Prospective Study

Lidocaine Injection in the Intramuscular Innervation Zone Can Effectively Treat Chronic Neck Pain Caused by MTrPs in the Trapezius Muscle

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Background: An increasing number of people suffer from neck pain due to life style and prolonged use of computers. Research has revealed that myofascial trigger points (MTrPs) and the intramuscular innervation zone (IZ) are involved in neck pain. MTrPs are induced mainly by IZ dysfunction of the affected skeletal muscle and the 2 do not overlap in location. The question is whether injection treatment in MTrPs or in the IZ is more effective to relieve MTrPs-associated pains. The precise location and body-surface map of the intramuscular IZ in the trapezius muscle and a clinical injection study in the IZ may provide a useful answer to the question.

Objectives: This study aimed to investigate the efficacy of lidocaine injection in the intramuscular IZ for the treatment of chronic neck pain caused by MTrPs in the trapezius muscle.

Study Design: Prospective observational study, approved by the local research ethics.

Setting: University hospital, departments of Anesthesiology and Anatomy.

Methods: First, for the determination of IZ distribution and body-surface mapping, a modified intramuscular Sihler's neural staining technique was applied to elucidate nerve distribution patterns of the trapezius muscle. Then, 120 patients with myofascial pain syndrome (MPS) of the trapezius muscle were randomly divided into 5 groups for analysis. Group 1 (n = 24) received injections of saline (0.9% NaCl) at the MTrPs. Group 2 (n = 24) received injections of 0.5% lidocaine at the MTrPs. Group 3 (n = 24) received injections of saline (0.9% NaCl) at the mid-upper trapezius (Point E). Group 4 (n = 24) received injections of 0.5% lidocaine at Point E. Group 5 (n = 24) received a combined injection of 0.5% lidocaine treatment at both Point E and the lower trapezius (Point F). The injection dose was 4 mL at each injection site. All patients received injections once a week for 4 weeks. The visual analogue scale (VAS) and the frequency of painful days per month (FPD) were obtained before treatment and at 2, 4, and 6 months after treatment.

Results: The intramuscular terminal nerve branches presented a "dendritic" distribution in the trapezius muscle and were connected with each other to form an S-shaped IZ belt in the middle of the muscle belly. Compared with the MTrP injection group, lidocaine-injection therapy in the IZ significantly reduced the degree and frequency of neck pain in patients at 6 months after treatment, especially the combined lidocaine-injection therapy in the IZ of both the mid-upper trapezius and the lower trapezius are more effective (all $P < 0.05$).

Conclusions: This study confirms that lidocaine-injection therapy in the IZ significantly reduces the degree and frequency of neck pain in patients at 6 months after treatment. The combined lidocaine-injection therapy in the IZ of both the mid-upper trapezius and the lower trapezius is more effective. In addition, this study establishes a clear distribution map of intramuscular nerves that will be conducive to the future use of chemical blockers and electrical stimulation in the nervous system in treating MPS of the trapezius muscle.

Limitations: The small number of patients and the short duration of follow-up.

Key words: Neck pain, intramuscular innervation zone, myofascial trigger points, lidocaine

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Because of work conditions and life styles, many people often maintain the same posture for long hours. Frequent and prolonged use of computers and long hours of working at desks keep the neck muscles in a persistent fatigue and strain status. As a result, an increasing number of people suffer from neck pain. Currently, approximately 67% of the population is experiencing neck skeletal muscular injury (1) and neck pain has affected the health conditions of 50% of the ordinary population (2). Neck pain is a non-fatal chronic disease, however, it can result in a loss of capability to work (3) and causes tremendous economic and social burdens to patients and their families (4,5).

Research has revealed that myofascial trigger points (MTrPs) are involved in neck pain (6-8). Excessive use (9) and long hours of maintaining an adverse posture of the neck and shoulder muscles can lead to disorders of muscle dynamic balance and can result in MTrPs occurrence (10). Simons et al (11) defined MTrPs as highly localized and irritable spots that are indurated and cord-shaped and can be palpated in the skeletal muscle. These spots are fine, hypersensitive points on the muscle. Stretching, pressing, or contracting of the skeletal muscles may trigger characteristic pain, which can spread to remote body areas. This is known as referred pain. Based on the absence or presence of spontaneous pain, MTrPs can be divided into active MTrPs and latent MTrPs. In general, active MTrPs refer to the points where spontaneous pain or motion-induced reactive pain occurs, while latent MTrPs refer to the sensitive spots where pain or discomfort occurs only when the spots are pressed.

As one of most vulnerable muscles in working populations (12-15), the trapezius muscle is where MTrPs occur very frequently, particularly the upper trapezius muscle (16-19). MTrPs in the trapezius muscle may cause not only neck pain and limited motility of the neck but also tension-type headaches, dizziness, and shoulder dysfunction (20-23).

In recent years, to effectively improve the treatment outcomes of MTrPs-caused pain, researchers have conducted a large number of pathogenic studies, among which the "motor end-plate region dysfunction" hypothesis provides the most reasonable explanation regarding the pathophysiologic mechanism of MTrPs (24,25). The end-plate region is also called the intramuscular innervation zone (IZ), where the intramuscular terminal nerve fibers of α–motor neurons attach to the skeletal muscular fibers (26-28). Dysfunction of the IZ might induce MTrPs occurrence. However, in a recent study, surface electromyography (EMG) revealed that MTrPs in the upper trapezius muscle did not overlap with the IZ (29). At present, injection therapy of MTrPs has been widely used in clinical practice due to its rapid pain-relieving effect and easy application in outpatients (30-34). However, because the pain-relieving effect of MTrPs injection sometimes lasts only a short period of time, a number of patients have to re-visit outpatient clinics for frequent treatments.

