validate the findings of our study.

Declarations

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Compliance with ethical standards

Conflict of interest

The authors declare that they have no conflict of interest.

Author contributions

J.L.H. and C.C. contributed with conceptualization, investigation, and writing of the original draft. D.O. contributed with conceptualization, supervision and funding acquisition. All authors reviewed and approved the final version of the paper.

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Tables

Due to technical limitations, table 1 and 2 is only available as a download in the Supplemental Files section.

Figures

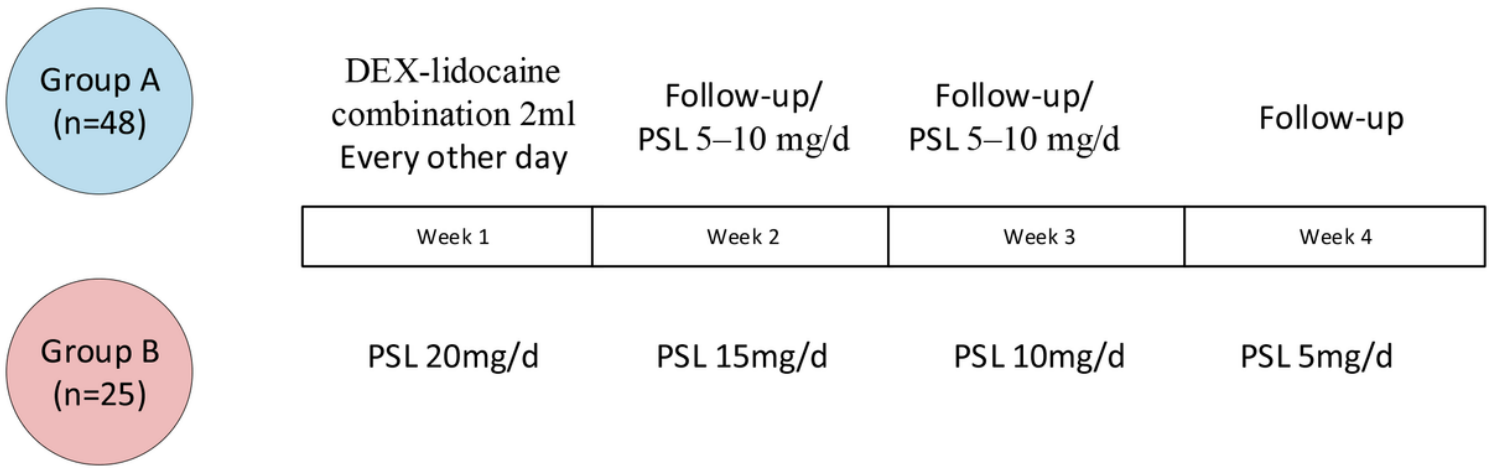

Figure 1

Comparison of the treatment between the two groups.DEX: dexamethasone; PSL: prednisolone.

