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COMPARATIVE EFFECTS OF MAGNESIUM SULPHATE IONTOPHORESIS ON POST-STROKE ELBOW FLEXORS SPASTICITY

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Abstract

Background: Controversy continues to trail the best physiotherapeutic approach to adopt in effectively managing hypertonicity in stroke patients. Magnesium sulphate is a muscle relaxant whose efficacy is relatively unexplored, and is unknown if it will be more effective than conventional cryotherapy.

Aim: The aim of this study was to compare the effects of cryotherapy, magnesium sulphate iontophoresis and the combination of both on the spastic elbow flexor muscles of stroke survivors.

Material and methods: Fifty-two stroke survivors were purposively recruited for the pre and post experimental study. They were randomly assigned to three groups, and the interventions were cryotherapy alone, magnesium sulphate iontophoresis (40 mA- mins) only and combination of both. The interventions were administered twice a week for six weeks for each group. The Modified Ashworth scale was used to grade the spasticity at baseline, 3rd and 6th week. Descriptive and Inferential statistics of Kruskal Wallis and Friedman tests were used to analyze the data obtained at $p<0.05$.

Results: Cyotherapy and Magnesium sulphate iontophoresis significantly ($p = 0.003$ and $p = 0.02$ respectively) reduced elbow flexors spasticity at 6th week. However, there were no significant differences ($p > 0.05$) when the three interventions were compared.

Conclusion: The three interventions were effective in alleviating spasticity of the elbow flexors of stroke survivors but none was superior over the other.

Keywords: *Stroke, Spasticity, Elbow Flexors, Cryotherapy, Magnesium sulphate Iontophoresis*

Introduction

Spasticity is best described as an increased, involuntary and velocity-dependent muscle tone that causes resistance to movement after damage to the central nervous system and this is as a result of an imbalance in the inhibitory and excitatory signals to the muscles[1]. Spasticity is one of a multitude of factors, leading to hypertonia, subsequently; there is hyper-reflexia, an exaggerated deep tendon reflex[2]. There are also features of involuntary movements, pain, decreased functional abilities and delayed motor development. Furthermore, spasticity had been reported to have significant impact on motor functions; hence, there is likelihood that it may affect Activities of Daily Living[3].

Spasticity can be highly debilitating as a result of flexor pattern of spasticity in the upper limbs and the extensor pattern in the lower limbs and it has been considered to be a major determinant of activity limitations[4]. It has been reported that spasticity restricts functional abilities and reduces quality of life[5,6]. These have made the management of muscle hypertonicity to be considered as an important goal in post-stroke patient care and rehabilitation[4,7]. The aims of interventions are to improve functions by managing spasticity so as to prevent contractures and correct deformities[8].

There are both pharmacological and non-pharmacological means of managing spasticity. Most mild and moderate spasticity cases are effectively managed with the conservative measures using available oral therapies such as Dantrolene, Diazepam tizanidine, Baclofen, Magnesium sulphate and Clonazepam. However, in cases of severe spasticity, there is less responsiveness to drug therapies[9]. Amongst drugs being considered for therapy is Magnesium Sulphate ($MgSO_4$), which is a naturally occurring mineral and it is often seen in the heptahydrate sulphate mineral epsomite. Magnesium sulphate has been known to be a muscle relaxant and vasodilator for over a century and it is considered physiologically to be an antagonist of calcium. In a systematic review reported by Nepal et al, it was found that magnesium sulphate was able to relieve muscle spasms in cases of tetanus[10.] Claudia et al, also observed that it was relevant in anesthesiology as an adjuvant for sedation, analgesia, neuromuscular relaxation, motor relaxation [11]. Ante-natal magnesium sulfate was also associated with a significant reduction in the risk of cerebral palsy by preventing preterm birth[12]. There are also reports of effectiveness in treating myalgia's, neuritis, deltoid bursitis, low back pain spasm and anti-arrhythmia in cases of cardiac arrest[13].