Because MTrPs are induced mainly by IZ dysfunction of the affected skeletal muscle and the 2 do not overlap in location, a question arises regarding whether MTrPs injection is a clinically reasonable treatment method. This concern also leads to another question regarding whether injection treatment in the IZ of the affected skeletal muscle can consistently and effectively relieve MTrPs-associated pains. Although the intramuscular nerve distribution in the trapezius muscle has been described previously, only the course of the main nerve trunk in the muscles was clarified (35,36). The precise location and body-surface map of the intramuscular IZ in trapezius remain unclear.

Based on the above discussion, this study adopted 2 experimental steps. First, a modified intramuscular Sihler's neural staining technique was used to elucidate intramuscular nerve distribution patterns and to identify the area innervated by "dendritic" branches in the trapezius muscle. This step helped clarifying the intramuscular IZ distribution and its body-surface projection map. Second, lidocaine injection therapy at corresponding IZ sites was performed for the treatment of neck pain caused by MTrPs in the trapezius. The efficacy of the treatment was evaluated.

Methods

This study received approval from the Local Human Research Ethics Committee.

Gross Anatomical Observation

All cadavers were obtained from donors who voluntarily agreed to using their bodies for education and scientific research after their death. The use of the bodies was approved by the donors and their families in writing and by the Ethics Committee. Twenty-two adult cadavers (14 women and 8 men; age range 21 – 64 years) were collected locally during the period between 2006 and 2008. All cadavers were routinely fixed with formalin for 2 years. No noticeable pathological changes or surgical or traumatic lesions were observed on the head, the neck, the shoulders, or the back. Forty-

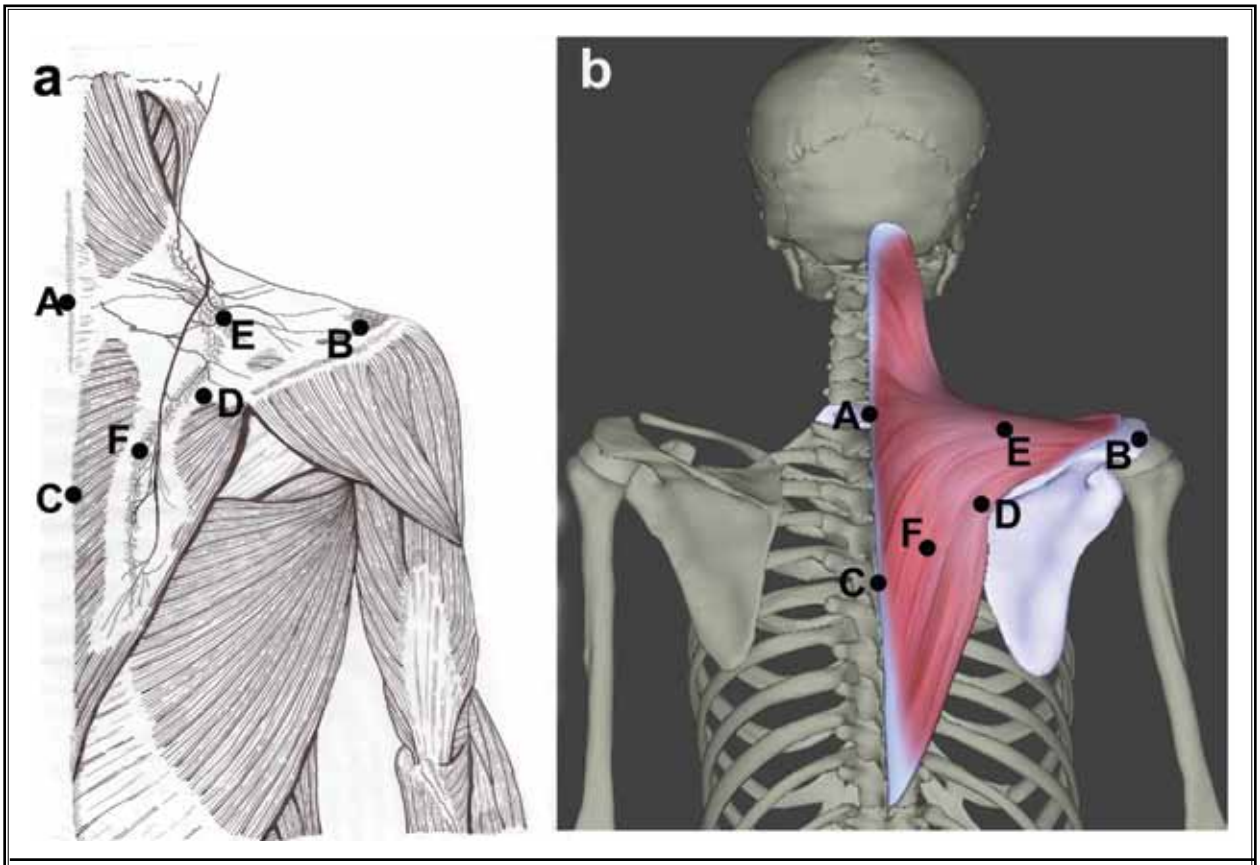

Fig. 1. *(a) A schematic diagram demonstrating the actual distribution of Sihler-stained intramuscular nerves of the trapezius muscle in the human body. (b) Point E is the intersection of the line AB connecting the spinous process of the seventh cervical vertebra (C7) (Point A) and the midpoint at the lateral margin of the acromion (Point B) with the IZ; Point F is the intersection of the line CD connecting the spinous process of the fifth thoracic vertebra (T5) (Point C) and the tubercle at the medial edge of the scapula (Point D) and the IZ.*

