

Original Article

Low dose high frequency ultrasound therapy for stellate ganglion blockade in complex regional pain syndrome type I: a randomised placebo controlled trial

Ayhan Askin¹, Serpil Savas², Hasan Rifat Koyuncuoglu³, Hale Hekim Baloglu⁴, Mehmet Fatih Inci⁵

¹Department of Physical Medicine and Rehabilitation, Katip Çelebi University Atatürk Education and Research Hospital, Izmir, Turkey; ²Department of Physical Medicine and Rehabilitation, School of Medicine, Süleyman Demirel University, Isparta, Turkey; ³Department of Neurology, School of Medicine, Süleyman Demirel University, Isparta, Turkey; ⁴Physical Medicine and Rehabilitation Clinic, State Hospital, Cankiri, Turkey; ⁵Department of Radiology, Katip Celebi University Atatürk Education and Research Hospital, Izmir, Turkey

Received September 27, 2014; Accepted November 25, 2014; Epub December 15, 2014; Published December 30, 2014

Abstract: Background: We aimed to determine the sympatholytic and clinical effects of low dose high frequency ultrasound (US) applied on stellate ganglion in Complex Regional Pain Syndrome (CRPS) type I patients. Material and method: Forty-five patients with CRPS type I were randomly allocated into three groups. Pharmacological treatment, transcutaneous electrical nerve stimulation (TENS), contrast bath and exercise were applied to all groups for 20 sessions. In addition to this treatment protocol, low dose high frequency US was applied on stellate ganglion as 0.5 watts/cm² in group I; 3 watts/cm² in group II and as placebo in group III. Forty age and sex matched healthy controls were served as controls. Sympathetic skin response (SSR) was used for determining the sympatholytic effects of US. Pain was assessed with visual analog scale (VAS), limitation of total finger flexion was assessed with finger pulp-distal crease distance, muscle strength was assessed with measuring the grip strength, upper extremity disability was assessed with Disability of the Arm, Shoulder and Hand (DASH) scale before and after the treatment. Results: All groups evaluated in terms of VAS score, finger pulp-distal crease distance, grip strength and DASH score after the treatment. The improvements in those parameters were not statistically significant between the groups ($P > 0.05$). SSR latency was significantly shorter in CRPS patients than controls ($P < 0.05$). Pre- and post-treatment SSR amplitude and latency values were not different within patient groups ($P > 0.05$). The differences in pre- and post-treatment SSR amplitude and latency values were not statistically different between patient groups ($P > 0.05$). Conclusion: Low dose high frequency US applied on stellate ganglion did not make a sympathetic blockade and was not of further benefit for pain, range of motion, grip strength and upper extremity disability in CRPS type I patients.

Keywords: Complex regional pain syndromes, ultrasonic therapy, stellate ganglion

Introduction

Complex Regional Pain Syndrome (CRPS) type I and II usually develops after a preceding noxious event with or without a definable nerve lesion and is characterized by continuous pain or hyperalgesia/hyperesthesia disproportionate to any initiating event, edema, skin blood flow or sudomotor abnormalities on the affected limb [1]. Treatment of CRPS remains controversial because of the multifactorial nature of its pathophysiological mechanisms [2]. Various clinical treatments are used for CRPS such as pharmacological therapy, physiotherapy and occupational therapy, motor imaginary program

and some invasive procedures such as epidural clonidine, intratecal baclofen, spinal cord stimulation, intravenous regional blockade, stellate ganglion blockade and lumbar sympathetic blockade with variable therapeutic success [3]. The presumed role of excessive sympathetic nervous system outflow in key CRPS characteristics was the traditional rationale for clinical use of selective sympatholytic blocks (e.g. stellate ganglion) for pain and symptom relief in CRPS patients [2].

Stellate ganglion blockade is widely used, valuable but an invasive anesthetic technique in CRPS treatment with possible serious side

Therapeutic ultrasound in complex regional pain syndrome

effects such as cardiac arrest [4], locked-in syndrome [5] and convulsions [6]. Electrophysical agents, for example diadynamic currents are successfully used for stellate ganglion blockade in CRPS and its sympatholytic effect is shown by sympathetic skin responses (SSR) [7]. Therapeutic ultrasound (US), a non-invasive and easily applicable electrophysical agent with no side effects has been used for sympatholytic effect in CRPS patients [8-10]. Although good clinical response had been reported, the sympatholytic effect has not been objectively documented in those studies.