The quest to find best and effective techniques to adopt to reduce muscle spasticity is a continuing process[5]. Considering side effects of most drugs, the use of alternate means to administer medications is gaining wider acceptance. This includes the use of electromotive forces to administer medications through the skin without passing through the gastro-intestinal system[14,15,16]. Electromotive Drug Administration (EMDA) is a technique in which an electric current is used to deliver a medicine or other chemical through the skin. It is basically referred to as an 'injection without needle'[17]. Iontophoresis is a non-invasive technology that uses controlled low level electrical energy to transport ionized drugs through the skin in a safe and effective manner[17].

Cryotherapy is a conventional approach usually administered to manage spasticity. There are documentations with the potentiality of significantly reducing spasticity, and improving hand functions in children with spastic cerebral palsy[8] Also, a not too old literature, reported that long-term cryotherapy induced prolonged inhibitory effects on the clonus, thereby resulting in muscle relaxation[18]. Physiotherapists are still facing challenges on best approach to adopt to alleviate muscle spasticity arising from upper motor neuron lesions. Cryotherapy is a non-pharmacological therapy but iontophoretic administration of topical drug relaxant is an emerging trend in physiotherapy. Spruyt et al, and Hassan et al reported that magnesium sulphate has therapeutic benefits in controlling muscle spasms, alleviating pain and reducing autonomic instability[19,20]. However, there are very few clinical trials in the use of magnesium sulphate to alleviate muscle spasticity among stroke survivors[21].Onigbinde et al. observed that magnesium sulphate iontophoresis alone was not significantly better than the application of cryotherapy alone in the reduction of biceps brachii spasticity among stroke survivors[21]. The generalization of the finding Onigbinde et al is limited as a result of the small sample size of stroke survivors that participated in the study. There is still dearth of empirical data to ascertain the combined effects of therapies, that is, combining magnesium sulphate iontophoresis and cryotherapy. Aside from these, contradiction of findings is still trailing the effects of cryotherapy in alleviating spasticity[22]. Hence, the need to investigate the most effective between cryotherapy and magnesium sulphate iontophoresis in alleviating posts stroke elbow flexor spasticity.

Methodology

Participants

The participants in this study were stroke survivors receiving treatment at the Physiotherapy Department of Obafemi Awolowo University Teaching Hospital Complex, Ile- Ife. Sixty-one stroke survivors were recruited for the study; however, 52 stroke survivors completed the study.

Inclusion and Exclusion Criteria

The major inclusion criteria were that the participants must have developed spasticity post-stroke and should not be on any anti-spasticity medication. Also, the duration of onset must not be more than 3 months and the blood pressure must be relatively stable at 140/90mm/Hg. Excluded criteria were having co-morbidities like diabetes mellitus, impaired skin sensation, metallic implants, cardiac pacemakers and those with history of allergy to magnesium sulphate.

Sampling Technique

The sample size for this study was determined using a sample size formula (Cohen, 1988). A total of 61 stroke survivors were purposively recruited for the study and were randomly assigned to three groups using fish bowl technique. Seven were excluded for not meeting the inclusion criteria/irregular clinic attendance. Only 52 stroke survivors completed the study. Seventeen participants completed the study in cryotherapy group while there were 15 in the magnesium sulphate iontophoresis group while the combined therapy group had 20 (Figure).