four pieces (both sides) of trapezius muscles were dissected and carefully observed for the nerves' entrance into the muscle and whether there are anatomical variations. Two straight-line distances were measured on the bodies; from the spinous process of the seventh cervical vertebra (C7) (Point A) to the lateral margin of the acromion (Point B, line AB), and from the spinous process of the fifth thoracic vertebra (T5) (Point C) to the medial end of the spine of the scapula (Point D, line CD) (Fig. 1b).

A Modified Intramuscular Sihler's Neural Staining Technique

Forty-four pieces of trapezius muscles were harvested from 22 cadavers, and the fat and fascial tissues were removed. Based on our previous studies, a modified intramuscular Sihler's neural staining technique was performed with the following steps: depigmentation, decalcification, staining, destaining, neutralization, and clearing. This method was described in detail in previous publications (37,38). The whole process took approximately 3 months. Finally, the specimens were stored in 100% glycerin with a few thymol crystals added.

After completion of the above staining procedures, the specimens were placed on an x-ray film viewing box for observation of the intramuscular nerve distribution patterns and the distribution of the IZ, which is the location where the terminal dendritic nerve branches were concentrated. In addition, we carefully observed the anatomical variations of the distribution of the IZ, variations were excluded from our study. Finally, the intramuscular distributions of the IZ and the nerves were projected to the trapezius muscle of the original

size for the measurement of the straight-line distances between Point A and Point E (the midpoint of the intersection between AB and IZ) and between Point C and Point F (the midpoint of the intersection between CD and IZ) (Fig. 1a).

Participant Selection

All participants signed informed consent forms prior to the study. This study recruited 120 patients ranging in age from 20 to 50 years who had neck pain and had visited our hospital's outpatient setting during the period from February 2012 to March 2014. The inclusion criteria were as follows (29,39-42): (1) history of neck pain longer than 3 months, accompanied in some cases by either limited mobility of the neighboring joints or referred pain in the occipital area or the head; (2) one active MTrP in the left or right mid-upper trapezius muscle; (3) palpable taut ribbon-shaped or cord-shaped structures at the MTrP sites; (4) local muscular twitch response with snapping palpation of MTrPs; (5) accompanied often by insomnia and neck muscle fatigue; and (6) long history of long hours working at a desk or history of neck muscle strain and fatigue.

The exclusion criteria included histories of fibromyalgia, temporomandibular joint disorders, rheumatic or neurological diseases, cervical spondylosis, neck muscle sprain, or severe systemic diseases such as diabetes mellitus. In addition, patients with depression; mental retardation; pregnancy; bone and joint diseases; local anesthetic allergy; history of malignancy; bleeding diathesis and anemia; neuromuscular dysfunction; hyperthyroidism and hypothyroidism; recent usage of antiepileptic, antipsychotic, and antidepressant; or a history of surgery of the neck or the cervical spine were also excluded. In this study, magnetic resonance imaging or computed tomography were performed when considered necessary.

A doctor with 10 years of experience in myofascial pain syndrome (MPS) diagnosis and treatment identified the MTrPs in the trapezius muscles of all patients. MTrPs were defined as the sites where painful taut ribbon-shaped or cord-shaped structures were palpable and were accompanied by remote referred pain.

Study Design

Based on the determined distribution pattern of the IZ, 120 patients who met the inclusion criteria were randomly divided into 5 groups: Group 1 (n = 24) received injections of saline (0.9% NaCl) at the MTrPs. Group 2 (n = 24) received injections of 0.5% lidocaine at the MTrPs. Group 3 (n = 24) received injections of saline (0.9% NaCl) at Point E. Group 4 (n = 24) received injections of 0.5% lidocaine at Point E. Group 5 (n = 24) received a combined injection of 0.5% lidocaine treatment at both Point E and Point F (Fig. 1b). The injection dose was 4 mL at each injection site. All patients received injections once a week for 4 weeks.

Measurement Procedures

The examiner was blinded to the paitent grouping. The following indicators were obtained before treatment and at 2, 4, and 6 months after treatment: (1) the visual analogue scale (VAS) score: score 0 indicated no pain, and score 10 indicated the most serious pain; (2) the frequency of painful days per month (FPD).

Statistical Analysis

SPSS 17.0 software (SPSS Inc., Chicago, IL) was used for data analysis. For parametric tests, except for the data from the paired-designed experiments, independent sample t tests were used for comparisons between 2 groups, and one-way analysis of variance (ANOVA) was used for comparisons among groups.

Results

The Extramuscular Course of the Nerves

In this study, we did not find any anatomic variations. The trapezius muscle can be divided into 3 portions (upper, middle, and lower). It is innervated by the spinal accessory nerve (SAN) and the trapezius branches of the cervical plexus (TBCP) C2-C4. After entering the anterior edge of upper trapezius muscle, one main trunk of the SAN courses 2 – 3 cm before it reaches the deep middle portion. Afterwards, the TBCP joins the main trunk of the SAN, continues downwards into the deep lower portion and eventually sends branches into the muscle bundles. One branch innervating the upper trapezius muscle originates from the main trunk of the SAN 1.5 cm from the anterior edge of the muscle and sends another 1 – 2 branches into the deep upper muscle part. One to 3 branches (mostly one) originate from the TBCP and enters the trapezius muscle from the underneath of the main trunk of the SAN. After the merging of the TBCP and SAN, they together send 4 – 5 branches in the deep middle muscle to innervate the mid-upper portion and 2 – 4 branches in the deep lower muscle to innervate the lower portion (Fig. 2).

