Original Article

Effect of magnesium sulfate iontophoresis on myofascial trigger points in the upper fibres of the trapezius

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Abstract

Objective: To investigate the immediate and post-treatment effect of magnesium sulfate (MgSO4) iontophoresis on myofascial trigger points (MTrPs) in the upper fibres of the trapezius muscle.

Method: Sixty participants (41 women and 19 men, aged 19–24 years) with active MTrPs on the dominant upper fibres of trapezius were enrolled in this study. They were randomly divided into 2 equivalent groups: the intervention and the control group. The intervention group (iontophoresis group; \( n = 30 \)) was treated with MgSO4 iontophoresis on the upper fibres of the trapezius twice a week for four weeks, and the control group (direct current group; \( n = 30 \)) received direct current (without medication) in the upper fibres of the trapezius twice a week for four weeks. The outcome measures were: pain intensity, pain threshold, neck range of motion, and neck function. The participants were assessed before treatment, immediately after the first session, and finally after treatment.

Results: The differences within and between groups were measured using a mixed design, multivariate analysis of variance (MANOVA). The within- and between-group analysis of all outcome measures in both groups revealed significant differences in favour of the intervention group \( (p < 0.05) \).

Conclusion: MgSO4 iontophoresis is effective in improving pain level, neck ROM, and neck function immediately after the first session and causes more...
significant improvement after treatment in subjects with active MTrPs on the dominant upper fiber of trapezius.

**Keywords:** Iontophoresis; Magnesium sulfate; Pain; Trapezius muscle; Trigger points

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**Introduction**

In recent decades, myofascial pain syndrome (MPS) is one of the most common clinical musculoskeletal disorders, characterised by the existence of one or more myofascial trigger points (MTrPs).1 MTrPs are hyperirritable spots associated with palpable nodules in the taut bands of the skeletal muscle.2 Clinically, about 85% of patients who attend pain clinics have MTrPs.1 The incidence rate is higher among women (54%) than men (45%)2 and they are found more on the dominant side (82.1%) than on the non-dominant side (79%) in the upper trapezius (UT) muscle.4 The highest prevalence is in trapezius muscles (93.75%), then in the levator scapulae (82.14%), and finally in the multifidi (77.68%).4

MTrPs are the most important causes of musculoskeletal pain, and are often located in the neck and shoulder muscles. Further, lack of good treatment for a long period may result in headaches, dizziness or vertigo, neck and shoulder pain, sleep disorders, autonomic dysfunction, sensory abnormality, and limited neck and shoulder range of motion (ROM).5

MTrPs are classified as either active or latent.6 Active MTrPs are characterised by persistent pain, referred pain, decreased muscle elasticity, and muscle weakness.7 Latent MTrPs have similar clinical features to active MTrPs but seem less severe, and the pain is induced rather than constant.8 Numerous researchers have studied the effects of various therapeutic techniques—such as ischemic compression, spray and stretch techniques, dry needling, injections, electrical stimulation, laser, and ultrasound/phonophoresis, iontophoresis—on MTrP treatment.1

Iontophoresis or ion transfer involves the administration of a therapeutic substance to the body through direct current, which is an alternative to the oral administration of drugs.9 Direct current by itself is successful in treating MPS. Kaya et al. revealed that direct current therapy with without lidocaine iontophoresis is effective in treating MPS.10 There are many advantages of iontophoresis, including the prevention of absorption variation (known with oral administration by bypassing hepatic ‘first-pass’ metabolism), which decreases the opportunity of dosing variation by giving a programmed delivery of medications, leading to increased patient improvement; at this point, medications can begin to circulate directly without delay.11 Further, iontophoresis is a painless, sterile, and non-invasive procedure.12

For many years, iontophoresis has been used to treat oedema, hyperhidrosis, gout arthritis, functional infections, ischemic skin ulcers, and musculoskeletal conditions (such as carpal tunnel syndrome, tendinopathy, degenerative joint disease, and MPS).9,12–15 Moreover, iontophoresis has been gaining popularity in MTrP management. Evans et al. investigated the immediate effects of lidocaine iontophoresis on trigger point pain and concluded that the lidocaine iontophoresis treatment increased the pain threshold of sensitive MTrPs.12

