Effects of Phonophoresis with Hydrocortisone Alone and in Combination with 10% Dimethylsulfoxide on Myofascial Trigger Points in the Upper Trapezius Muscle

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Abstract

Dimethylsulfoxide is a potent solvent which is used to increase the transdermal transport of medicines. The aim of this study was to examine the effects of phonophoresis with hydrocortisone alone and in combination with dimethylsulfoxide on the upper trapezius trigger points. Sixty patients were divided into three groups and received ten treatment sessions with different protocols using ultrasound: 1% hydrocortisone gel, a solution of 10% dimethylsulfoxide and 1% hydrocortisone gel, and a neutral ultrasound gel. The pain, pressure pain threshold, and the range of motion of the neck were assessed at four intervals in all three groups. The results revealed that phonophoresis with the two treatment gels and ultrasound with neutral gel significantly reduced the pain and the pressure pain threshold (P=0.01). The range of ipsilateral lateral flexion and contralateral lateral flexion of the neck was significantly improved following phonophoresis with 10% DMSO and 1% hydrocortisone gel (P=0.01 and P=0.02, respectively). Thus, it was concluded that the addition of 10% DMSO to 1% hydrocortisone gel enhanced the persistence of the beneficial effects of hydrocortisone on the pain, pressure pain threshold, and the range of motion of the neck.

Keywords: Myofascial trigger point, Phonophoresis, Hydrocortisone, Dimethylsulfoxide

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Introduction

Myofascial trigger points are considered to be the most common causes of musculoskeletal pain. These hyperirritable points are located in taut skeletal muscle bands and can cause pain or autonomic symptoms as well as movement limitations of the joints (1). About 95% of people with chronic pain suffer from myofascial trigger point pain (2, 3). There are two types of myofascial trigger points: active and latent. Active myofascial trigger points may cause local or referred pain whose touching can lead to a local twitch response. Touching or needling a latent myofascial trigger point can cause local and/or referred pain. Both types of myofascial trigger points show spontaneous EMG activity when the muscle is at rest (4).

The upper trapezius muscle is probably one of the muscles most affected by a myofascial trigger point1. The common myofascial trigger point in this muscle is often accompanied by referred pain on the posterolateral side of the neck and postauricular to the temporal area (5). A person with latent myofascial trigger points in the upper trapezius muscle can be at risk of the involvement of the rotator cuff muscles, impingement of the shoulder muscles, and musculoskeletal pain when the muscle activation pattern is disturbed during scapular elevation (6).

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Various methods have been proposed for the treatment of myofascial trigger points. For example, iontophoresis and phonophoresis have been widely used as effective interventions in physiotherapy (6). Phonophoresis refers to the use of ultrasound to enhance the transdermal delivery of medicine to the blood circulation and is regarded as a noninvasive method with local and systemic effects. In contrast with taking oral medicines, the appropriate amount of medicine is administered during phonophoresis; as such, there are no digestive complications, and the patients are not prone to medicinal poisoning.

Hydrocortisone, a corticosteroid, is used to treat musculoskeletal inflammation and can be delivered using phonophoresis. Hydrocortisone passes through the cell membrane, combines with cytoplasmic receptors, and stimulates the production of different proteins for specific enzymes. It also plays a role in treating symptomatic inflammation by increasing the surface blood circulation. Although phonophoresis with a corticosteroid is a very common treatment for musculoskeletal inflammations, there is little scientific evidence to support the effectiveness of using phonophoresis to deliver the medicine to the muscle. There is also little information about the mechanism of phonophoresis involved in the treatment of myofascial trigger points (1). It is thought that hydrocortisone can provide more oxygen to the myofascial trigger points by promoting the blood flow. Thus, phonophoresis with hydrocortisone can be effective in improving the symptoms of the myofascial trigger points by increasing the local circulation (7).

Dimethylsulfoxide (DMSO) is a potent solvent which is used to boost the transdermal transport of medicines by changing the configuration of the stratum corneum cells. DMSO can also help muscles relax by controlling ATPase and promoting the reabsorption of calcium into the sarcoplasmic reticulum. In addition, the absorption of steroids would triple in the presence of DMSO (7). However, very few studies have investigated the clinical application of DMSO and there is little evidence about its effectiveness in treating musculoskeletal problems in humans. So far, no study has examined the effect of DMSO on the myofascial trigger points in humans.

