Electromotive Drug Administration of Magnesium Sulphate on Spastic Gastrocnemius Muscle of Stroke Patients

Ibrahim. M. Hassan¹, Maher A. Elkebalawy¹, Ahmed E. Elerian¹, Hatem S. Shehata², Abdelaziz A. M. Elsherif³, Ahmed M. Elkebalawy⁴

¹Department of Basic Science, Faculty of Physical Therapy, Cairo University
²Faculty of medicine, Cairo University
³Department of physical therapy for neuromuscular disorders and its surgery, Faculty of Physical Therapy
⁴Researcher in national center of research

DOI: 10.47750/pnr.2022.13.S0.6

Abstract

Objective: This study aimed to investigate the effects of Magnesium sulfate (MgSO₄) iontophoresis on electrical activity and functional ability (step length of the affected side) of the gastrocnemius muscle Methods: A total of 50 patients aged 45-65 years of both genders who were diagnosed with chronic cerebrovascular accident (29 females and 21 males) were recruited in this study and randomly assigned into 2 equal groups. Subjects in Group A received MgSO₄ iontophoresis in addition to passive stretching of the gastrocnemius for two session per week for 4 weeks, whereas group B underwent calf, quadriceps and hamstring muscle stretching for two sessions per week for 4 weeks. Electromyography was used to measure the electrical activity of the gastrocnemius muscle during rest and activity times (active plantar flexion) whereas the Biodex Gait Trainer 2 was used to measure the step length of the affected side; thus, patients were evaluated twice before and after allocation to each group. Results: Statistical analysis showed a significant change within all study variables when comparing pretreatment with posttreatment values in group A (p < 0.05) but not in group B (p > 0.05). Between-group analysis showed no significant changes in pretreatment values of all variables as (p > 0.05), whereas a significant change in all variables was observed in posttreatment values (p < 0.05). Conclusion: MgSO₄ iontophoresis is more effective than traditional therapy (stretching) in managing the spasticity of poststroke patients.

Keywords: EMG, Iontophoresis, Spasticity, Stroke.

INTRODUCTION

Stroke is one of the leading causes of disability and mortality worldwide [1]. It occurs when blood flow to the brain is restricted due to a blocked or ruptured artery; and when the cerebral energy supply is interrupted, resulting in tissue damage and widespread neuronal impairment [1]. Secondary limb abnormalities, physical disability, and pain are the most common complications of stroke due to spasticity that reduce the ability to perform basic daily tasks, including holding and picking up objects, self-care, and ambulation [2].

Spasticity is a motor disorder characterized by hypertonia and a velocity-dependent increase in muscle tone or tonic stretch reflexes [3]. It is commonly referred to as “tightness” or “stiffness” a severely increased muscle tone leading to joint immobility [4]. The most common spastic pattern in the lower limbs is knee adduction and extension with an equinovarus foot [5], which affected gait patterns and daily functioning activities [6].

Spasticity has been treated with various methods, such as physical therapy, splinting, oral medicines, chemical neurolysis, surgical procedures, and therapeutic exercises [7]. Therapeutic exercises were used to manage obesity [8], pain and muscle strength [9], balance [10] and spasticity [11].

Furthermore, oral anti spasticity drugs, such as baclofen, tizanidine, and diazepam, act on the central nervous system to reduce muscle tone, although they might have systemic adverse effects, such as lethargy or drowsiness [12]. Since baclofen has a short half-life of 2.6 h, regular administration is necessary to obtain the best results [13].
However, chemo denervation (e.g., phenol block) result in sensory loss and dysesthesia across the injected limb [14]. One of the most effective anti-spasticity treatments is the injection of botulinum toxin (BoNT), a protein neurotoxin generated from Clostridium botulinum, which selectively inhibits acetylcholine release at the neuromuscular junction [15].

However, BoNT injections costly, can result in the development of neutralizing antibodies after repeated injections, and may have unfavorable side effects such as post injection weakness if the dose is not ideal. When noninvasive treatments fail to control severe spasticity, surgical options, such as selective peripheral neurotomy or intrathecal baclofen pump implantation, are typically reserved [16].