The aim of this study was to examine the sympatholytic effect of low dose high frequency US applied on stellate ganglion in two different doses (0.5 watts/cm² vs 3 watts/cm², both at 1 MHz frequency) in upper extremity CRPS type I by using SSR for determining the sympathetic effect. We also investigated the clinical effects of low dose high frequency US in CRPS type I in terms of pain, range of motion, grip strength and upper extremity disability.

Material and methods

Forty-five patients with upper extremity CRPS type 1 who admitted to outpatient clinic of our hospital and 40 healthy controls were included in this randomised controlled, parallel group study with a 1:1:1 allocation ratio. CRPS type I diagnosis was made according to IASP Consensus Report [11]. The patients with peripheral or central nerve lesions, diabetes mellitus, severe heart failure, severe hypertension, cardiac conduct disorders, chronic obstructive pulmonary disease, chronic alcoholism, rheumatologic disease, malignancy or thyroid disease and/or patients using anticholinergic or antihypertensive medications were not included in the study. Age, gender and the type of injury that caused CRPS were recorded. Body mass index (BMI) was calculated with the formula kg/m². Blood count, biochemistry, C-reactive protein and erythrocyte sedimentation rates were recorded.

Patients were randomly divided into 3 groups by picking cards in different colors. First, three groups of cards (each group consisted of 15 cards) in 3 different colors (blue for 3 watts/cm², pink for 0.5 watts/cm², yellow for placebo) were prepared. Patients were asked to choose a card before starting the treatment. The US

dose was determined according to the color of the selected card and it was recorded. The randomization process was performed by another physician. No information was given to patients and to the physician who will make assessments and US application about the randomization process until the end of the study. Group I (n = 15) received 0.5 watts/cm²; group II (n = 15) received 3 watts/cm² and group III received placebo US (n = 15) on stellate ganglion for 5 minutes/day, for 20 sessions.

All the patients took the same medication including 500 mg/day vitamin C, Gabapentin (dose: 1800 mg/day) and Prednisolone (dose: 30 mg/day-2 weeks, stopped within next 2 weeks). Before and after the treatment the severity of the pain experienced at rest was assessed on a 10 cm visual analog scale (VAS) (0 = no pain, 10 = severe pain).

Therapeutic US applications on stellate ganglion were applied by placing the ultrasound heading on the level of transverse process of the seventh vertebra and 3-4 cm above the sternoclavicular joint [12]. Therapeutic US doses were 0.5 watts/cm² and 3 watts/cm², both in 1 MHz frequency, for 5 minutes, by using 1 cm² US heading and therapeutic US device Enraf Nonius brand Sonopuls 590 model. Pulsed pattern was 1:4. Placebo application was performed with the same technique and duration as the other applications when the device was off.

Conventional transcutaneous electrical nerve stimulation (TENS) applications were performed with Enraf Nonius brand Endomed 582ID product to the painful area of the affected extremity once a day, 20 minutes for a period of 100 hertz (Hz) frequency, to the level that the amplitude would remain under the motor threshold level [13]. Contrast bath applications were performed by using Ewac brand device, made of stainless steel, ground-mounted with faucets and tubs input for hot and cold water. By putting the affected upper extremity into the 38°C hot water for 4 minutes and then putting into the 4°C cold water for 1 minute and in total 20 minutes of contrast bath application was performed [13].

Active, active assistive and passive range of motion (ROM) exercises to the wrist and fingers, stretching exercises, progressive resis-

tance exercises were performed once a day, as 2 sets with 15 repetitions for each exercise [14]. The mirror box exercises were applied for 30 minutes [15].

Outcome measures of our study were finger pulp-distal crease distance for determining the limitation of total finger flexion, grip strength for muscle strength and disability of the arm, shoulder and hand (DASH) scale for determining the upper extremity disability. All tests were performed before and after the treatment protocol.