The addition of DMSO to hydrocortisone may facilitate its absorption. The purpose of the present study was to examine the effects of phonophoresis with hydrocortisone alone and in combination with 10% DMSO on pain intensity as measured on a visual analogue scale (VAS), the pressure pain threshold (PPT) of the myofascial trigger points, and the range of motion of the neck in people affected by myofascial trigger points in the upper trapezius muscle.

Materials and Methods

The study was a double-blind clinical trial carried out on 60 patients (51 females and 9 males) with an age range of 18–25 years. The patients had palpable nodules in their upper trapezius muscles which were painful under 25 units of pressure on the Newton scale. The patients had no previous history of neck pain for at least 6 months before the study and had received no treatment for myofascial pain at least 1 month prior the study. All the patients were voluntarily assigned to groups using a nonrandom sampling method (convenience sampling) whereby each patient picked up a card labeled as A, B, or C in the physiotherapy clinic. The therapeutic gels were prepared and labeled as A, B, or C by one pharmacologist. Thus, both the therapist and the patients were blinded to the type of gel used for treatment. The stages of the study and the probable effects of the medications were explained to the patients and they voluntarily signed the consent forms to participate in the study. Patients in group A received gel A: 1% hydrocortisone (Daru Pakhsh Company, Iran); patients in group B received gel B: solution of 10% DMSO and 1% hydrocortisone gel (Merck Company, Canada); and patients in group C received gel C: a neutral gel (Abzar Darman Company, Iran) used in ultrasound. The patients received ten treatment sessions and four assessments, performed by the same physiotherapist at four intervals: before beginning the treatment, at the end of the fifth treatment session, at the end of the tenth treatment session, and two weeks after the last treatment session, which was the follow-up. To determine if there was a possible dermal allergy to any of the gels, the patients were asked to apply the gel to one hand and not to wash it for two hours. None of the patients showed any signs of allergy. One week before initiating the treatment, the patients were asked to avoid taking any sedatives or medicines that would relax their muscles. The study protocol was approved by the local ethics committee of Shahid Beheshti University of Medical Sciences. The study was conducted for 8 months at the School of Rehabilitation in 2015.

To begin the treatment, the patients were examined for the presence of myofascial trigger points in their upper trapezius muscles using both manual palpation and an algometer with a disc surface of 1 cm^2 (Model FG-5005; Lutron Electronic Enterprise Co. Ltd., Taiwan). The positions of the myofascial trigger points were designated using skin markers. The patients lied in a prone position with their neck in a neutral position. A pillow was then placed under the patient's pelvis and they were asked to put their forehead on their hands. A therapeutic pulse

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Table 1. Demographic characteristics of the patients (n=60) (Mean± SD)

Variable	Group A (Hydrocortisone gel)	Group B (DMSO and hydrocortisone gel)	Group C (Ultrasound gel)	P
Age (year)	22.10±1.16	22.15±1.22	21.85±1.08	0.68
Height (cm)	165.35±8.75	165.15±8.11	165.50±7.09	0.99
Weight (kg)	56.70±7.79	58.55±7.08	56.20±6.51	0.55

ultrasound unit (BMS Company, England) with an effective radiating area of 5cm^2, frequency of 1MHz, intensity of 1W/cm^2, and a duty cycle of 50% was used for all patients after calibration. The applicator was moved in a circular motion at a similar speed and pressure for all patients.

The pain intensity, the PPT of the myofascial trigger points, and the range of ipsilateral lateral flexion (ILLF) as well as the contralateral lateral flexion (CLLF) of the neck were examined before beginning the treatment, at the end of the fifth treatment session, at the end of the tenth treatment session, and two weeks after the last treatment session, which was considered as follow-up. The PPT was assessed using an algometer. The algometer was applied to the myofascial trigger point at a speed of 1 kg/cm^2/s until pain developed. The intensity of the force exerted was recorded. This process was repeated three times with a time interval of 10 seconds whose mean was calculated. The reliability and the validity of the algometer had been established in previous studies (8, 9). A goniometer (MSD Company, Korea) was used for measuring the range of ILLF and CLLF of the neck. The patients were asked to sit on a chair with their face looking forward, their mouth in a horizontal position, and their nose in a vertical position, while holding the lower part of the chair with their hands. The fulcrum of the goniometer was set along the spinous process of the first thoracic vertebra, while the center of the moving arm of the goniometer was on the occipital protuberance. The moving arm was held horizontally and the patient was asked to move their neck without moving their shoulder. The moving arm of the goniometer was then displaced in proportion with the movement of the head. The active and painless range of motion was assessed three times with their mean calculated.