Iontophoresis was used in various trials to prevent potential systemic side effects of oral and injectable medicines [17, 18]. It was becoming widely known in the area of spasticity relief with different types of medications; however, to date literature regarding the impact of MgSO4 iontophoresis on calf muscle spasticity in stroke patients has been limited.

**MATERIALS AND METHODS**

This randomized control trial, involved participants from Cairo University's Faculty of Physical Therapy's Outpatient Rehabilitation Program. Participants were referred to a physiotherapy program in the outpatient rehabilitation center as chronic spastic hemiplegic patients (>6 months after a cerebrovascular event).

In this study, a randomly selected sample (n = 50) from each gender was recruited (Fig. 1). The inclusion criteria were as follow: patients (1) aged 45-65 years, (2) with moderate spasticity grade of 3 according to the Modified Ashworth Scale, (3) who are responsive to verbal instructions (>13° on Glasco Coma Scale) and (4) who can walk independently without any assistive device.

To ensure an appropriate sample size, a power analysis was performed. The sample size was calculated to be 46 patients at a 95 % confidence interval, with an 80.0 % study power. Finally, the study involved 50 participants. Each participant provided informed permission before enrolment (NO: P. T. REC/012/002708), as required by our faculty ethical committee. This investigation was submitted to the Pan African Control Trial (Approval ID: PACTR202011752304906).

Patients were excluded if they had any other co-existing progressive neurological disorder and unstable cardiac function (acute myocardial infarction and severe cardiac failure), take any antispastic drugs, had any previous contracture or deformities, were un cooperative, and took oral magnesium sulfate (MgSO4).

Patients were randomly assigned to an experimental (n = 25) or control group (n = 25) using the simple random randomization of closed envelops as shown in (Fig. 1).

An independent researcher with >7 years of expertise in the electromyograph (EMG) and gait analysis analyzed both groups at 1-week pre- and postintervention program.
Electromyograph (EMG)

The muscle (calf muscle) surface was cleansed with cotton wool and alcohol pretreatment to reduce skin resistance. To facilitate access to the calf muscle, all treatments were performed while patients were lying on their faces with their feet outside the plinth. The active electrode was placed on the bulkiest area of the calf muscle and the dispersive electrode was placed 5 in distal to the active (around the ankle joint) [19]. The EMG (amplitude-time) was recorded during the resting state, active plantar flexion, and maximum planter flexion three times, and root mean squares (RMS) were calculated (Reid et al., 2012). A fresh towel was used to clean the treatment area post procedure.

Analysis of EMG data:

To ensure that no noticeable artifacts remained, EMG responses were visually examined on an amplitude-time display of EMG recordings. Direct current artifact, motion artifact, and electrode noise were subtracted before quantifying of EMG variables [20]. RMS normalization is performed [20], and RMS percentage is calculated during rest and activity times [21].
Gait analysis

At the Biodex Gait Trainer 2 laboratory, spatiotemporal aspects of gait were assessed. Before starting the examination, all processes were explained to the patients. Each patient was instructed to stand on the Biodex Gait Trainer. Before the evaluation, each patient’s velocity (or speed) was changed based on one’s capacity to walk as measured by the 10-meter walk test (10-MWT). The patient was asked to walk with the regular walking pattern on the trainer for 3 min. Thereafter, they were instructed to adjust their feet at the center while walking on the trainer to ensure the feet were printed on the screen. The instrument measures the spatial parameter of gait (step length). Data generated from the device were printed in a comprehensive report [22].

Treatment procedures

Group A: Experimental group

To determine the skin sensitivity preintervention, skin feeling was measured using warm water in a test tube (temperature), a pinprick (pain), and cotton wool (light touch) [17].

To reduce skin resistance, cotton wool and alcohol were used to wipe the muscle’s surface area before each treatment. To facilitate easy access to the calf muscle, all procedures were performed on a patient lying on their abdomens, in a comfortable position, and relaxed. A 2.5 mL of MgSO4 at a concentration of 100 mg/cm2 was applied using a syringe to the active positive electrode, which was then placed directly over the gastrocnemius muscle. The dispersive electrode was placed on the skin 6 in. apart from the active electrode [23].