Finger pulp-distal crease distance were measured with a ruler and recorded [16]. Grip strength was evaluated with Jamar hydraulic hand dynamometer (Sammons Preston, Inc., Bollingbrook, IL) as "kg" unit. To measure grip strength, standard test positions of the American Physiotherapists Hand Association were used [17]. All measurements were performed by the same physician when the patients were sitting and the shoulders were in adduction and neutral rotation, 90° elbow flexion, neutral forearm position, 0°-30° wrist dorsiflexion and 0°-15° ulnar flexion. Measurements were done 3 times to calculate the average value. The Jamar dynamometer was held from the top and the bottom by the person in charge to make sure that the weight of the device itself does not effect the measurement when estimating the values. To evaluate the upper extremity functional disability, the Turkish version of DASH scale was used. This scale is accepted as the easiest and the most valid criteria which assesses upper extremity disability and symptoms and which is used in the measurement of upper extremity function. The main part of the DASH scale consists of 30 items assessing the health status of the patient. These items contain scaling the patient's difficulties in performing different physical activities because of arms, shoulder and hand problems (21 items); assessment of the status of the pain, activity-related pain, weakness, stiffness (5 items) and social activities, work, sleep, personality (4 items). Every item contains 5 answers. The DASH score is calculated through the total scores and low score indicates good function [18].

Sympathetic skin response measurements were performed from the affected extremities of the patients before and after the treatment;

from the dominant hand of controls before the treatment. The recordings were conducted with the device Cadwell Sierra Wedge brand 2-channel EMG, in a calm and bright room with a 22-24°C room temperature between 03:00 pm-05:00 pm when the patient was in supine position. Prior to measurement, patients' vital signs were watched closely to make sure they are normal. Measurements were done after 10 minutes of rest. After the patients' hands and wrists were wiped with alcohol to reduce the skin resistance, the active electrode was placed to palmar surface of the third metacarpal bone and the reference electrode was placed on the dorsal surface of the hand. To increase the transmission, ultrasound gel was applied under the electrodes. The ground electrode was placed on the same forearm area. The stimulations were given 5 times with at least a 30 second break from the opposite side of the wrist median nerve for a period of 0.2 milliseconds, between 15-30 mA. The obtained appropriate latency and amplitude values were recorded by taking the average [7].

Informed consent was obtained from all patients according to the Declaration of Helsinki. The study was approved by the Ethical Committee of our institution.

Statistical analyses

The statistical analyses of the study were performed by using the program Statistical Package for Social Sciences (SPSS) 15.0. Age, BMI, SSR amplitude and SSR latency values of the patients and healthy controls were compared by using Independent Samples t test. Chi-square test was performed to compare the groups for gender, type of the injury, affected side and dominant hand. Kruskal-Wallis test was performed to compare the groups for the median age, BMI, duration between the on set of disease and start of the therapy, pre- and post-treatment median VAS score, finger pulp-distal crease distance, grip strength, DASH score, SSR amplitude and SSR latency. The median pre- and post-treatment VAS, pulp-distal crease, grip strength, DASH, SSR amplitude, and SSR latency values within the study groups were compared with Wilcoxon test. The difference in the pre- and post-treatment median values of VAS, finger pulp-distal crease distance, grip strength, DASH score, SSR amplitude, and SSR latency values were calculated by sub-