The data were analyzed using SPSS software. The measurements of the central tendency and the distribution of the variables (mean, variance, and standard deviation) were determined using descriptive statistics. The Kolmogorov–Smirnov (K–S) test was used to determine the normal distribution of the variables. A one-way analysis of variance (ANOVA) was employed to ensure that the three groups were equal in terms of age, height, and weight. A two-way repeated measures ANOVA was also utilized to compare the changes in the numerical values of pain, PPT, and the range of motion of the neck in the three groups, while the Bonferroni test was used for post hoc comparison. Finally, the Tukey post hoc test was used to study the differences between the treatment groups. In all statistical calculations, the significant level was set at $P \leq 0.05$.

Results

The study was conducted on 60 patients, and there were 20 patients (17 females and 3 males) in each group. The one-way ANOVA showed that there were no significant differences between the three groups in terms of the demographic variables of the study (Table 1). The K–S test revealed a normal distribution of the variables. All the assessments that were conducted at the end of the fifth treatment session indicated that there was no reduction in pain and no improvement in the PPT and range of ILLF and CLLF of the neck.

Pain intensity

The two-way repeated measures ANOVA indicated that all three gels significantly reduced the pain at the end of the tenth treatment session and there were no significant differences between the three groups (P=0.09). While all three gels were effective in reducing pain, the results of the Tukey test showed that gel B had a more persistent effect on pain than the other two gels (P=0.001) (Figure 1). The patients also had increased sensitivity to palpation during phonophoresis with gel B.

Pressure pain threshold (PPT)

The two-way repeated measures ANOVA revealed that all three gels significantly improved the PPT at the end of the tenth treatment session (P=0.01) and there were no significant differences between the groups (P=0.19). The one-way ANOVA showed that there were significant differences between the three gels in terms of the duration of their effects on the PPT (Figure 2). Finally, the Tukey test exhibited that gel B had a more persistent effect on the PPT than the other two gels (P=0.001) (Figure 3).

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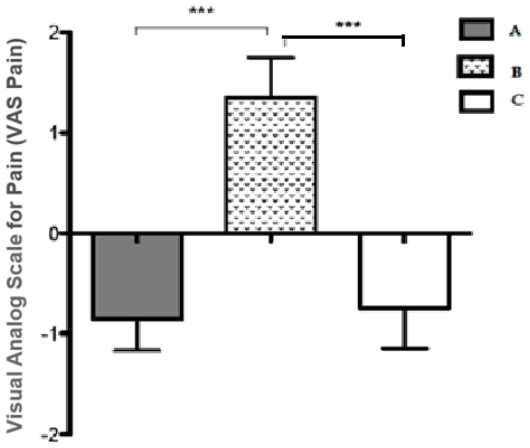

Figure 1. The effects of different interventions on pain (VAS) after two weeks' follow-up in the three groups (Group A: hydrocortisone gel; Group B: DMSO and hydrocortisone gel; Group C= ultrasound gel), ***: *P*<0.001

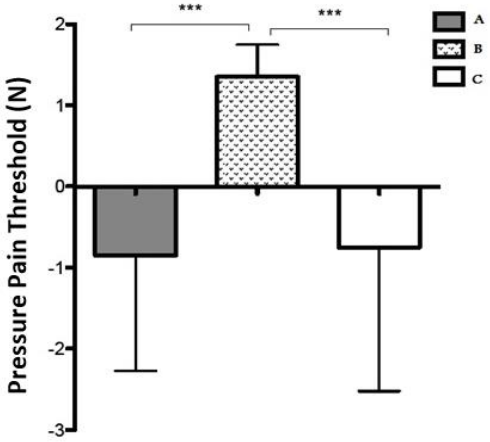

Figure 3. The effects of different interventions on the pressure pain threshold (PPT) after two weeks' follow-up in the three groups (Group A: hydrocortisone gel; Group B: DMSO and hydrocortisone gel; Group C: ultrasound gel), ***: *P*<0.001