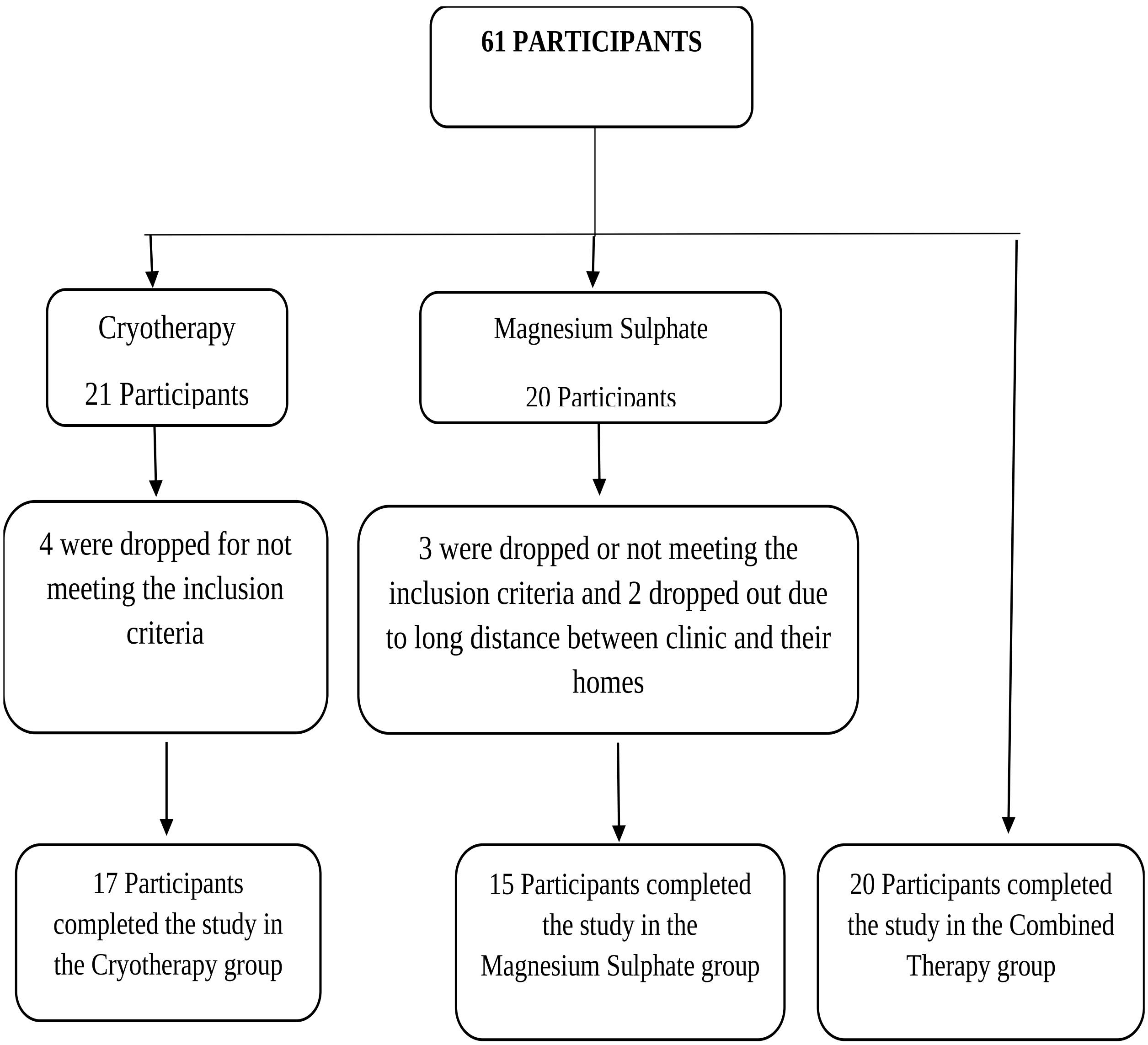

Fig: Flow chart for participants' recruitment

Instruments

The major test instrument was an Electrical stimulator with surface circular electrodes (Model: Endomed 582, India). The Magnesium Sulphate gel was compounded using the method of Onigbinde et al[20] while ice flakes were used for the application of cryotherapy, wrapped in a clean towel. Other instruments were mercury sphygmomanometer, stop watch, cotton wool, methylated spirit (Lifesign Healthcare Limited) and gauze bandage.

Research Design

The study was a pre and post experimental design.

Procedure

Ethical clearance was obtained from the Ethics and Research Committee, Obafemi Awolowo University Teaching Hospitals Complex. Participants were informed about the purpose of the study and they consented to participate. The surface area of the skin where electrodes were placed was cleaned with cotton wool soaked in 3ml of 95% ethanol[20].