Therapeutic ultrasound in complex regional pain syndrome

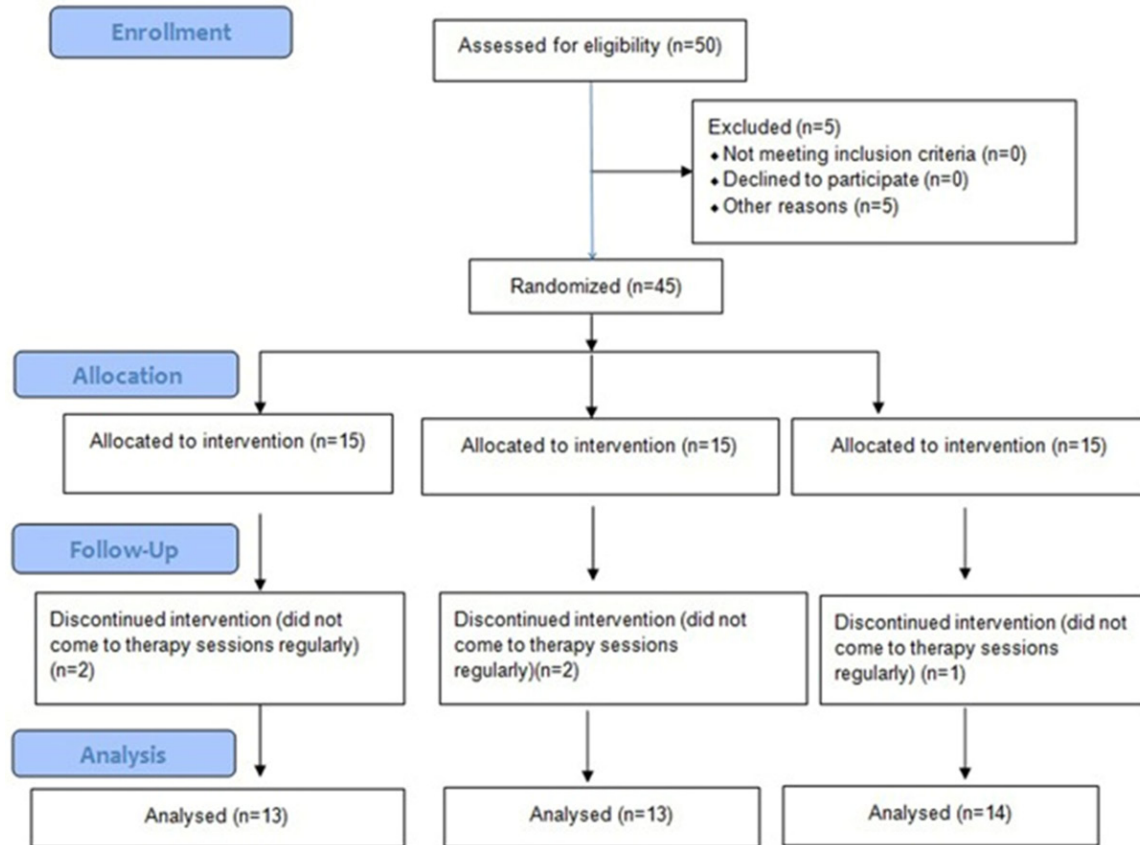


Figure 1. Flow diagram of the study.

Table 1. Characteristics of the CRPS type-1 patient groups

	Group I (n = 13) (0.5 wt/cm ²)	Group II (n = 13) (3 wt/cm ²)	Group III (n = 14) (Placebo)	P
Age (years)	45.0 (23.0-69.0)	46.0 (23.0-69.0)	44.0 (22.0-69.0)	0.971
Gender (female/male)	7/6	7/6	5/9	0.816
BMI (kg/m ²)	24.5 (19.1-35.0)	27.3 (21.5-32.4)	30.5 (20.9-37.7)	0.084
Dominant hand (right/left)	12/1	12/1	14/0	0.567
Affected side (right/left)	6/7	5/8	2/12	0.180
Duration between the onset of disease and start of therapy (day)	57.0 (38.0-156.0)	62.0 (25.0-161.0)	70.5 (15.0-162.0)	0.477

straction of pre-treatment values from post-treatment values and compared with Kruskal-Wallis test. Results were given as mean \pm standard deviation (SD) and median (min-max) values.

Results

Fifty patients with CRPS type I were assessed for eligibility. Five patients who declined to participate were excluded. Forty-five patients were randomised. Two patients from group I, 2 patients from group II and 1 patient from group III who did not come to therapy sessions regu-

larly were excluded. Thirteen patients from group I, 13 patients from group II and 14 patients from group III, a total of 40 patients (F/M:19/21) completed the study (Figure 1).

The mean age of the patients was 45.17 ± 13.44 years and the mean BMI of the patients was 27.53 ± 4.74 kg/m². The mean age of the controls (F/M:23/17) was 45.82 ± 13.54 years and the mean BMI of the controls was 27.56 ± 5.05 kg/m². There was no statistically significant difference between the patients and controls for age and BMI (P = 0.826 and P = 0.974 respectively). The median age and median BMI

Therapeutic ultrasound in complex regional pain syndrome

Table 2. Comparison of SSR amplitude and SSR latency between CRPS patients and controls at the beginning of the study (mean ± SD)