The device’s required dose of 75 mA/min was used, which was gradually increased between 2 and 4 mA based on the patient’s tolerance. The device then calculated the necessary time for the specified dose. For 4 weeks, the interventions were repeated twice a week [17]. If a patient reported any sensation other than tingling, the treatment was discontinued, the electrodes were removed and the skin was inspected. If the skin displayed signs of blistering, the session was discontinued and the patient was removed from the study. If the skin appeared normal, we continued the treatment at a lower current [23].

Group B: Control group

The control group received ten repetitions of passive stretching for the calf, quadriceps, and hamstring muscles with a 5 min hold and a 30 s break between stretches.

Statistical Analysis:

With the alpha level set at 0.05, the measured variables were statistically evaluated and compared using the SPSS for Windows version 25 (SPSS, Inc., Chicago, IL). Data were checked for the existence of extreme scores, homogeneity of variance, and assumption of normality. The measured variables were found to be normally distributed using the Shapiro-Wilk test (p > 0.5).

RESULTS

Figure 1 shows the flowchart for study participants. Table 1 lists the baseline demographic and clinical data for each participant in the MgSO4 and stretching activity groups. Regarding age, body mass index, gender, and afflicted side, findings revealed no statistically significant differences between groups (P > 0.05).

Repeated measures multivariate analysis was undertaken to compare how the participants’ scores change the outcome measures between the two groups. Multivariate effects were found to be statistically significant for the main effects of groups (Wilk’s Λ = 0.258, F = 12.75, P 0.001, 2 = 0.742), for time (Wilk’s Λ = 0.06, F = 69.37, P 0.001, 2 = 0.94), and for the interaction of groups and time (Wilk’s Λ = 0.078, F = 52.64, P 0.001).
Follow-up univariate analysis of variance reveals significant change in EMG during rest time (F=37.52, p< 0.001, \( \eta^2 =0.439 \)), for EMG during the activity time (planter flexion) (F=56.64, p< 0.001, \( \eta^2 =0.541 \)), and step length (F=24.41, p< 0.001, \( \eta^2 =0.337 \)).

Table (1): One Way ANOVA of the Baseline Demographic Characteristics of Subjects(N=50)*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group A (n=25)</th>
<th>Group B (n=25)</th>
<th>F-Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(years)</td>
<td>59.4±7.9</td>
<td>53.8±9.2</td>
<td>2.257</td>
<td>0.29</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.5 ± 2.4</td>
<td>27.8±3.4</td>
<td>-.434</td>
<td>.66</td>
</tr>
<tr>
<td>Sex(M/F)</td>
<td>9/16</td>
<td>12/13</td>
<td>0.089</td>
<td>0.76</td>
</tr>
<tr>
<td>Affected side (R/L)</td>
<td>13/12</td>
<td>15/10</td>
<td>0.738</td>
<td>0.39</td>
</tr>
</tbody>
</table>

BMI, body mass index; M, males; F, females; R, right; L, left; F, fisher test; p, probability value; X 2, Data are mean± SD for age and BMI and counts for gender and affected side, P-Value < 0.05 indicate statistical significance.

Between-group comparison

All parameters pretreatment did not significantly differ between the study and control groups (P > 0.05). Tables 1 and 2 demonstrate that a significant increase in the step length for the study group compared to the control group (P 0.001) and a significant decrease in EMG during rest and activity times for the study group compared to that of the control group (P 0.001) were observed following the treatment.

Table (2): One Way ANOVA Between Groups Effects after 4 weeks of intervention

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>MgSo4 group (n=25)</th>
<th>Stretching group (n=25)</th>
<th>MD</th>
<th>99% CI</th>
<th>F-Value</th>
<th>sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMG during Rest</td>
<td>2.75±1.53</td>
<td>7.06±3.17</td>
<td>-4.32</td>
<td>(2.89-5.73)</td>
<td>37.5</td>
<td>0.0001</td>
</tr>
<tr>
<td>EMG during Activity</td>
<td>8.88± 2.5</td>
<td>14.4± 2.7</td>
<td>-5.56</td>
<td>(4.07-7.05)</td>
<td>56.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>Step length</td>
<td>0.41± 0.065</td>
<td>0.34± 0.03</td>
<td>0.71</td>
<td>(0.042-0.01)</td>
<td>24.4</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

EMG, Electromyography; MD, mean difference; CI, Confidence interval; p, probability value, P-Value < 0.05 indicate statistical significance.