The blood pressure of each participant was measured with a mercury sphygmomanometer and pulse rate was taken using the radial pulse; and recorded. Skin sensation was assessed from response to pin prick test. Thermal and cold sensations were assessed using test tubes filled with hot and cold water to ascertain normal skin sensation. A pre- treatment assessment of spasticity was carried out by passively flexing and extending the elbow while the patient was in a seated position. The level of spasticity was graded using the Modified Ashworth Scale[23]. The level of spasticity was graded as: 0- No increase in muscle tone (scored as Grade 0), 1- The presence of slight increase in muscle tone characterized by a catch and release at the end of range of motion when affected part is moved in flexion or extension (scored as Grade 1), 1^+- The presence of slight increase in muscle tone characterized by a catch followed by minimal resistance throughout the range of motion (scored as Grade 2), 2- The presence of marked resistance in muscle tone throughout the ROM but affected part can be easily moved (scored as Grade 3), 3- The presence of considerable increase in muscle tone and passive movement is difficult (scored as Grade 4), 5- Affected part is rigid in flexion and extension (scored as Grade 5).

Procedure for the Administration of Magnesium Sulphate Iontophoresis`

Patients were instructed to lie on the treatment couch, facing upward (supine position) and the surface area of the biceps brachii muscle was cleaned with cotton wool and methylated spirit. The electrodes were wrapped in wet gauze. 0.5g of magnesium sulphate gel (Finger Tip Unit) was applied to the positive electrode (anode). The electrodes (both positive and negative) were placed on the bicep brachii muscle using the labile electrode placement method. The electrical stimulator was preset to positive polarity and the cables of the electrodes were plugged into it and the current intensity was gradually increased using a dose of

40mA-min for 15 minutes[14,15, 21] in each participant. A clean towel was used to clean the area after treatment. After a brief period of 5 minutes, participants received 10 repetitions of passive stretching of the biceps brachii muscle and then the level of spasticity was assessed using the Modified Ashworth Scale pre and post intervention at onset, and post intervention at 3rd and 6th week respectively.

Application of Cryotherapy

This procedure was also carried out with the patient lying supine, relaxed and well positioned. A clean towel was used to wrap the ice flakes and it was placed on the bicep brachii muscle for 15 minutes[22]. The participants in this group also received 10 repetition of passive stretching of the arm flexors after application of the ice which was baseline for all the groups. The spasticity was also assessed using the Modified Ashworth scale and recorded pre- and post-intervention at onset, and post intervention at 3rd and 6th week.

Administration of Both Magnesium Sulphate Iontophoresis and Cryotherapy

The participants in this group received both interventions of groups 1 and 2. First to be administered was magnesium sulphate iontophoresis followed by the application of cryotherapy with 5 minutes' interval in between. This was to allow the permeation of magnesium sulphate gel through the skin and avoid washing away effect that may arise from the application of cryotherapy. All documentations were recorded.

Data analysis

The data were analyzed using descriptive statistics of frequency, means, standard deviation and percentage. Analysis of Variance (ANOVA) was used to compare age, height and weight of the groups. The Wilcoxon signed rank test was used to determine the immediate effects of intervention, Friedmann test was utilized for comparing pre and post intervention scores within the groups while Kruska-Wallis was used to compare the spasticity grades across the 3 groups. SPSS version 23 was used and Alpha level was set at $p < 0.05$.

Results

There were 10 (58.8%) males and 7 (41.2%) females among participants in the cryotherapy group. The sex distribution of participants in magnesium sulphate iontophoresis group and the group that had a combination of both magnesium sulphate iontophoresis and cryotherapy are presented in table 1. Twelve stroke survivors (70.6%) in the cryotherapy group had ischemic stroke; while five (29.4%) presented with hemorrhagic stroke. In the magnesium sulphate iontophoresis group, 12 participants (80%) and three (20%) presented with ischemic and hemorrhagic stroke respectively. In the combined therapy group, there were 14 (77.8%) ischemic and four (22.2%) hemorrhagic stroke patients. The type of stroke and side of affectation are presented in Table 2.