Intramuscular Nerve Distribution Pattern and Iz Localization

After the modified intramuscular Sihler's nerve staining, the trapezius muscle presented an intact morphology; the muscle tissue appeared transparent or like translucent jelly and the nerve branches were stained purple-black (Fig. 3). At the anterior edge of the trapezius muscle, the main trunk of the SAN sends one primary branch to innerve the upper trapezius before it enters the deep trapezius muscle. The main trunk of the SAN travels downwards in the deep trapezius muscle and sends 1 – 3 primary branches into the upper portion (Figs. 3 and 4). In the deep middle trapezius muscle, the TBCP merges with the main trunk of the SAN and together they send 4 – 5 primary branches to innerve the mid-upper portion and 2 – 4 primary branches to the lower trapezius muscle. The primary branches distributed in the middle trapezius mostly course to the insertion end of the muscle and send secondary branches into the muscle after coursing parallel to the muscular fibers for a certain length. The primary branches supplying the lower trapezius mostly course to the origin end of the muscle and send the secondary branches into the muscle after coursing parallel to the muscular fibers for a certain length (Figs. 4 and 5). The secondary branches innervating the upper, middle, and lower trapezius muscle regions send a large number of terminal nerve branches showing a "dendritic"

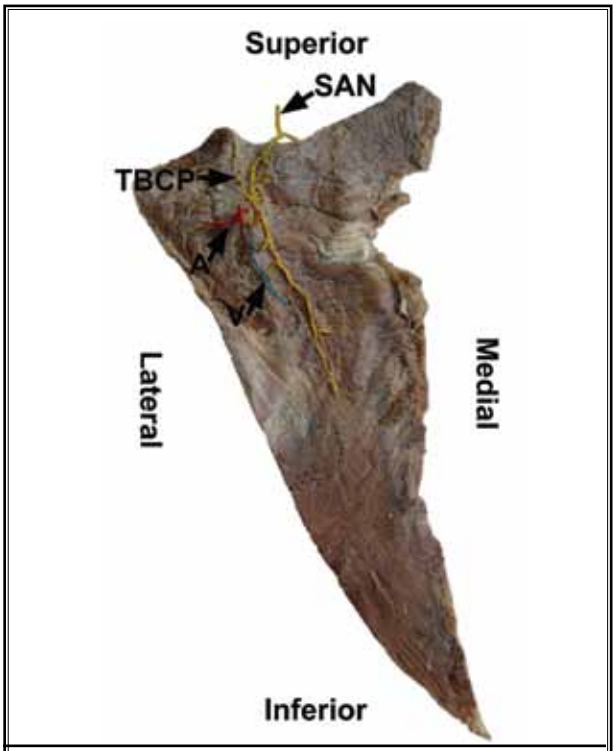

Fig. 2. *The branches, course, and entrance of the extramuscular nerve trunks into different portions of the trapezius muscle (right side, deep side view; SAN: the spinal accessory nerve; TBCP: the trapezius branches of the cervical plexus; A: the artery of trapezius muscle; V: the vein of trapezius muscle).*

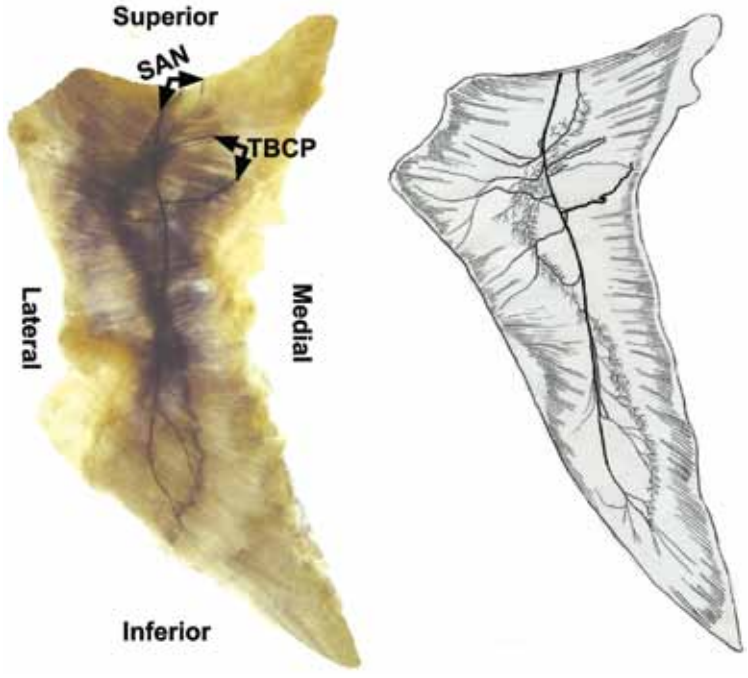

Fig. 3. *The spatial distribution of the SAN and TBCP in the right trapezius muscle stained with Sihler's technique. View from the "deep" side: the left panel shows an actual image and the right panel is a graphic representation (right side; SAN: the spinal accessory nerve; TBCP: the trapezius branches of the cervical plexus).*