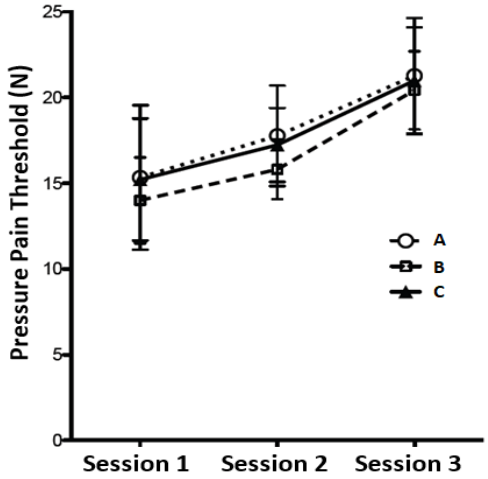

Figure 2. The effects of different interventions on the pressure pain threshold (PPT) during the 10 sessions across the three groups (Group A: hydrocortisone gel; Group B: DMSO and hydrocortisone gel; Group C=ultrasound gel) (n=60).

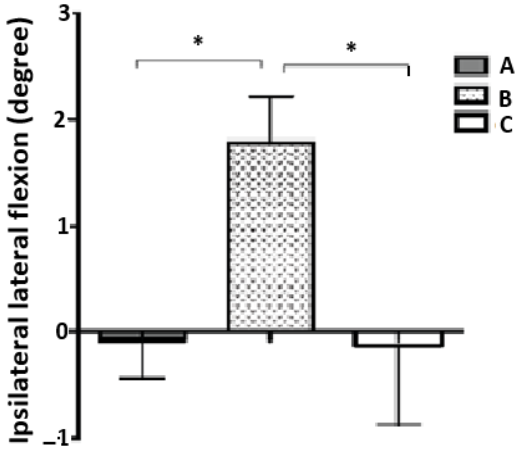

Figure 4. The effects of different interventions on the range of ipsilateral lateral flexion (ILLF) of the neck after two weeks' follow-up across the three groups (Group A: hydrocortisone gel; Group B: DMSO and hydrocortisone gel; Group C= ultrasound gel), *: P<0.001

Ipsilateral lateral flexion (ILLF) range of motion

The two-way repeated measures ANOVA suggested that the three gels significantly improved the range of ILLF of the neck at the end of the tenth treatment session (*P*=0.01). However, there were significant differences across the three groups (*P*=0.01). The Bonferroni test showed that the improvement in the ILLF range of motion of the neck was significantly greater for gel A (*P*=0.03) and gel B (*P*=0.01) than for gel C. On the other hand, there were no significant differences between gel A and gel B (*P*=0.93). The Tukey test revealed that gel B had a more significant persistent effect on improving the range of ILLF of the neck compared to gel A (*P*=0.03) and gel C (*P*=0.02) (Figure 4).

Contralateral lateral flexion (CLLF) range of motion

The two-way repeated measures ANOVA showed that the three gels significantly improved the range of CLLF of the neck at the end of the tenth treatment session (*P*=0.01). However, there were significant differences between the three groups (*P*=0.02). The Bonferroni test revealed that the range of CLLF of the neck was more significantly improved in group B than in group C (*P*=0.02), and that there were no significant differences between groups A and B (*P*=0.78) or groups A and C (*P*=0.11). Although there was some improvement observed with gel A compared with gel C, this difference was not significant. Ultimately, the Tukey test showed that gel B had a significant persistent effect on improving the range of CLLF of the neck than the other two gels (*P*=0.01) (Figure 5).

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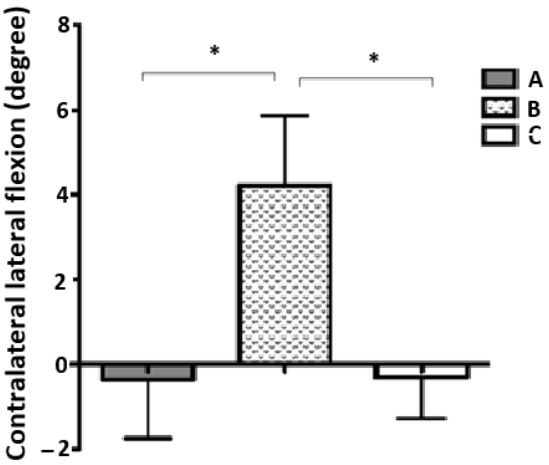