For musculoskeletal inflammatory conditions, the following substances have been used with iontophoresis: acetic acid, sodium diclofenac, sodium salicylate, ketorolac, benzoylamino, ketamine, lidocaine and naproxen, dexamethasone, hydrocortisone, and magnesium sulfate (MgSO4).16 MgSO4 is employed a muscle relaxant and a vasodilator, and also has an analgesic effect. Some studies have observed its impact on the management of neuritis, deltoid bursitis, and myalgias.17–19

Due to its ability to penetrate undamaged skin, MgSO4 has a superior effect, which is proven by increasing the serum magnesium level. In addition, the transdermal absorption of MgSO4 increases linearly with the solution concentration and the skin surface area. These properties of MgSO4 become more effective when used together with the added benefit of iontophoresis.20

The ideal physicochemical property selected for cutaneous administration is a low molecular weight, as this will cause a high diffusion coefficient; in other words, the smaller the molecular weight, the deeper the drug’s penetration.21 Compared with other drugs used in iontophoresis with higher molecular weights such as dexametason (392.467 g/mol)22 and lidocaine (234.34 g/mol),23 the molecular weight of MgSO4 is low (120.36 g/mol),24 so MgSO4 may be the preferred choice and can be used to treat deeper structures.21–24

To the best of our knowledge, there is a gap in the literature about the effects of MgSO4 iontophoresis on MTrPs, so this study aimed to investigate the immediate impact and post-treatment outcomes of MgSO4 iontophoresis on MTrPs in the UT muscle.

**Materials and Methods**

**Design of the study**

This is a single-blind, randomised, controlled study performed between October 2019 and February 2020 at the outpatient clinic of Cairo University’s Faculty of Physical Therapy. All procedures were conducted following the Declaration of Helsinki.

**Subjects**

This study included 60 subjects (41 females and 19 males), ranging in age from 19 to 24 years, with heights between 153 and 179 cm, and weights of 50–100 kg, who were diagnosed with active MTrPs on the UT muscle of the dominant side. They were recruited from among undergraduate and post-graduate students of the Faculty of Physical Therapy and provided institutionally approved informed consent before data were gathered.

The inclusion criteria encompassed having active MTrPs on the UT muscle on the dominant side, pain at rest, and having a local twitch response, jump sign, limited ROM, and referred pain lying over the lateral aspect of the UT fibres and superior to the ipsilateral occiput.25,26 The exclusion...
Effect of magnesium sulfate iontophoresis

371

criteria included latent MTrPs, serious pathologies such as cervical radiculopathy or myelopathy, fractures of the cervical spine, malignancy, and vascular syndromes such as vertebrobasilar insufficiency. Twenty subjects were excluded as they did not meet the inclusion criteria during the initial assessment for eligibility.

The subjects were randomly divided into two equivalent groups: the intervention (iontophoresis) group and the control (direct current) group. The randomisation process was performed using permuted blocks with a number generator. In our study, only the subjects were blinded to the intervention arm (see Figure 1).

Interventions

The subjects in the iontophoresis group received MgSO4 iontophoresis using an iontophoretic drug delivery system (Phoresor® II Auto, Model PM850, IOMED; Figure 2). MTrPs were examined using pincher palpation and marked by pin. MgSO4 was applied to the active positive electrode using a syringe with a concentration of 100 mg/cm². The active electrode was placed directly over the marked area where the sensitive MTrPs were located. The dispersive electrode was applied to the skin 6 inches distal from the active electrode (Figure 3). The dose required was selected on the device, which was 75 mA-min; depending on the subject's tolerance, the current intensity was gradually increased, ranging from 2 to 4 mA. The device automatically calculated the required time for the selected dose, and the treatment was repeated twice a week for four weeks.

The same procedures previously performed on the iontophoresis group were conducted on the subjects in the direct current group. Also, the same treatment-dosage (mA.min) guideline was followed, but MgSO4 was substituted with 1.0 ml of distilled water, and the treatment was repeated twice a week for four weeks.

Outcome measures

The assessment of the outcome measurements occurred at three time points: before treatment, immediately after the first session, and after treatment.