	Group I (n = 13) (0.5 wt/cm ²)			Group II (n = 13) (3 wt/cm ²)			Group III (n = 14) (Placebo)		
	Pre-treatment	Post-treatment	p	Pre-treatment	Post-treatment	p	Pre-treatment	Post-treatment	p
VAS score (0-10)	4.0 (2.0-8.0)	0 (0.0-6.0)	0.001	3.0 (2.0-7.0)	0 (0.0-1.0)	0.001	4.0 (2.0-6.0)	0 (0.0-1.0)	0.001
Finger pulp-distal crease distance (cm)	3.0 (0.0-7.0)	0 (0.0-5.0)	0.002	1.5 (0.0-5.0)	0 (0.0-2.0)	0.001	3.2 (0.0-6.5)	0 (0.0-4.0)	0.001
Grip strength (kg)	5.0 (0.5-19.0)	14.0 (1.0-24.0)	0.002	8.0 (2.0-28.0)	15.0 (8.0-41.0)	0.008	3.5 (2.0-12.0)	12.0 (5.0-22.0)	0.003
DASH score	88.3 (50.0-114.0)	51.6 (31.6-105.0)	0.001	72.5 (49.1-110.8)	37.5 (25.0-71.6)	0.001	77.9 (60.8-106.0)	37.4 (25.0-96.6)	0.001

Table 4. Comparison of pre- and post-treatment SSR amplitude and SSR latency within the groups [median (min-max)]

	Group I (n = 13) (0.5 wt/cm ²)			Group II (n = 13) (3 wt/cm ²)			Group III (n = 14) (Placebo)		
	Pre-treatment	Post-treatment	p	Pre-treatment	Post-treatment	p	Pre-treatment	Post-treatment	p
SSR amplitude (µv)	700.0 (333.2-1840.7)	555.2 (203.1-1451.3)	0.861	729.5 (311.1-2134.2)	694.4 (410.9-2075.4)	0.972	685.6 (230.1-1512.4)	693.5 (133.7-1961.6)	0.925
SSR latency (sec)	1447.2 (527.3-2030.0)	1350.0 (1071.8-1900.0)	0.701	1420.3 (1100.0-1626.5)	1515.6 (1251.4-1704.6)	0.071	1424.2 (786.4-1925.7)	1445.5 (1025.9-1862.3)	0.433

Therapeutic ultrasound in complex regional pain syndrome

Table 3. Comparison of the pre-treatment VAS, finger pulp-distal crease distance, grip strength, DASH score within the groups [median (min-max)]

	CRPS patients (n = 40)	Controls (n = 40)	p
SSR amplitude (μv)	800.87 \pm 448.88	901.89 \pm 642.02	0.409
SSR latency (sec)	1376.18 \pm 290.21	1510.49 \pm 223.76	0.018

of group I (F/M:7/6) were 45.0 (23.0-69.0) years and 24.5 (19.1-35.0) kg/m²; the median age and the median BMI of group II (F/M:7/6) were 46.0 (23.0-69.0) years and 27.3 (21.5-32.4) kg/m²; the median age and the median BMI of group III (F/M:9/5) were 44.0 (22.0-69.0) years and 30.5 (20.9-37.7) kg/m². There were no statistically significant differences between the groups for age, gender and BMI ($p = 0.971$, $P = 0.816$ and $P = 0.084$ respectively).

The duration between the development of CRPS and the start of therapy were 57.0 (38.0-156.0) days in group I; 62.0 (25.0-161.0) days in group II and 70.5 (15.0-162.0) days in group III. There were no significant differences between the groups regarding the duration to the development of CRPS and the start of therapy ($P = 0.477$), the dominant hand ($P = 0.567$) and the affected side ($P = 0.180$) (**Table 1**).

Eighteen patients were house-wives, 10 were laborers, 7 were retired, 3 were officers, 1 was manager and 1 was student. Fracture of distal radius (n = 17), tendon injury (n = 10), contusion of the hand (n = 5), surgery for carpal tunnel (n = 4), fracture of elbow (n = 2), fracture of humerus (n = 1) and fracture of finger (n = 1) initiated CRPS type I.

The median pre-treatment VAS was 4.0 (2.0-8.0) in group I, 3.0 (2.0-7.0) in group II and 4.0 (2.0-6.0) in group III. The median pre-treatment DASH score was 88.3 (50.0-114.0) in group I, 72.5 (49.1-110.8) in group II and 77.9 (60.8-106.0) in group III. There was no significant difference between the groups for the median pre-treatment VAS and DASH scores ($P = 0.128$ and $P = 0.173$ respectively). The median pre-treatment pulp-distal crease distance was 3.0 (0-7.0) cm in group I, 1.5 (0-5.0) cm in group II and 3.2 (0-6.5) cm in group III. The median pre-treatment grip strength was 5.0 (0.5-19.0) kg in group I, 8.0 (2.0-28.0) kg in group II and 3.5 (2.0-12.0) kg in group III. No statistically signifi-

cant difference was detected between the groups for the pre-treatment pulp-distal crease distance and hand grip strength ($P = 0.317$ and $P = 0.161$, respectively). There were statistically significant differences for the median pre- and post-treatment

VAS score, pulp-distal crease, grip strength and DASH score values within the groups ($P < 0.001$) (**Table 2**).