Figure 5. The effects of different interventions on the range of contralateral lateral flexion (CLLF) of the neck after two weeks' follow-up in the three groups (Group A: hydrocortisone gel; Group B: DMSO and hydrocortisone gel; Group C= ultrasound gel), *: $P<0.05$

Discussion

The present study revealed that although phonophoresis with the three types of gels significantly reduced the pain intensity and improved the PPT, there were no significant differences between the gels. Phonophoresis with 1% hydrocortisone and with a solution of 10% DMSO plus 1% hydrocortisone gel were not preferable to the neutral ultrasound gel in terms of their effects on the pain intensity of the myofascial trigger points. Kuntz found that phonophoresis of 10% hydrocortisone in comparison with the topical application of 10% hydrocortisone had no boosting effect on the amount of hydrocortisone absorbed in muscles[10]. Ebrahimi et al. compared the effects of a pulsed ultrasound with continuous ultrasound and reported that the pulsed ultrasound was far more effective on the amount of medicine absorbed through the skin (11). In the present study, pulsed ultrasound was used for phonophoresis though the results revealed no differences for pain and the PPT of the myofascial trigger points in the upper trapezius muscle compared to pulsed ultrasound with neutral gel.

Sarrafzadeh et al. compared the effects of pulsed ultrasound, 1% hydrocortisone phonophoresis, and 90s of ischemic pressure on the latent myofascial trigger points in the upper trapezius muscles of 60 patients. They reported that the three interventions were all effective in reducing the pain and the PPT of the myofascial trigger points; however, ischemic pressure and phonophoresis were far more effective than the pulsed ultrasound. The authors suggested that phonophoresis could affect the dermal absorption of hydrocortisone. They also indicated that the effectiveness of the hydrocortisone on the pain intensity and the PPT of the myofascial trigger points showed the presence of an inflammatory area and a pain-inducing latent myofascial trigger point (1). Shah et al. (2008) reported that the levels of intermediary biochemicals that were related to pain and inflammation might increase around the myofascial trigger points in the upper trapezius muscle. However, they found that there was no significant difference between the levels of inflammatory and pain-inducing biochemicals around the latent myofascial trigger points and healthy muscles (2). The results of our study were similar to those of the study by Shah et al. We could attribute the reduction of pain and the increase of the PPT to the nonthermal effect of the pulsed ultrasound after using phonophoresis with hydrocortisone gel along with the solution of hydrocortisone with DMSO. By stimulating the mechanical receptors, the pain gate mechanism will be activated, which will inhibit the pain signals in the spinal cord. However, this issue needs to be further studied.

In a review article, Jacob stated that DMSO could increase the permeability of the skin, mitigate inflammation, cause local anesthesia, inhibit cholinesterase, improve circulation, and relax the muscles (12). Silveira et al. studied the effect of DMSO on pain reduction and oxidative stress in rat muscles after mechanical damage. They found that phonophoresis with DMSO gel could reduce pain and improve muscle ability (13). Maibach et al. used a DMSO solution to enhance the local absorption of hydrocortisone and testosterone in humans. They found that the local absorption of these steroids tripled in the presence of DMSO (14). In a similar study, Weissmann et al. examined the anti-inflammatory effect of DMSO combined with cortisone; their results showed that cortisone boosted the resistance of lysosomes against dangerous elements and its combination with DMSO enhanced its effectiveness from 10 to 100 times (15).

Contrary to these studies, the present study revealed that the DMSO solution did not increase the effectiveness of hydrocortisone on pain reduction in the myofascial trigger points. Additionally, patients who received phonophoresis with gel B (DMSO and hydrocortisone gel) had an unpleasant feeling in the applied area, which increased their sensitivity to palpation. There are two reasons for this contradiction. First, we used phonophoresis with a solution of DMSO and hydrocortisone gel in our study, while the previous studies employed a local application of a combination of DMSO and hydrocortisone. It is possible that the phonophoresis with the solution produced a local tenderness lowering the effectiveness

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of the hydrocortisone on the pain intensity and the PPT of the myofascial trigger points. The second reason for the differences between the studies is that the previous studies did not use phonophoresis with DMSO on humans, while they used a high percentage of DMSO.