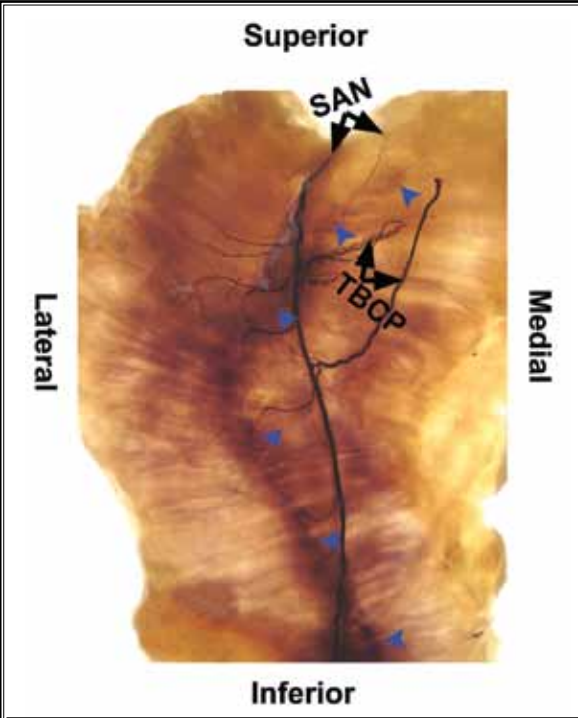

Fig. 4. *The intramuscular nerve distribution in the mid-upper trapezius muscle, the blue arrowheads denote the anastomosis of terminal nerve branches (right side, deep side view; SAN: the spinal accessory nerve; TBCP: the trapezius branches of the cervical plexus).*

distribution pattern and anastomosing with each other (Figs. 4 and 5). Enormous anastomosing branches are found in all muscle bellies where the terminal nerve branches are concentrated. These areas are connected with each other to form an S-shaped IZ belt throughout the muscle (Figs. 3 and 6).

The average length of line AB and line CD is 17.86 ± 0.64 cm and 13.24 ± 0.58 cm, respectively. When projecting the IZ and the intramuscular nerve distribution to the original-sized trapezius muscle (muscle before staining), the straight line distances are 9.14 ± 0.35 cm between Point E and Point A; and 6.62 ± 0.43 cm between Point F and Point C. Point E is the spot where enormous terminal branches of the SAN anastomose with a small number of terminal branches of the TBCP in the middle and upper trapezius regions. Point F is the spot where the terminal nerve branches of the SAN anastomose with a relatively large number of terminal branches of the TBCP in the lower trapezius muscle (Fig. 1a).

Clinical Research

This study enrolled 120 patients (77 women and 43 men) with a mean age of 36.26 ± 4.51 years (20 – 50 years). Forty-five patients were affected on the left upper trapezius muscle by MTrPs and 75 patients on