Within-group comparison

The EMG during rest and activity times post treatment in the MgSO4 group was significantly lower than that during those times prior to treatment (P 0.001), but not significantly lower than in the stretching exercise group (P > 0.05). In addition, there was a nonsignificant increase in the step length posttreatment compared to that pretreatment in the group participating in stretching exercises (P > 0.05), whereas there was a significant increase in the step length posttreatment than that pretreatment in the MgSO4 group (P 0.001) (Table 3).
Table (3): EMG during rest and activity times and step length pre and at 4 weeks Follow-Up for MgSo4 Group and stretching group

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>MgSo4 Group</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>MD</td>
<td>99% CI</td>
</tr>
<tr>
<td><strong>EMG during</strong></td>
<td>8.06±5.5</td>
<td>2.75±1.53</td>
<td>-5.32</td>
<td>(3.84-6.77)</td>
</tr>
<tr>
<td><strong>Rest</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.0001</td>
</tr>
<tr>
<td><strong>EMG during</strong></td>
<td>13.2±2.19</td>
<td>8.88±2.5</td>
<td>-4.31</td>
<td>(3.52-5.09)</td>
</tr>
<tr>
<td><strong>Activity</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.0001</td>
</tr>
<tr>
<td><strong>Step length</strong></td>
<td>0.36±0.06</td>
<td>0.41±0.065</td>
<td>0.046</td>
<td>(0.058-0.035)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.0001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Stretching group</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characteristics</strong></td>
<td>Pre</td>
<td>Post</td>
<td>MD</td>
<td>99% CI</td>
</tr>
<tr>
<td><strong>EMG during</strong></td>
<td>7.33±3.2</td>
<td>7.06±3.17</td>
<td>0.273</td>
<td>(-1.12-1.72)</td>
</tr>
<tr>
<td><strong>Rest</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.706</td>
</tr>
<tr>
<td><strong>EMG during</strong></td>
<td>14.2±2</td>
<td>14.4±2.7</td>
<td>0.242</td>
<td>(-1.03-0.55)</td>
</tr>
<tr>
<td><strong>Activity</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.542</td>
</tr>
<tr>
<td><strong>Step length</strong></td>
<td>0.34±0.03</td>
<td>0.34±0.03</td>
<td>0.002</td>
<td>(-0.01-0.13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.787</td>
</tr>
</tbody>
</table>

EMG, Electromyography; MD, mean difference; CI, Confidence interval; p, probability value, P-Value < 0.05 indicate statistical significance.

DISCUSSION

This study investigated the effect of MgS04 iontophoresis on calf muscle spasticity versus stretching exercises of calf muscle, hamstring and quadriceps muscles on EMG (during rest and activity) of gastrocnemius muscle and functional ability (step length of affected side) in stroke survivors; 50 patients were randomly assigned into two equal groups: group A (MgS04 iontophoresis) and group B (stretching exercises).

Patients ages were 45 yrs to 65 yrs and females (29 patients) more than males (21patients) which is convenient with the prevalence rate of stroke patients worldwide [17, 24]. Data obtained from the two groups regarding EMG during rest time, EMG during activity time (planter flexion) and functional ability (step length during gait) were measured before starting treatment and 4 weeks of intervention for all groups. It conducted at the Outpatient Clinic and The Laboratory of Electromyography at the Faculty of Physical Therapy, Cairo University.

Regarding the effects of MgSo4 iontophoresis on EMG during rest time, EMG during activity time (planter flexion) and functional ability (step length during gait) in stroke survivors:

According to the data analysis in the current study, the results of (MgS04 iontophoresis) group revealed that there was a significant decrease after treatment in the values of EMG gastrocnemius during rest time by 64.69%, EMG gastrocnemius during activity time by 32.67% and increase in step length by 12.7 %.

Significantly lower spasticity scores indicated that magnesium sulphate iontophoresis might lessen spasticity during a single therapy session. By lowering acetylcholine release at the myoneural junction and inhibiting skeletal muscle contraction, the decrease of spasticity can be attributed to the restriction of magnesium sulphate to peripheral neuromuscular transmissions [25].