To assess pain intensity, the visual analog scale (VAS) is considered a valid and reliable tool. It consists of a line that is 10 cm long and has 2 ends: one end represents no discomfort or pain, and the other end denotes the severest degree of pain. The subjects were instructed to place a vertical mark to indicate their level of pain. Pressure pain threshold (PPT) assessment was performed using the Digital Electronic Pressure Algometer (Wagner Instruments, FDX, Greenwich, CT), which is a valid and reliable tool for gauging active MTrP tenderness. The transducer probe tip was applied perpendicularly to the MTrP. The exerted pressure was held and gradually increased until the subject expressed the first sign of pain; this point was the PPT value (see Figure 4).

To assess neck function, the Arabic neck disability index (ANDI) was used, which is widely regarded as a valid and reliable tool. It contains 10 classes/categories; in each category, six choices are presented (0–5). Each question in the questionnaire was explained in detail, and the subjects were asked to choose one out of six sentences that best described their function.

Neck ROM was assessed with a Myrin gravity-reference goniometer (Myrin OB Goniometer; OB Rehab Co. Anlic Company, 5-17182 Solana, Sweden), which is effective and has moderate to good reliability. The subject is instructed to perform the full available ROM to evaluate neck flexion. The strap was placed around the head at forehead level, and the dial was placed on the lateral aspect of the head (Figure 5). During the assessment of neck lateral flexion, the strap was placed around the head at forehead level, and the dial was placed on the forehead (Figure 6). During the assessment of neck rotation, the strap was placed at the centre of the top of the head, and the dial was placed at the centre of the top of the head (Figure 7).

Sample size determination

The pain score measured by VAS is the primary outcome measure. Based on a pilot study conducted on 10 subjects, it is used to calculate the required sample size using G*Power software (version 3.1.9.2). For a t-test with a Type I error rate of 5% (alpha level: 0.05), the effect size was 0.77, and the Type II error rate (beta) was set at 0.20 (power of 0.80). The total sample size estimated for the study was at least 56 patients (28 for each group). To compensate for possible withdrawals, 30 subjects per group were included in this study.

Data analysis

In the beginning, the Shapiro–Wilk test was employed to test the normality of the data distribution. Additionally, the data were screened for homogeneity of variance. Next, a parametric analysis was conducted once data were found not to violate the normality and homogeneity of variance assumptions. T-tests were used to perform baseline comparisons between both groups for patient characteristics (weight, age, and height), and a chi-square test was conducted to compare the distribution of sex and the affected side between the two groups. Moreover, to determine the main effect of time, the main effect of the interventions, and the main interaction effects of VAS, PPTs, ANDI, and neck ROM scores, a mixed multivariate analysis of variance (MANOVA) was carried out. Post-hoc tests using Bonferroni corrections were performed for subsequent multiple comparisons. For all statistical analyses, the significant point was set to \( p \leq 0.05 \). All analyses were conducted using the Statistical Package for the Social Sciences (SPSS), Version 25 for Windows.

Results

Subject characteristics

Sixty subjects (41 females and 19 males) from both groups were matched with consideration given to age, weight, height, affected side, and sex (Table 1).
To investigate the effects of treatment on VAS, PPT, ANDI, and neck ROM, mixed MANOVA was conducted, which revealed a significant interaction effect between treatment and time ($p = 0.0001; F = 24.702$). There was a significant main effect of treatment ($p = 0.0001, F = 24.038$), and a significant main effect of time ($p = 0.0001; F = 264.314$).

Within-group analysis of all measured variables showed significant differences immediately after the first session and after treatment in both groups, and the level of improvement in the iontophoresis group was greater than that of the direct current group ($p < 0.05$).

Between-group analysis indicated no statistically significant differences in the VAS, PPT, ANDI, and neck ROM before treatment between the iontophoresis and direct current groups ($p > 0.05$). On the other hand, there were significant differences in all outcome measures between groups immediately after the first session and after treatment in both groups; the level of improvement was greatest in the iontophoresis group ($p < 0.05$) (Table 2).