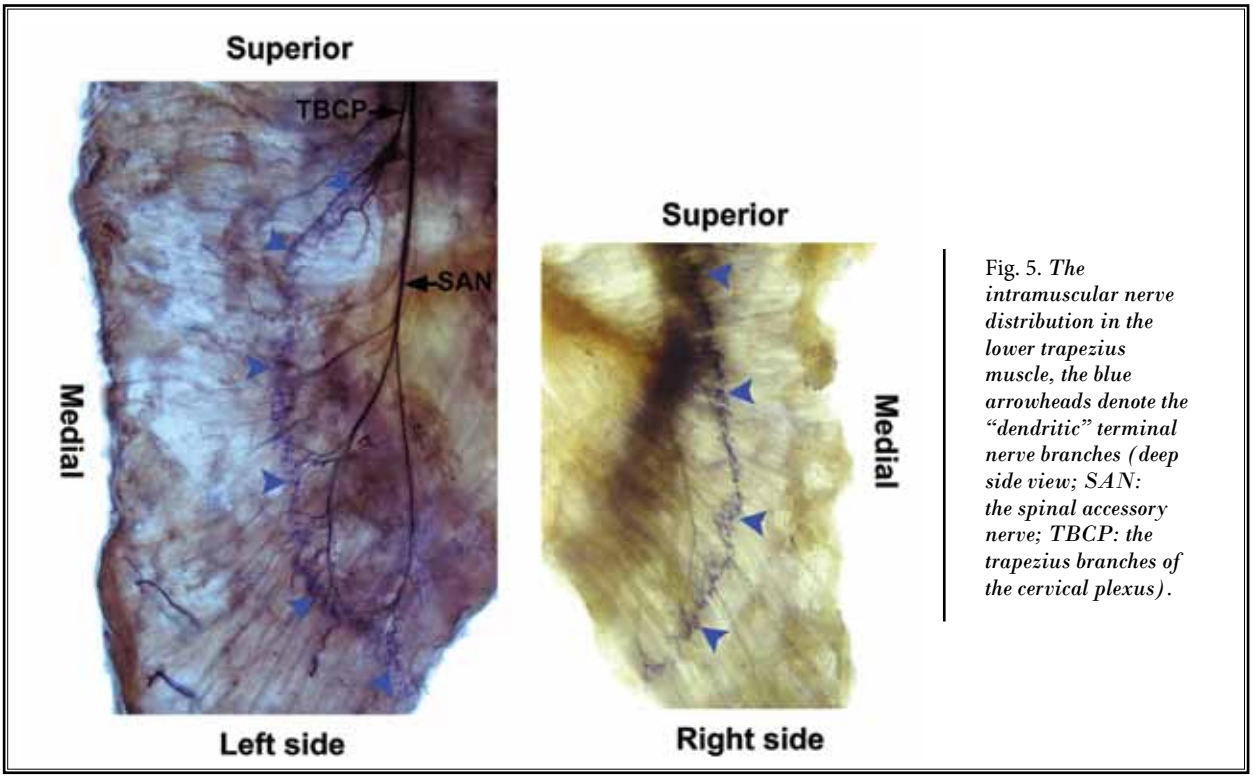

Fig. 5. *The intramuscular nerve distribution in the lower trapezius muscle, the blue arrowheads denote the "dendritic" terminal nerve branches (deep side view; SAN: the spinal accessory nerve; TBCP: the trapezius branches of the cervical plexus).*

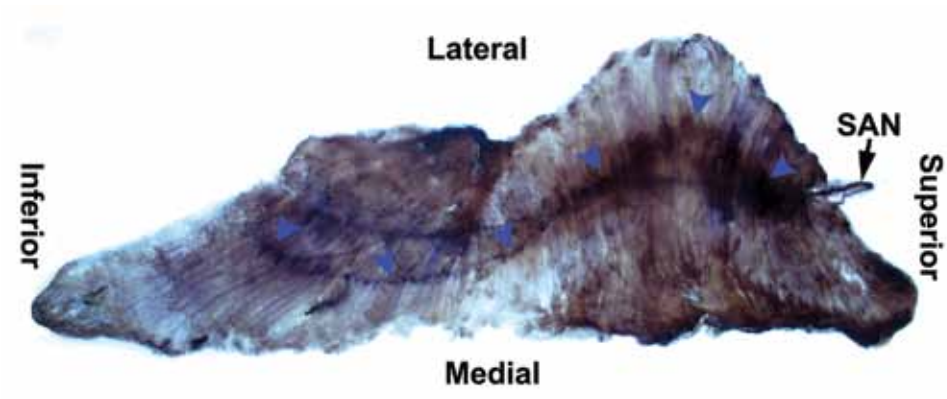

Fig. 6. *The IZ formed through anastomosis of intramuscular "dendritic" terminal nerve branches in the trapezius muscle, the blue arrowheads denote an S-shaped structure where the intramuscular terminal nerve IZ is located (Left side, superficial side view; SAN: the spinal accessory nerve).*

Table 1. *Demographic data of patients with neck pain.*

	Group 1	Group 2	Group 3	Group 4	Group 5
N (Men/Women)	9/15	8/16	9/15	8/16	9/15
Affected side (Left/Right)	8/16	10/15	10/14	8/16	9/15
Age (Years)	36.58 ± 3.84	37.21 ± 6.81	38.42 ± 4.64	36.67 ± 4.81	35.83±5.40
Weight (kg)	58.34 ± 4.52	59.10 ± 4.98	57.88 ± 5.14	58.91 ± 5.32	58.83±4.76
Height (cm)	161.93 ± 5.17	160.64 ± 5.93	161.44 ± 6.26	160.89 ± 5.17	160.87±6.39

Data are expressed as means ± SD.

the right. Table 1 displays the general patient information. There were no differences in age, gender, height, weight, or affected side between the groups.

Table 2 shows that the average VAS scores during pre-treatment and at the 2, 4, and 6 months after injection in Group 1 are 7.06 ± 0.88, 6.81 ± 0.90, 6.89 ± 0.89, 6.98 ± 0.90; in Group 2: 7.03 ± 1.25, 2.67 ± 0.70, 5.06 ± 0.93, 6.83 ± 1.20; in Group 3: 7.03 ± 0.88, 6.71 ± 0.88, 6.77 ± 0.90, 6.85 ± 0.92; in Group 4: 7.02 ± 0.97, 2.55 ± 0.54, 4.44 ± 0.80, 5.23 ± 0.85; and in Group 5: 7.05 ± 1.06, 1.80 ± 0.43, 3.33 ± 0.66, 4.12 ± 0.44, respectively.

Tables 2 and 3 display the VAS and FPD scores of the 5 groups before treatment and 2, 4, and 6 months after treatment. There were no differences in the VAS and FPD scores among the 5 groups before treatment (all $P > 0.05$). Compared with the data before treatment, the VAS and FPD scores were significantly improved in Groups 2, 4, and 5 at post-treatment months 2 and 4 (all $P < 0.05$), and this improvement remained at post-treatment month 6 in Groups 4 and 5 (all $P < 0.05$) (Tables 4 and 5).

Compared with Group 1, Group 2 had a significantly improved VAS and FPD scores at post-treatment months 2, 4, and 6 ($P < 0.05$); compared with Group 3, Group 4 showed significantly improved treatment outcomes in terms of the VAS and FPD scores at post-treatment months 2, 4, and 6 ($P < 0.05$); but there were no differences in the VAS and FPD scores between Group 1 and 3 ($P > 0.05$) (Tables 2 and 3). Compared with Group 2, the VAS and FPD scores improvement persisted at post-treatment month 6 in Group 4 ($P < 0.05$). In addition, Group 5 had better VAS and FPD scores than Group 4 at post-treatment months 2, 4, and 6 (Tables 2 and 3).

No serious adverse responses were observed during the treatment and follow-up periods except Group 1 had 2 cases of slight muscle spasm.