Pre-treatment SSR latency were significantly shorter in CRPS patients than controls ($P = 0.018$). Pre-treatment SSR amplitude values were not different between CRPS patients and controls ($P = 0.409$) (**Table 3**). The median pre-treatment SSR amplitude was 700.0 (333.2-1840.7) μv in group I, 729.5 (311.1-2134.2) μv in group II and 685.6 (230.1-1512.4) μv in group III. The median pre-treatment SSR latency was 1447.2 (527.3-2030.0) sec in group I, 1420.3 (1100.0-1626.5) sec in group II and 1424.2 (786.4-1925.7) sec in group III. Groups were not statistically different from each other for the median pre-treatment SSR amplitude and SSR latency ($P = 0.875$ and $P = 0.947$). When pre- and post-treatment SSR amplitude and SSR latency values were compared within groups, no statistically significant difference was found ($P > 0.05$) (**Table 4**). No significant differences were detected between the groups for the pre- and post-treatment median values of VAS, finger pulp-distal crease distance, hand grip strength, DASH score, sympathetic skin response amplitude and latency values ($P > 0.05$) (**Table 5**).

Discussion

This is the first randomized placebo-controlled study which evaluates the sympatholytic and clinical effects of low dose high frequency therapeutic ultrasound applied on stellate ganglion in patients with CRPS type 1. Applying therapeutic US on stellate ganglion for sympatholytic effect has been known for a long time but few studies were performed in this issue. Four decades ago, Goodman [8] applied pulsed US on stellate ganglion in 7 CRPS type 1 patients and reported excellent outcome. Portwood [9] reported daily therapeutic low dose ultrasound therapy (0.5 watts/cm²) to the tarsal tunnel and plantar nerve distribution to be a safe and use-

Therapeutic ultrasound in complex regional pain syndrome

Table 5. Comparison of the differences in the pre- and post-treatment values of VAS score, finger pulp-distal crease distance, grip strength, DASH score, SSR amplitude and SSR latency between the groups [median (min-max)]

	Group I (n = 13) (0.5 wt/cm ²)	Group II (n = 13) (3 wt/cm ²)	Group III (n = 14) (Placebo)	P
VAS score (0-10)	-2.0 [-5.0(-1.0)]	-3.0 [-6.0(-2.0)]	-3.5 [-5.0(-2.0)]	0.067
Finger pulp-distal crease distance (cm)	-2.0 (-4.0-0.0)	-1.5 (-5.0-0.0)	-2.2 (-4.5-0.0)	0.729
Grip strength (kg)	8.0 (0.0-15.0)	6.0 (1.0-37.0)	7.0 (2.0-14.0)	0.879
DASH score	-26.7 [-54.2(-6.7)]	-30.8 [-72.5(-5.8)]	-32.1 [-71.6(-4.1)]	0.320
SSR amplitude (μv)	-91.7 (-1285.4-496.4)	45.0 (-1228.6-474.8)	108.6 (-1327.4-891.6)	0.926
SSR latency (sec)	-101.5 (-350.0-777.3)	82.8 (-176.3-241.0)	-14.4 (-346.9-602.6)	0.387

ful treatment in three cases of lower extremity CRPS who refused surgical sympathectomy. Hazneci et al. [10] applied pulsed US on stellate ganglion in 3 watts/cm² dose in 14 CRPS type 1 patients and reported more pain relief and better muscle power measurements when added to physical activity program than physical therapy program alone. We applied therapeutic US to our patient groups in 0.5 watts/cm² or 3 watts/cm² doses to compare the effects of the two different doses which previously have been used in the literature and therapeutic US did not provide an additional clinical benefit in either doses in our patient groups. The disparity between our results and the previous studies may be due to the different study methodologies. The number of patients included in those studies were quite limited and none of them had placebo or control groups. The results were highly observational and the response of the sympathetic system to US application was not documented.