**Figure 1:** Flowchart for patients in the study. (Consolidated Standards of Reporting Trials).

**Figure 2:** Iontophoretic drug delivery system: (n).

**Figure 3:** Iontophoresis treatment with magnesium sulphate.
Figure 4: Pressure Pain Threshold Assessment.

Figure 5: Neck flexion assessment using OB goniometer.
Figure 6: Neck lateral flexion assessment using OB goniometer.

Figure 7: Neck rotation assessment using OB goniometer.

Table 1: Baseline comparisons of Subject's characteristics in both groups.

| Variables      | Iontophoresis group | Direct current group | MD   | p-value |
|----------------|---------------------|----------------------|------|---------|
|                | \(\bar{X} \pm SD\) | \(\bar{X} \pm SD\)  |      |         |
| Age (years)    | 20.53 \(\pm 1.71\) | 20.56 \(\pm 1.79\)  | -0.03| 0.94**  |
| Weight (kg)    | 65.96 \(\pm 10.49\) | 68.53 \(\pm 8.10\)  | -2.57| 0.29**  |
| Height (cm)    | 166.70 \(\pm 6.18\) | 165.83 \(\pm 6.58\) | 0.87 | 0.60**  |

Non parametric

| Sex            | Iontophoresis group | Direct current group | \(\chi^2\) value | p-value |
|----------------|---------------------|----------------------|------------------|---------|
| Females        | 21 (70%)            | 20 (66.66%)          | 0.077            | .781**  |
| Males          | 9 (30%)             | 10 (33.33%)          |                  |         |
Table 1 (continued)

| Affected side | Iontophoresis group | Direct current group | $\chi^2$ value | p-value |
|---------------|---------------------|----------------------|----------------|---------|
| Right         | 16 (53.33%)         | 18 (60%)             | 0.271          | .602**  |
| Left          | 14 (46.66%)         | 12 (40%)             |                |         |

σ: mean; SD: Standard deviation; MD: mean difference; t value: Unpaired t value; p value: Probability value; **: Non significant; $\chi^2$: Chi squared value.

Table 2: within and between group comparison for both iontophoresis group and direct current group.