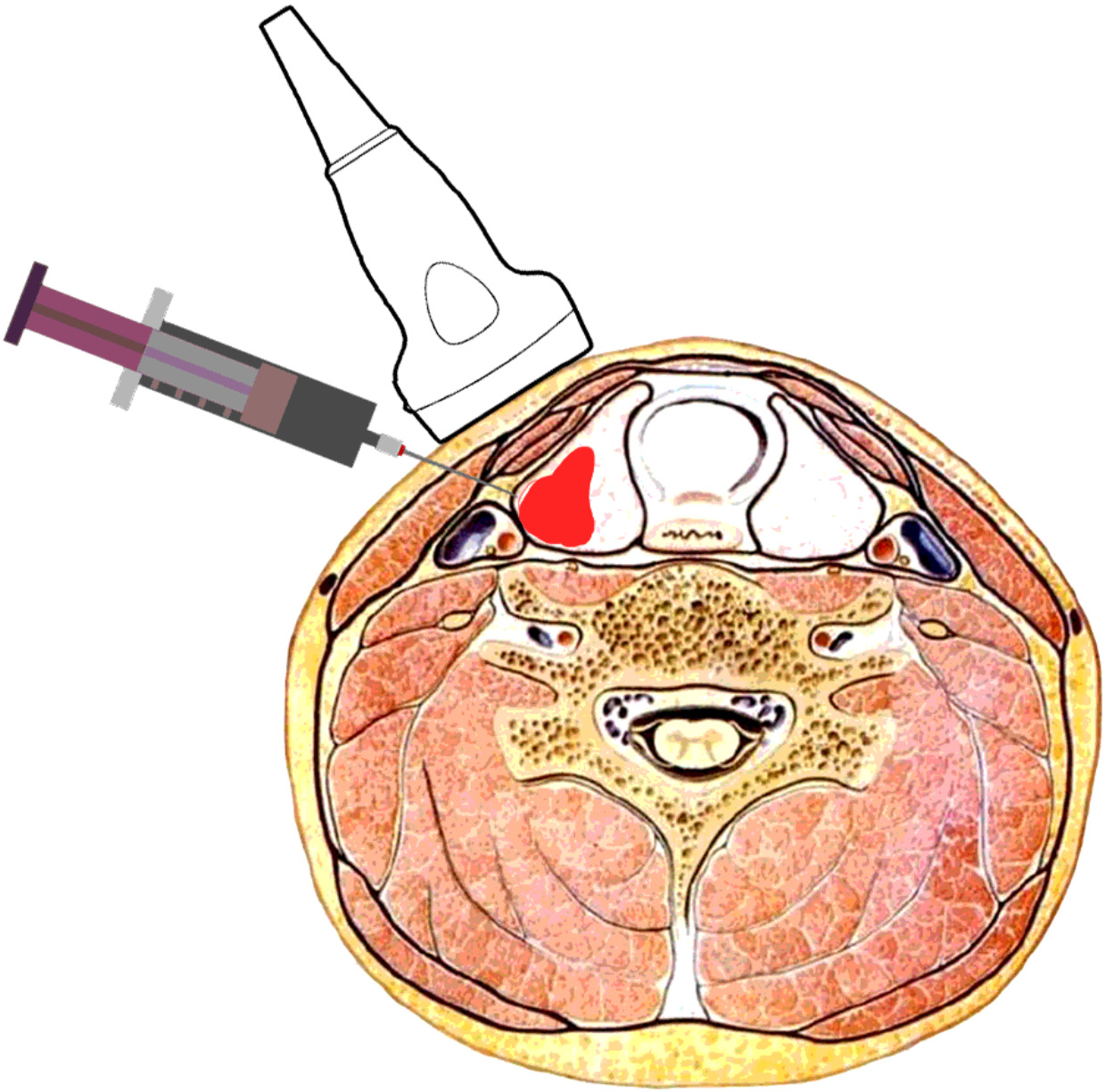

Figure 2

Schematic diagram of injection sites. The irregular area in red indicates the lesion area.