Additionally, the ions in magnesium raise the firing threshold in both myelinated and unmyelinated axons, and magnesium is a cofactor for enzymatic activities that play a critical role in neurochemical transmission and muscle excitability [26]. The mechanism of mgSo4 action is opposing to the action of spasticity on the muscles (Hyperexcitability) which lead to spontaneous electrical discharges from the motor nerve fibers that promote muscular activation [27].

The results of the study are convenient with the results of [28] who discovered that magnesium sulphate was useful for treating paraplegic patients' painful spasms and lowering low back spasm, respectively. Similarly, [29] discovered that the action of anesthetics and other muscle relaxants was boosted by magnesium sulphate.
Also, [30] reported that magnesium sulphate reduces the discomfort associated with protective spasms, which may help to reduce spasticity. [17] concluded that administering magnesium sulphate through iontophoresis was successful in lowering spasticity of the bicep brachii muscle in stroke survivors, but the study was just a technical report because of the study’s small sample size, which limited the findings' generalization.

Improved walking is one of the most important goals for stroke survivors [31]. Walking is a bipedal locomotion mode in which both feet remain in touch with the ground, followed by a single stance on one limb while the other is swung forward [31].

Regarding the results in our study improvement in gait function (step length) is postulated to decreased spasticity of the calf muscle which is combined with improve in joint flexibility (range of motion) [32], motor control and performance of spastic muscle [33]. Also, spasticity reduction makes it possible to learn normal movement patterns [34] and permit more efficient and useful use of selective motor control [35].

The result of the study is accepted with the result of [36] who observed that decreasing of spasticity using botulinum Botox improve the gait parameters (stride length and velocity) However, botulinum toxin injections have a high price tag, the potential for post-injection weakness, and the potential to produce neutralizing antibodies after repeated injections [16].

Furthermore [18], found that decreasing spasticity in the calf muscle using lidocaine iontophoresis improve gait parameters (stride length, velocity and cadence) in spastic diplegic cerebral palsy children.

Regarding the effects of stretching exercises on EMG during rest time, EMG during activity time (planter flexion) and functional ability (step length during gait) in stoke survivors:

According to the data analysis in the current study, the results of stretching exercises group revealed that decrease in the values of EMG gastrocnemius during rest by 3.7 %, EMG gastrocnemius during activity by 1.7 % and increase in step length by 0.6% and the change in these values was non-significant.

The non-significant decrease in the values is postulated to the viscous deformation of the tissue, stretching causes a temporary increase in tissue extensibility. This effect disappears soon as the tension is removed [37]. This result is compatible with the result of [38] who found that stretching exercises for wrist flexors is not significant to reduce spasticity and [39] claimed that stretching the ankle plantar flexors for 30 minutes improved ankle joint stiffness but had no impact on gait. Also, stretching exercises do not result in the plastic changes in the central nervous system needed to permit adaptation to the demands of any motor activity after repeated training, it makes sense that a few muscle stretching sessions have little to no impact on the functional plasticity of the neuronal circuits in the spinal cord [40]. had no effect on the gait [39].

The clinical implications of this study include that electromotive magnesium sulphate injection may be an effective way to manage common spasticity linked to upper motor neuron lesion. Iontophoresis using magnesium sulphate may be used in a cost-effective manner, while simultaneously reducing the risk of negative effects linked to oral MgSO4 because it is a local substance and the therapist can control the degree of spasticity by controlling the number and dose of MgSO4 iontophoresis sessions.

There were some limitations to the present study that should be considered. The lack of a follow-up period. Further study to be conducted to investigate the effects of MgSO4 iontophoresis on calf muscle power, ankle range of motion and compare the effects of MgSO4 iontophoresis and botulinum Botox A on muscle spasticity in stroke survivors.

**LIMITATIONS**

There are no limitations were obvious in the study.
CONCLUSION

MgSO4 iontophoresis is more effective than stretching exercises in reducing spasticity of the calf muscle and improve functional ability (step length) of stroke survivors.

ACKNOWLEDGMENTS

The authors would like to thank all the contributor authors in the study.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

REFERENCES


7. Bethoux F. Spasticity management after stroke


41. Bressel E, McNair PJ. The effect of prolonged static and cyclic stretching on ankle joint stiffness, torque relaxation, and gait in people with stroke. Phys ther. 2002 Sep 1;82(9):880-7. doi.org/10.1093/ptj/82.9.880