|                      | Iontophoresis group | Direct current group | P value (Between group) | F (between) | Partial Eta Squared |
|----------------------|---------------------|----------------------|-------------------------|-------------|---------------------|
| **VAS**              |                     |                      |                         |             |                     |
| Pre (Mean ± SD)      | 6.566 ± 0.935       | 6.566 ± 0.626        | 1.000**                 | 29.698      | 0.000               |
| After 1st session    | 3.266 ± 1.142       | 4.833 ± 1.116        | 0.001*                  | 0.32        |                     |
| Percent of change (Pre vs 1st session) | 50.25%            | 26.39%               |                         |             |                     |
| Percent of change (Pre vs post session) | 85.79%            | 68%                  |                         |             |                     |
| P value within group (Pre vs 1st session) | 0.0001*           | 0.0001*              |                         |             |                     |
| P value within group (Pre vs. Post treatment) | 0.0001*           | 0.0001*              |                         |             |                     |
| F value (within)     | 613.046             |                      |                         |             |                     |
| **PPT**              |                     |                      |                         |             |                     |
| Pre (Mean ± SD)      | 0.676 ± 0.264       | 0.6003 ± 0.176       | 0.425**                 | 18.449      | 0.011               |
| After 1st session    | 1.458 ± 0.350       | 1.180 ± 0.251        | 0.001*                  | 0.177       |                     |
| Post (Mean ± SD)     | 2.462 ± 0.553       | 1.825 ± 0.703        | 0.001*                  | 0.208       |                     |
| Percent of change (Pre vs 1st session) | 115.68%           | 96.56%               |                         |             |                     |
| Percent of change (Pre vs post session) | 264.2%            | 204%                 |                         |             |                     |
| F value (within)     | 250.285             |                      |                         |             |                     |
| **ANDI**             |                     |                      |                         |             |                     |
| Pre (Mean ± SD)      | 17.433 ± 2.079      | 17.966 ± 1.751       | 0.287**                 | 69.360      | 0.020               |
| After 1st session    | 13.966 ± 1.956      | 16.200 ± 2.091       | 0.001*                  | 0.239       |                     |
| Post (Mean ± SD)     | 3.466 ± 1.332       | 11.166 ± 2.755       | 0.001*                  | 0.766       |                     |
| Percent of change (Pre vs 1st session) | 115.68%           | 96.56%               |                         |             |                     |
| Percent of change (Pre vs post session) | 264.2%            | 204%                 |                         |             |                     |
| F value (within)     | 763.971             |                      |                         |             |                     |
| **Neck flexion**     |                     |                      |                         |             |                     |
| Pre (Mean ± SD)      | 54.033 ± 4.552      | 54.333 ± 6.233       | 0.832**                 | 19.617      | 0.001               |
| After 1st session    | 65.700 ± 5.760      | 59.466 ± 5.888       | 0.001*                  | 0.229       |                     |
| Post (Mean ± SD)     | 48.200 ± 5.422      | 45.200 ± 5.074       | 0.031*                  | 0.078       |                     |
| Percent of change (Pre vs 1st session) | 21.59%            | 9.44%                |                         |             |                     |
| Percent of change (Pre vs post session) | 36.95%            | 16.32%               |                         |             |                     |
| F value (within)     | 340.348             |                      |                         |             |                     |
| **Neck side bending**|                     |                      |                         |             |                     |
| Pre (Mean ± SD)      | 41.100 ± 4.787      | 41.833 ± 5.382       | 0.579**                 | 6.375       | 0.005               |
| After 1st session    | 48.200 ± 5.422      | 45.200 ± 5.074       | 0.031*                  | 0.078       |                     |
| Post (Mean ± SD)     | 55.666 ± 5.377      | 48.400 ± 6.267       | 0.001*                  | 0.286       |                     |
| Percent of change (Pre vs 1st session) | 17.27%            | 8%                   |                         |             |                     |
| Percent of change (Pre vs post session) | 35.44%            | 15.69%               |                         |             |                     |
| F value (within)     | 204.895             |                      |                         |             |                     |
| **Neck rotation**    |                     |                      |                         |             |                     |
| Pre (Mean ± SD)      | 61.733 ± 3.226      | 63.466 ± 4.754       | 0.104**                 | 9.512       | 0.045               |
| After 1st session    | 70.933 ± 3.647      | 66.433 ± 5.276       | 0.031*                  | 0.203       |                     |
| Post (Mean ± SD)     | 77.4 ± 3.024        | 70.80 ± 6.138        | 0.001*                  | 0.325       |                     |
| Percent of change (Pre vs 1st session) | 14.9%             | 4.67%                |                         |             |                     |
| Percent of change (Pre vs post session) | 25.37%            | 11.55%               |                         |             |                     |
| F value (within)     | 276.278             |                      |                         |             |                     |

σ: mean; SD: Standard deviation; MD: mean difference; t value: Unpaired t value; VAS: Visual Analogue Scale; PPT: Pressure Pain Threshold; p value: Probability value; ANDI: Arabic Neck Disability Index; **: Non significant; *: Significant; F value: MANOVA test.
Discussion

The aim of this study was to investigate the immediate outcomes and post-treatment effects of MgSO4 iontophoresis on MTrPs in the UT muscle. To the best of the authors' knowledge, this is the first study to use MgSO4 iontophoresis on MTrPs. Few researchers have studied the effect of MgSO4 on other modalities and different musculoskeletal disorders. The results revealed decreased pain levels, improved neck function, and increased neck ROM. Immediately after the first session, both groups improved in all outcome measures. After treatment, increasingly significant improvement appeared, although the level of improvement was greater in the iontophoresis group than in the direct current group.

Energy crisis theory is a widely accepted theory for the aetiology of MTrPs; it states that MTrPs are caused by a recurrent microtrauma or macrotrauma to the muscle fibres, leading to an excessive release of calcium and a persistent shortening of the sarcomeres, which decreases the blood and oxygen supply, causing inadequate adenosine triphosphate (ATP) synthesis, which is essential to initiate muscle relaxation. This sustained contraction causes metabolic waste products to accumulate, which results in pain. Further, the motor endplate theory asserts that MTrPs are formed due to the abnormal and excessive release of acetylcholine from the motor endplate—even during relaxation—producing a persistent shortening of sarcomeres and the formation of contraction knots in the muscle fibres. These theories may be helpful in explaining the effects of MgSO4 iontophoresis on the management of MTrPs.