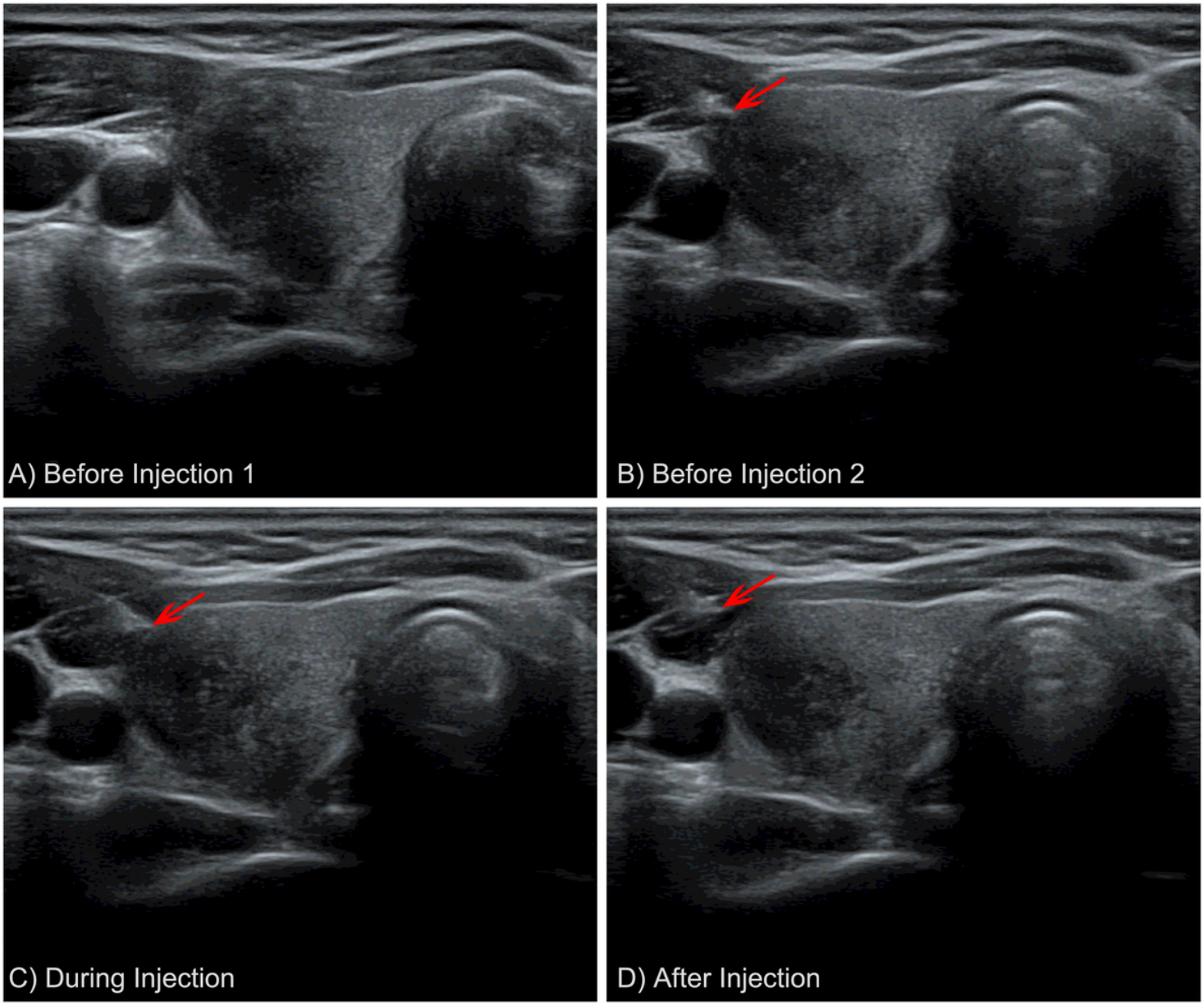

Figure 3

Schematic of the ultrasonic tracking system.A) An ultrasound image of a patient with pSAT before injection.B) The needle tip reaches the injection site.C)The DEX-lidocaine combination was slowly injected into the capsule of the thyroid.D) The needle was removed gently. Note: Red arrows indicate the tip of needle.

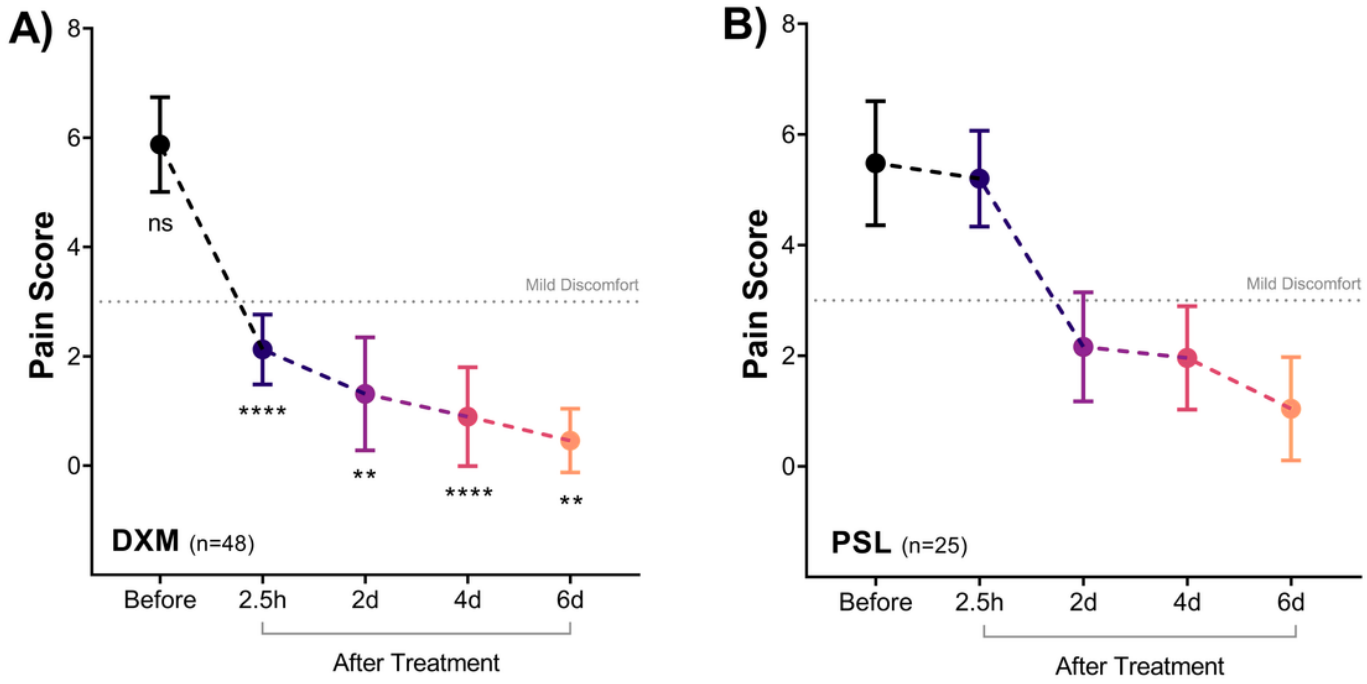

Figure 4

Pain scores after treatment between group A and group B.

Supplementary Files

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- Table1.xlsx
- table2.xlsx