The mean ages of participants in cryotherapy, magnesium sulphate iontophoresis and the combined therapy groups are 55.35±4.60, 56.53±5.42 and 59.11±4.39 years respectively. The vital signs of the stroke survivors are presented in Table 3. The result of the Analysis of Variance showed that there were no significant differences in the cardiovascular parameters of the participants in the three groups, at the onset of interventions (Table

3). The mean height and weight of the participants in the cryotherapy group were 1.69±0.13m and 79.11±8.15kg respectively. Other means of height and weight of participants in the magnesium sulphate iontophoresis and combined therapy groups are also presented in Table 3. The results of the Analysis of Variance (ANOVA) showed that there were no significant differences in the height and weight of the participants.

Table 1: Gender distribution of participants in the groups

Groups	Male		Female	
	F	**%**	**F**	**%**
Cryotherapy	10	58.8	7	41.2
Magnesium Sulphate	10	66.7	5	33.3
Combined Therapy	11	61.1	7	38.9

Table 2: **Pattern of distribution of Types of Stroke**

Types		Cryotherapy		Magnesium Sulphate		Combined Therapy	
		F	**%**	**F**	**%**	**F**	**%**
Ischemic		12	70.6	12	80	14	77.8
Hemorrhagic		5	29.4	3	20	4	22.2
Affectation:	Right	3	17.6	1	6.7	3	16.7
	Left	14	82.4	14	93.3	15	83.3

Table 3: Age, cardiovascular parameters, height and weight of the participants

Variables	CRYO	MSI	CMT	F	p
Systolic BP (mmHg)	125±21.83	122.80±10.68	126.94±12.14	0.28	0.76
Diastolic BP (mmHg)	76.06±7.58	73.80±6.05	75.89±6.20	0.56	0.57
Pulse rate (bpm)	80.71±8.30	76.67±4.87	76.00±6.17	2.49	0.09
Height (in m)	1.69±0.13	1.70±0.13	1.74±0.12	0.86	0.43
Weight (in Kg)	79.12±8.15	79.73±7.72	79.72±5.74	0.40	0.96

*Key: **CRYO:** Cryotherapy **MSI:** Magnesium Sulphate Iontophoresis **CmT:** Combined Therapy group*

The mean ranks of biceps brachii muscle at onset and immediately after first treatment session are presented in table 4. The results showed that there was significant difference in the spasticity grades immediately after cryotherapy intervention (Z =3.32, p= 0.001). Similarly, significant differences were observed after interventions using magnesium sulphate iontophoresis and combination of both therapies (Z =-3.05, p= 0.002 and Z =-3.61, p=0,001) respectively (Table 4).

The mean rank at onset, 3rd week and 6th week post intervention was 35.03, 21.94 and 21.03 respectively. For the magnesium sulphate iontophoresis group the mean rank at baseline, 3rd and 6th week was 30.43, 18.33 and 20.23 respectively (Table 5). There are significant differences in the reduction of spasticity within cryotherapy, magnesium sulphate iontophoresis and combined therapy groups (T = 11.33, p = 0.003; T = 8.42; T= 22.81, p = 0.001 respectively). There were no significant differences in the level of spasticity across the groups at baseline, 3rd and 6th week of intervention (Table 6).