In the study, the improvement in pain occurred in two dimensions: pain intensity (using VAS) and PPT. After one session and after treatment, the improvement in the value of VAS reached 50.25% and 85.79%, respectively, in the iontophoresis group compared to 26.39% and 68% in the direct current group. For the PPT, after one session and after treatment, the percentage of change reached 115% and 264.2%, respectively, in the iontophoresis group compared to 10.9% and 60.9% in the direct current group. These findings are consistent with those of Mizutani et al., who explored the analgesic effect of iontophoresis with MgSO4 on healthy adult volunteers. They concluded that MgSO4 iontophoresis is effective in improving pain level, neck ROM, and neck function immediately after the first session and causes increasingly significant improvement after treatment in subjects with active MTrPs on the dominant upper fibres of the trapezius.

In the present study, after one session and after treatment, the improvement in neck function (ANDI) reached 24.82% and 402.9%, respectively, in the iontophoresis group compared to 10.9% and 60.9% in the direct current group. Fejer and Hartvigsen investigated the relationship between neck pain and disability, and found that pain is moderately correlated with disability, and that neck disability increases linearly with the rising number of pain sites and factors causing pain. Thus, the current study's results revealed that pain improvement enhances neck function.

There was a strong relationship between MTrPs in the UT muscle and the existence of joint hypomobility. Many theories have explored the relationship between MTrPs and joint hypomobility. Due to the increased tension of the muscular band and the facilitation of motor activity, muscle shortening and spasms occur. This leads to abnormal joint tension and dysfunction. Also, it is believed that MTrPs in the muscle send nociceptive stimulation to the dorsal horn neurons, thereby producing segmental hypomobility.

In this study, after one session and after treatment, the level of improvement in neck ROM reached 115.68% and 264.2%, respectively, in the iontophoresis group compared to 96.56% and 204% in the direct current group. These findings are consistent with those of Teslim et al., who scrutinised the effect of applying MgSO4 using electromotive force (iontophoresis) on the spastic biceps brachii muscle of stroke patients. They deduced that, with the application of MgSO4 using electromotive force, the spasticity of the biceps brachii muscle of stroke patients decreases significantly. These results are in line with those of Clinton et al., who examined the impact of MgSO4 in reducing painful muscle spasms; they concluded that the intravenous injection of 2 g of MgSO4 produces immediate relief of muscle spasms.

One possible explanation for the increasing neck ROM is the muscle relaxation effect of MgSO4 by lowering acetylcholine release at the myoneural junction, since this blocks peripheral neuromuscular transmissions, causing the inhibition of skeletal muscle contractions.

Study limitations

This study was limited by only reporting on the immediate and post-treatment outcomes of MgSO4. As such, the findings cannot be used to generalise about the long-term effects.

Conclusion

MgSO4 iontophoresis is effective in improving pain level, neck ROM, and neck function immediately after the first session and causes increasingly significant improvement after treatment in subjects with active MTrPs on the dominant upper fibres of the trapezius.

Recommendations

We recommend replicating the study using different age groups and assessment of the long-term effects of MgSO4.
Sources of funding

This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors have no conflicts of interest to declare.

Ethical approval

This study protocol was accepted before commencement by the Research Ethics Committee of the Faculty of Physical Therapy at Cairo University (NO: P. T. REC/012/002139). It was prospectively registered in the Pan African Clinical Trial Registry accepted at 30 July 2018 (registration number ID PACTR: 201807754550712).

Consent

All subjects signed a consent form before the start of the study after a detailed explanation of the treatment procedures.

Authors contributions

N.A.I came up with the idea, performed the research, gathered the data, and organised them. S.T.A was responsible for clinical assessment and statistical analysis. D.M assisted in writing the original draft and reviewed the final one. N.A.A reviewed and approved of the final draft. All authors have reviewed and approved of the final draft, and are responsible for the content and similarity index of the manuscript.

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