The findings of the present study suggested that phonophoresis with a combination of hydrocortisone and DMSO produced a more persistent effect than the other two gels did. In addition to increasing the skin permeability to steroids, DMSO may produce a reservoir of steroids in the skin, which are resistant to water, soap, and alcohol for a maximum of 16 days, as previously discussed by Jacob and Herschler (12). Therefore, it might be claimed that DMSO can enhance the persistency of the effect of hydrocortisone by storing steroids in the skin.

The function of the upper trapezius muscle is necessary for the ipsilateral elevation of the shoulder, the ipsilateral bending of the head and neck, and the rotation of the head to the opposite side. When the muscle is affected by the myofascial trigger points, the function of the muscle and the range of neck movements will be limited; because of the shortening of the sarcomeres in the muscle, the head and neck movements to the opposite side may be limited to 45 degrees or less. The results of this study revealed that phonophoresis with the three gels significantly improved the range of ILLF of the neck. Phonophoresis with hydrocortisone gel and a solution of DMSO plus hydrocortisone gel were far more effective than using ultrasound gel alone for the range of ILLF of the neck. However, there were no significant differences between phonophoresis and 1% hydrocortisone and between the solution of 10% DMSO and 1% hydrocortisone gel in terms of their effects on the range of ILLF of the neck.

After 10 sessions of treatment, phonophoresis with the three gels had significant effects on the range of CLLF of the neck. Note that, the effect of phonophoresis with the solution of 10% DMSO and 1% hydrocortisone on the range of CLLF of the neck was greater than the impact of the ultrasound with neutral gel. Sarrafzadeh et al. reached a similar conclusion in their comparison of three interventions on the latent myofascial trigger points in the upper trapezius muscle (1). However, Aguilera et al., who compared the effects of ischemic pressure and pulsed ultrasound in the treatment of the latent myofascial trigger points of the upper trapezius muscle, reported that, although it decreased the pain, ultrasound did not have any effect on the active range of motion of the neck (16). The contradictory results of this study with the previous studies may be due to the different measurement methods used. In addition, Aguilera et al. examined the active range of motion of the neck as a single general parameter, and did not view the range of CLLF and ILLF individually.

It can be stated that the three interventions used in this study are effective in improving the range of motion of the neck in people who are affected by the myofascial trigger points of the upper trapezius muscle. However, the phonophoresis of 1% hydrocortisone gel and a solution of 10% DMSO and 1% hydrocortisone gel were far more effective than the mechanical effect of ultrasound. The reason is that they increased the surface blood circulation, which enhanced the provision of oxygen for the affected muscle. In addition, DMSO can help to relax the muscles by controlling ATPase and increasing the reabsorption of calcium into the sarcoplasmic reticulum. Thus, it can be stated that the range of motion in the neck, especially in the range of CLLF, will improve more via phonophoresis with a solution of 10% DMSO and 1% hydrocortisone gel than with a 1% hydrocortisone gel, although the difference has not been significant. The insignificant difference may be due to the low percentage of DMSO used. In addition, the present study revealed that phonophoresis with a solution of DMSO and hydrocortisone had a more persistent effect on the range of motion of the neck than the other two gels. One probable explanation for this improvement is that the DMSO may increase the delivery of steroids and produce a reservoir of steroids in the skin which is resistant to water, soap, and alcohol for a period of time. This confirmed the explanation stated by Jacob and Herschler who conducted a similar study on animals (12). However, more studies are required to provide evidence for the effect of the solution of DMSO and hydrocortisone on relaxing the affected muscles in humans.

A limitation of this study was that we used a low percentage of DMSO because of the probable complications associated with its use. Most of the previous studies used a high percentage of DMSO on animals. We did not find any study employing phonophoresis with DMSO on humans. Therefore, more study should be performed on human subjects using different percentages of DMSO.

Conclusion

The present study suggested that DMSO not only potentiated the effects of hydrocortisone on reducing pain and increasing the pressure pain threshold, it also improved the range of ILLF and CLLF of the neck. The study also revealed that the effect of DMSO persisted two weeks after the last treatment.

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M.M.R., designed and drafted the manuscript; Z.T., had executive role and helped to design the manuscript; M.G. helped to draft and check the manuscript; K.K. helped to draft and translate the manuscript; A.A. performed the statistical analysis.

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Authors' contributions:

All authors made substantial contributions to conception, design, acquisition, analysis and interpretation of data.

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