Pain reduction is not supposed to be a reliable indicator of successful sympathetic blockade, because patients may suffer from SIP (sympathetic independent pain), or factors like placebo response may contribute to a false interpretation of pain relief after stellate ganglion blockade. Thus, only a physiological measurement of sympathetic nervous function is able to prove sympathetic blockade efficacy [19]. SSR is defined as a change in the electrical potential of the skin after arousing stimuli, e.g. by activation of mechanosensitive A-beta or A-delta fibers. Thus, while skin response is not specific for painful stimuli, it usually allows differentiating the autonomic response in respect to stimulus intensity. The reflex loop includes the anterior cingulate cortex, the anterior hypothalamus, the intermediolateral column of the spinal cord and the sympathetic ganglia [20]. Bolel et

al. [7] reported SSR as a useful method for evaluating the response to sympathetic blockade in CRPS type 1. SSR is supposed to be increased because of the excessive sympathetic activity in CRPS [21, 22]. SSR latency was less in our patients with CRPS when compared to healthy controls at the beginning of our study. This result is in compatible with the previous work in terms of latency which had reported shorter SSR latency [7, 21, 23]. However in the present study we did not find a higher SSR amplitude in CRPS patients as detected in those studies. As the density of sweat glands determines the amplitude of SSR, the reason for the absence of amplitude change may be due to the unchanged density of sweat glands due to the absence of peripheral nerve lesion in CRPS type I.

In the present study low dose high frequency US therapy used on stellate ganglion did not make a sympathetic blockade at either 0.5 watts/cm² or 3 watts/cm² doses. We could not meet any other similar studies in the literature, which measured SSR after stellate ganglion application of low dose high frequency US in CRPS. Therefore, we could not compare our results with such a study.

The action mechanism of US on stellate ganglion remains largely unknown. In general, 'low' intensity therapeutic US (0.125-3 W cm²) has been used as a standard treatment option for soft tissue injuries in physiotherapy clinics, and it is used in some centres for wound healing and treating venous leg ulcers [24, 25] Low intensity US was reported to stimulate normal physiological responses to injury to aid repair [25]. Hong and Henneman [26] reported that US therapy at a therapeutic dosage (0.5-2 watts/cm²) may cause a reversible conduction block in peroneal nerves with painful polyneu-

ropathy. Portwood et al. [9] hypothesized that the action mechanism of US may be that US affected peripheral sympathetic nerve fibers and/or increased blood flow. However Portwood et al.'s hypothesis was not supported with an objective data. These studies were methodologically different from our study because Hong and Henneman and Portwood et al. applied therapeutic US on the peripheral nerves instead of stellate ganglion.

In conclusion, we found that low dose high frequency US therapy used on stellate ganglion did not make a sympathetic blockade at either 0.5 watts/cm² or 3 watts/cm² doses and was not of further benefit for pain, pulp-distal crease distance, grip strength and upper extremity disability in patients with CRPS type I. However the limited number of patients in our study is an important limitation to make precise conclusions. Studies with larger sample size are needed in this issue.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Ayhan Askin, Department of Physical Medicine and Rehabilitation, Izmir Katip Çelebi University Atatürk Education and Research Hospital, Izmir 35360, Turkey. Tel: +90-2322444444; E-mail: ayhanaskin@hotmail.com