Discussion

Our study reveals that the intramuscular terminal nerve branches in the trapezius muscle has a "dendritic" distribution which forms an S-shaped IZ belt in the middle of the muscle belly through close interconnections. Compared with the MTrP injection group, lidocaine-injection therapy in the IZ significantly reduced

Table 2. *Comparison of the VAS of the 5 groups before and after treatment.*

		G1	G2	G3	G4	G5	* *P* value
VAS-BT	**N**	24	24	24	24	24	
	Mean	7.06	7.03	7.03	7.02	7.05	0.9998
	SD	0.88	1.25	0.88	0.97	1.06	
VAS-2 months-AT	**Mean**	6.81	2.67	6.71	2.55	1.80	< 0.0001
	SD	0.90	0.70	0.88	0.54	0.43	
	Comparison	G1 vs G2	G1 vs G3	G2 vs G4	G3 vs G4	G4 vs G5	
	***P* value**	< 0.0001	0.6430	0.5726	< 0.0001	0.0004	
VAS-4 months-AT	**Mean**	6.89	5.06	6.77	4.44	3.33	< 0.0001
	SD	0.89	0.93	0.90	0.80	0.66	
	Comparison	G1 vs G2	G1 vs G3	G2 vs G4	G3 vs G4	G4 vs G5	
	***P* value**	< 0.0001	0.6232	0.7603	< 0.0001	< 0.0001	
VAS-6 months-AT	**Mean**	6.98	6.83	6.85	5.23	4.12	< 0.0001
	SD	0.90	1.20	0.92	0.85	0.44	
	Comparison	G1 vs G2	G1 vs G3	G2 vs G4	G3 vs G4	G4 vs G5	
	***P* value**	0.5518	0.6180	< 0.0001	< 0.0001	< 0.0001	

VAS: visual analogue scale; BT: before treatment; AT: after treatment; N: number of patients; SD: standard deviation; * One way Analysis of Variance (ANOVA), if *P* value is < 0.05, *P* value of between groups are compared.

Table 3. *Comparison of the FPD of the 5 groups before and after treatment.*

		G1	G2	G3	G4	G5	* *P* value
FPD-BT	**N**	24	24	24	24	24	
	Mean	11.75	11.83	11.63	11.83	11.75	0.9960
	SD	2.01	2.32	1. 91	1.61	1.89	
FPD -2 months-AT	**Mean**	10.92	5.79	10.46	5.33	3.50	< 0.0001
	SD	1.82	1.79	1.84	1.05	0.98	
	Comparison	G1 vs G2	G1 vs G3	G2 vs G4	G3 vs G4	G4 vs G5	
	***P* value**	< 0.0001	0.2671	0.2670	< 0.0001	< 0.0001	
FPD -4 months-AT	**Mean**	11.04	8.46	10.75	8.33	6.08	< 0.0001
	SD	1.83	1.91	1.80	1.13	1.06	
	Comparison	G1 vs G2	G1 vs G3	G2 vs G4	G3 vs G4	G4 vs G5	
	***P* value**	< 0.0001	0.5263	0.7858	< 0.0001	< 0.0001	
FPD -6 months-AT	**Mean**	11.46	11.38	11.29	9.38	7.54	< 0.0001
	SD	1.89	2.41	1.78	1.24	1.41	
	Comparison	G1 vs G2	G1 vs G3	G2 vs G4	G3 vs G4	G4 vs G5	
	***P* value**	0.8724	0.7482	0.0002	0.0003	0.0006	

FPD: frequency of painful days per month; BT: before treatment; AT: after treatment; N: number of patients; SD: standard deviation; * One way Analysis of Variance (ANOVA), if *P* value is < 0.05, *P* value of between groups are compared.

the degree and frequency of neck pain in patients at 6 months after treatment. The combined lidocaine-injection therapy in the IZ of both the mid-upper trapezius (Point E) and the lower trapezius (Point F) was more effective.

Although the question regarding whether a central or peripheral mechanism is responsible for MTrPs remains unanswered (43,44), researchers believe that dysfunction of motor end-plates might be one of the major causes for MTrPs (24,28). A motor end-plate is

Table 4. *Comparison the VAS scores before and after treatment in each group.*

	BT vs 2 month-AT	BT vs 4 month-AT	BT vs 6 month-AT	2 month-AT vs 4 month-AT	2 month-AT vs 6 month-AT	4 month-AT vs 6 month-AT	*P* value
G1	> 0.05	> 0.05	>0.05	> 0.05	> 0.05	> 0.05	> 0.05
G2	< 0.0001	< 0.0001	>0.05	< 0.0001	< 0.0001	< 0.0001	< 0.0001
G3	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05
G4	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	> 0.05	< 0.0001
G5	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.001	< 0.0001

VAS: visual analogue scale; BT: before treatment; AT: after treatment

Table 5. *Comparison the FPD scores before and after treatment in each group.*

	BT vs 2 month-AT	BT vs 4 month-AT	BT vs 6 month-AT	2 month-AT vs 4 month-AT	2 month-AT vs 6 month-AT	4 month-AT vs 6 month-AT	*P* value
G1	> 0.05	> 0.05	>0.05	> 0.05	> 0.05	> 0.05	> 0.05
G2	< 0.0001	< 0.0001	>0.05	< 0.0001	< 0.0001	< 0.0001	< 0.0001
G3	< 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05
G4	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.05	< 0.0001
G5	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.001	< 0.0001

FPD: frequency of painful days per month; BT: before treatment; AT: after treatment

the site where an α-motor nerve ending attaches to the muscular fiber, namely, the IZ. Sustained depolarization on the postsynaptic membrane of the skeletal muscle end-plate may results in a "local hypoxic energy crisis," causing local ischemia and hypoxia, which may stimulate the release of various substances from the nervous and vascular systems. Ultimately, this leads to MTrPs through complex mechanisms such as sustained sensitizations in the sensory system and reflex arcs in the autonomic nervous system. Drug injection at MTrPs has been commonly used for MPS treatment in clinical practice, but this procedure has not achieved satisfactory performance in prolonged analgesic effects (45,46). Theoretically, MTrPs pain is caused by dysfunction of the IZ. Thus, one of the major objectives of this study was to address the question regarding whether IZ injection would prolong the analgesic effects of drugs.