Table 4: Comparison of immediate effects of Interventions for cryotherapy group

Period		**N**	**Mean rank**	**Sum of ranks**	***Z***	**p**
Cryotherapy						
At onset	Negative ranks	11[a]	6.00	66.00	-3.32	0.001
Post Intervention	Positive ranks	0[b]	0.00	0.00		
Magnesium Sulphate						
At onset	Negative ranks	10[a]	5.50	55.00	-3.05	0.002
Post Intervention	Positive ranks	0[b]	0.00	0.00		
Combined Therapy						
At onset	Negative ranks	13[a]	7.00	91.00	-3.61	0.001
Post Intervention	Positive ranks	0[b]	0.00	0.00		

a. *Spasticity grade immediately after Intervention < spasticity at onset*
b. *Spasticity grade immediately after Intervention > spasticity at onset*

Table 5: Results of Friedman test comparing the spasticity grades at baseline, 3rd and 6th week post intervention

Groups	**Mean spasticity grades**			**T***	**P**
	Baseline	**3rd week**	**6th week**		
Cryotherapy	35.03	21.94	21.03	11.33	0.003*
Magnesium Sulphate	30.43	18.33	20.23	8.42	0.02*
Combined Therapy	40.50	20.72	.28	22.81	0.001*

Friedman test

Table 6: Comparison of spasticity grades across the groups

	Cryotherapy	**Magnesium Sulphate**	**Combined Therapy**		
	Mean rank	Mean rank	Mean rank	**H**	**p**
Baseline	23.44	26.63	26.50	0.839	0.66*
3rd week	26.62	25.50	24.44	0.234	0.89*
6th week	24.74	27.43	24.61	0.470	0.79*

Discussion

The singular application of cryotherapy, Magnesium Sulphate iontophoresis or the combination of both therapies, resulted to reduction in the arm flexor spasticity of stroke survivors in each group. The current outcome of this study provided empirical support to numerous previous documentations on the effects of cryotherapy in decreasing spasticity[8,18,22,25,26,27,28,29,30]. The application of cold packs in combination with other physiotherapeutic modalities enhances muscle relaxation, including cases of spasticity. The administration of magnesium sulphate alone through iontophoresis also reduced the grade of arm flexors spasticity after six weeks of intervention. The outcome of this study is similar to the reports of Onigbinde et al and Geneviva et al, although, magnesium sulphate was administered through infusion in that of the later report[21,31]. Similarly, the finding is not different from that of when magnesium sulphate was administered orally[32.]

There are reports that magnesium was not toxic when administered through skin and it does not also vaporize easily[33]. The neurophysiological effect of magnesium sulphate is that it blocks peripheral neuromuscular transmission by reducing acetylcholine release at myoneural junction resulting in inhibition of skeletal muscle contraction[34]. The pharmacological form of magnesium, is a physiological voltage-dependent blocker of *N*-methyl-D-aspartate (NMDA)-coupled channels and there documentation that it has anti-nociceptive role, blocks calcium influx, which inhibits central sensitization and decreases preexisting pain hypersensitivity[16]. Magnesium is a cofactor for enzymatic reactions which play important role in neurochemical transmission and muscular excitability and the ions elevate the firing threshold in both myelinated and unmyelinated axons[35]. Magnesium results into the reduction of acetylcholine release and dimishes motor endplate sensitivity to acetylcholine coupled with reduction in the amplitude of the motor endplate potential[36,37]. However, it is noteworthy that magnesium levels should be kept at a serum range between 0.75 and 0.95mmol/L, and this should be applicable even when administering through iontophoresis, especially in the elderly because several changes of magnesium (mg) metabolism have been reported with aging, including diminished Mg intake, impaired intestinal absorption and renal wasting[38]. The combination of cryotherapy and magnesium sulphate iontophoresis to alleviate spasticity was comparable to the singular application of either cryotherapy or magnesium sulphate iontophoresis. This study is in a verdant area of physiotherapy, hence, little comparison could be made with previous studies.

The clinical implication of this study is that there is no added advantage to combine cryotherapy with magnesium sulphate in the management of spasticity of the arm flexors among stroke survivors, despite that the two techniques have different neurophysiological effects on spasticity.

Conclusion

It was concluded that combined therapies showed no superiority over individual use of cryotherapy and magnesium sulphate iontophoresis in alleviating spasticity among stroke survivors. The outcome of this study, however, provides preference of choice for patients who may have hypersensitive allergy to either cold or magnesium.

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