References

- [1] Harden RN, Bruehl SP. Diagnosis of complex regional pain syndrome: signs, symptoms, and new empirically derived diagnostic criteria. *Clin J Pain* 2006; 22: 415-9.
- [2] Bruehl S. An update on the pathophysiology of complex regional pain syndrome. *Anesthesiology* 2010; 113: 713-25.
- [3] Tran QH, Duong S, Bertini P, Finlayson RJ. Treatment of complex regional pain syndrome: a review of the evidence. *Can J Anesth* 2010; 57: 149-166.
- [4] Saxena AK, Saxena N, Aggarwal B, Sethi AK. An unusual complication of sinus arrest following right-sided stellate ganglion block: a case report. *Pain Pract* 2004; 4: 245-8.
- [5] Chaturvedi A, Dash H. Locked-in syndrome during stellate ganglion block. *Indian J Anaesth* 2010; 54: 324-6.
- [6] Mahli A, Coşkun D, Akçalı DT. Aetiology of convulsions due to stellate ganglion block: a review and report of two cases. *Eur J Anaesthesiol* 2002; 19: 376-80.
- [7] Bolel K, Hizmetli S, Akyüz A. Sympathetic skin responses in reflex sympathetic dystrophy. *Rheumatol Int* 2006; 26: 788-791.
- [8] Goodman CR. Treatment of shoulder-hand syndrome: Combined ultrasonic application to stellate ganglion and physical medicine. *NY State J Med* 1971; 71: 559-62.
- [9] Portwood MM, Lieberman JS, Taylor RG. Ultrasound treatment of reflex sympathetic dystrophy. *Arch Phys Med Rehabil* 1987; 68: 116-8.
- [10] Hazneci B, Tan KA, Özdem T, et al. The effects of transcutaneous electrostimulation and ultrasound in the treatment of reflex sympathetic dystrophy syndrome. *Turk J Phys Med Rehab* 2005; 51: 83-89.
- [11] Wilson PR. News-letter of the IASP special interest group on pain and the sympathetic nervous system. *Taxonomy* 2004; 9: 4-6.
- [12] Pappagallo M, Rosenberg AD. Epidemiology, pathophysiology, and management of complex regional pain syndrome. *Pain Practice* 2001; 1: 11-20.
- [13] Basford JR, Baxter GD. Therapeutic Physical Agents. In: Gans BM, Walsh NE, Robinson LR, editors. *De Lisa's Physical Medicine & Rehabilitation. Principles and Practice*. Philadelphia: Lippincott Williams & Wilkins; 2010. pp. 1691-1712.
- [14] Harden RN, Swan M, King A, Costa B, Barthel J. Treatment of complex regional pain syndrome: functional restoration. *Clin J Pain* 2006; 22: 420-4.
- [15] Cacchio A, De Blasis E, Necozone S, di Orio F, Santilli V. Mirror therapy for chronic complex regional pain syndrome type 1 and stroke. *N Engl J Med* 2009; 361: 634-6.
- [16] Cambridge-Keeling CA. Range-of-motion measurement of the hand. In: Mackin EJ, Callahan AD, Skirven TM, Schneider LH, editors. *Rehabilitation of the Hand and Upper Extremity*. Mosby; 2002. pp. 169-182.
- [17] Mathiaowetz V, Weber K, Volland G, Kashman N. Reliability and validity of grip and pinch strength evaluations. *J Hand Surg* 1984; 9: 222-6.
- [18] Hudak PL, Amadio PC, Bombardier C. Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand). The Upper Extremity Collaborative Group (UECG). *Am J Ind Med* 1996; 29: 602-8.
- [19] Schürmann M, Gradl G, Witzgal I, Tutic M, Moser C, Azad S, Beyer A. Clinical and physiologic evaluation of stellate ganglion blockade for complex regional pain syndrome type I. *Clin J Pain* 2001; 17: 94-100.
- [20] Gutrecht JA. Sympathetic skin response. *J Clin Neurophysiol* 1994; 11: 519-24.

Therapeutic ultrasound in complex regional pain syndrome

- [21] Ghahreman A, Bogduk N. Predictors of a favorable response to transforaminal injection of steroid in patients with lumbar radicular pain due to disc herniation. *Pain Medicine* 2011; 12: 871-9.
- [22] Ates Y, Asik I, Ozgencil E. Evaluation of the longus colli muscle in relation to the stellate ganglion block. *Reg Anesth Pain Med* 2009; 34: 219-23.
- [23] Hansen HC, Trescot AM, Manchikanti L. Stellate ganglion block. In: Manchikanti L, Singh V, editors. *Interventional techniques in chronic non-spinal pain*. Paducah: ASIPP Publishing; 2009. pp. 115-40.
- [24] Watson J, Kang'ombe AR, Soares MO, Chuang LH, Worthy G, Bland JM, Iglesias C, Cullum N, Torgerson D, Nelson EA; VenUS III Team. Use of weekly, low dose, high frequency ultrasound for hard to heal venous leg ulcers: the VenUS III randomised controlled trial. *BMJ* 2011; 342: d1092.
- [25] Datta S, Pai UT, Manchikanti L. Lumbar sympathetic blocks. In: Manchikanti L, Singh V, editors. *Interventional techniques in chronic non-spinal pain*. Paducah: ASIPP Publishing; 2009. pp. 141-67.
- [26] Hong CZ, Henneman E. Reversible nerve conduction block in patients with polyneuropathy after ultrasound thermotherapy at therapeutic dosage. *Arch Phys Med Rehabil* 1991; 72: 132-7.