The intramuscular Sihler's neural staining technique is the internationally accepted tool to elucidate the distribution of the intramuscular terminal nerve fiber branches without disruption of the integrity of skeletal muscle (37,47,48). This technique has the advantage of not only demonstrating the relationship between muscle bundles and intramuscular nerve distributions that cannot be observed by the naked eye but also directly elucidates the intramuscular terminal nerve branches and their anastomotic relationships. Using this technique, the entire specimen can become transparent, enabling the observation of a full 3-dimensional structure of nerve distribution.

As demonstrated in our observation, the main trunk of the SAN courses downwards inside the trapezius muscle and merges with the TBCP in the middle of the trapezius muscle. Two to 4 primary nerve branches originate from the merged nerve to innerve the mid-upper trapezius muscle. A large number of "dendritic" secondary branches (mainly consisting of the branches of the SAN) form the mid-upper IZ through anastomoses after originating from the primary branches within the muscle. Since the MTrPs were located in the mid-upper trapezius muscle in all selected patients, we chose the Point E of the straight line connecting the C7 spinous process (Point A) and the lateral margin of the acromion (Point B) with the IZ of the mid-upper trapezius muscle as one of the injection sites. In addition, from the perspective of the overall intramuscular nerve branching pattern, the IZ extends across the upper, middle, and lower portions of the trapezius muscle through intramuscular nerve terminal anastomoses. A larger number of IZ forming terminal branches are from the TBCP participation in the lower portion. Based on such an IZ distribution characteristic, we also chose Point F in the lower trapezius as an injection site.

Lidocaine is a common local anesthetic drug and can reversibly inhibit the transmission of nerve impulses. In general, intramuscular terminal nerve fibers,

ganglia, and the synaptic regions in the central nervous system are the most sensitive to local anesthetics, and thin nerve fibers can be blocked more easily than thick nerve fibers. In addition, local anesthetic drugs can block the transmission of peripheral pain signals to the central nervous system (49). The underlying mechanism of lidocaine is that it can block the voltage-gated sodium channels and reduce sodium ion influx, thereby reducing the depolarization frequencies of nerve fibers and other excitable cells and ultimately inhibiting the spontaneous discharge activities of excitable cells (50). In the present study, the lidocaine injection at MTrPs decreased the VAS and FPD scores in Group 2 at post-treatment months 2 and 4; however, these indicators returned to the pre-treatment levels at post-treatment month 6. Compared with Group 2, the lidocaine injection at the IZ of the trapezius muscle in Groups 4 and 5 greatly improved the VAS and FPD scores even 6 months after treatment. In addition, the saline injection at the MTrPs and IZ in Groups 1 and 3 didn't have any therapeutic effects. We deduced that the reason behind the superior outcomes of lidocaine injection in the IZ to MTrP injection might be that IZ injection could suppress the sensitization of terminal nerve fibers more effectively, thereby reducing the release of pain mediators and blocking pain propagation in skeletal muscle. Another possible mechanism might be that the nociceptive signals transmitted into the central nervous system were reduced due to the suppression of the sensitization of terminal nerve fibers in the IZ, thus weakening central sensitization and central regulation of MTrPs. From the angle of therapeutics, this study indirectly confirmed that IZ dysfunction could be one of reasons for MTrPs (24,28).

In addition, this study demonstrated that Group 5 patients had improved VAS and FPD scores compared to those of Group 4 at post-treatment months 2, 4, and 6. Although MTrPs were located in the mid-upper trapezius muscles in all patients enrolled in this study, the IZ in the upper, middle, and lower portions were not isolated and instead connected with each other to form an S-shaped belt structure, with relatively larger numbers of terminal nerve branches in the IZ of the lower trapezius. Therefore, Point F injection in Group 5 might inhibit the sensitization of terminal nerve fibers in the lower trapezius muscle, in particular the terminal fibers originating from the TBCP, thus decreasing the effect of the lower signals on the nerve fibers in the mid-upper muscle and reducing the possibility of nociceptive signal transmission from the lower trapezius to the central nervous system.

Conclusions

The findings of this study reveal that the intramuscular terminal nerve branches are anastomosed with each other and form an S-shaped IZ in the middle of the trapezius muscle belly. Further, this study confirms that lidocaine-injection therapy in the IZ significantly reduces the degree and frequency of neck pain in patients at 6 months after treatment. The combined lidocaine-injection therapy in the IZ of both the mid-upper trapezius and the lower trapezius are more effective. In addition, this study supports the hypothesis that IZ dysfunction can be a cause for trigger point development and establishes a clear distribution map of intramuscular nerves that will be conducive to the future use of chemical blockers and electrical stimulation in the nervous system in treating MPS of the trapezius muscle.

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