Original Article

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Efficacy of a multimodal therapy protocol for upper limb spasticity in post-stroke hemiplegic patients: a randomized controlled trial

Eficácia de um protocolo de terapia multimodal para a espasticidade de membro superior em pacientes hemiplégicos pós acidente vascular cerebral: um ensaio clínico randomizado

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ABSTRACT

Objective: To evaluate the efficacy of a comprehensive treatment protocol with four therapeutic modalities for the recovery of patients with chronic stroke by evaluating clinical, neurological, and functional outcomes. **Methods:** Thirty-two subjects with stroke at least six months prior to the study were randomized to receive ten sessions of either treatment protocol or sham intervention. Treatment protocol consisted of low-frequency transcranial electrical stimulation, paraspinous blocks, spastic muscle needling, and functional electrical stimulation. Spasticity, range of motion, pain, functionality, and quality of life were evaluated using the Modified Ashworth Scale (MAS), goniometry, Visual Analog Scale (VAS), Functional Independence Measure (FIM), and Short Form 36 (SF-36) questionnaires. **Results:** Active group showed a significant improvement in functionality (at one week [p= 0.02] and at three months [p= 0.03]), range of motion (active shoulder flexion p= 0.012; active shoulder internal rotation p= 0.01; active shoulder abduction p= 0.002; active elbow extension p= 0.042) and quality of life (improvement from 14.34% to 108.33% in all domains of SF-36). Both groups had significant improvement in pain (p≤0.001). **Conclusion:** This protocol is effective for post-stroke upper-limb spasticity and leads to improvements in functionality, quality of life, and spasticity. (ClinicalTrials.gov Identifier - NCT05940805).

Keywords: Stroke, Muscle Spasticity, Transcranial Direct Current Stimulation, Rehabilitation

RESUMO

Objetivo: Avaliar a eficácia de um protocolo de tratamento abrangente com quatro modalidades terapêuticas para a recuperação de pacientes com acidente vascular cerebral (AVC) crônico, por meio da avaliação de desfechos clínicos, neurológicos e funcionais. **Métodos:** Trinta e dois indivíduos com AVC ocorrido há pelo menos seis meses antes do estudo foram randomizados para receber dez sessões do protocolo de tratamento ou da intervenção simulada (SHAM). O protocolo de tratamento consistiu em estimulação elétrica transcraniana de baixa frequência, bloqueios paraespinhais, agulhamento de músculo espástico e estimulação elétrica funcional. A espasticidade, amplitude de movimento, dor, funcionalidade e qualidade de vida foram avaliadas usando a escala de Ashworth Modificada (MAS), goniometria, Escala Visual Analógica (VAS), Medida de Independência Funcional (FIM) e questionários Short Form 36 (SF-36). **Resultados:** O grupo intervenção mostrou uma melhora significativa na funcionalidade (na primeira semana [p= 0,02] e em três meses [p= 0,03]), na amplitude de movimento (flexão ativa do ombro p= 0,012; rotação interna ativa do ombro p=0,01; abdução ativa do ombro p= 0,002; extensão ativa do cotovelo p= 0,042) e na qualidade de vida (melhora de 14,34% a 108,33% em todos os domínios do SF-36). Ambos os grupos tiveram melhora significativa na dor (p≤0,001). **Conclusão:** Este protocolo foi eficaz para o tratamento da espasticidade de membro superior pós-AVC e levou a melhorias na funcionalidade, qualidade de vida e espasticidade. (Registro ClinicalTrials.gov - NCT05940805).

Palavras-chaves: Acidente Vascular Cerebral, Espasticidade Muscular, Estimulação Transcraniana por Corrente Contínua, Reabilitação

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INTRODUCTION

Stroke is the second leading cause of death and has a 70.0% increase in incidence from 1990 to 2019.[1] From a socioeconomic point of view, stroke is an extremely costly disease that is an increasing economic burden in many countries.[2,3] Furthermore, and is the primary cause of severe permanent disability in adults in the United States.[4]

Classically defined as "a group of pathological conditions characterized by sudden, non-convulsive loss of neurological function due to brain ischemia or intracranial hemorrhages",[5] stroke has a higher incidence level in older age groups.[6] Other risk factors for stroke include hypertension, diabetes, dyslipidemia, smoking, heart disease, AIDS, drug abuse, alcoholism and a family history of stroke.[7]

After a stroke, during the initial cerebral shock phase, the patient's reflexes and voluntary movements become depressed and the muscles become flaccid. The reflexes begin to return within days or weeks and then become hyperactive within weeks to months. Hyperactivity decreases as voluntary movements are reestablished. However, this re-establishment can stop at any point during the recovery process, resulting in weakness and hyperreflexia. After-stroke spasticity usually includes velocity-dependent resistance to stretching, hyperreflexia, and clonus.[8] upper-limb spasticity is considered one of the most detrimental effects of stroke in terms of quality of life.[9]

In general, the primary causes of post-stroke spasticity are synaptic changes between type IA afferent fibers and spinal motor neurons, changes in upper motor neuron activation, and changes in intrinsic muscle characteristics. Because spasticity is derived from muscle, spinal, and neural factors,[10] it is reasonable that therapeutics should target these three topographies that contribute to the pathophysiology of spasticity.[11]

Several studies have suggested various methods for treating spasticity.[12-21] However, to date, there is no consensus regarding the best modality for treating upper-extremity spasticity.[21]

Among therapeutic modalities, transcranial direct current stimulation (tDCS) is a non-invasive neuromodulation technique that has gained importance in neurological rehabilitation. The technique involves applying a low-intensity electrical current, typically between 1 and 2 mA, through saline-soaked sponge electrodes placed on the scalp. tDCS can be administered in several ways, with anodal (a-tDCS) and cathodal (c-tDCS) being the most common. Anodal stimulation tends to increase cortical excitability, while cathodal stimulation has the opposite effect, decreasing it.[22]

The proposed mechanisms of action for tDCS in the context of stroke include modulation of cortical excitability in the affected area, reduction of inhibitory effects from the uninjured hemisphere, and improvement of local cerebral blood flow, with the aim of protecting neurons in ischemic areas. These theoretical mechanisms provide the basis for its application in rehabilitation, with the expectation that tDCS may facilitate the brain reorganization and plasticity necessary for the recovery of motor function.[22,23]

The benefits of transcranial direct current stimulation (tDCS) for the treatment of post-stroke spasticity are multifaceted, with the strongest evidence pointing to its effectiveness as a complementary intervention.[24] Although meta-analyses have shown that tDCS alone may not have a significant direct effect on spasticity reduction, there is strong evidence that it enhances the effects of other rehabilitation therapies. Research indicates that, when combined with interventions such as mirror therapy or brain-computer interface, tDCS substantially improves motor function and balance in post-stroke patients, acting as a facilitator of neuroplasticity and optimizing the gains of conventional rehabilitation.[25,26] Furthermore, the application of tDCS may positively influence lower limb function in combination with robotic therapy.[26]

Paraspinal block, in turn, has demonstrated significant benefits in the treatment of post-stroke spasticity, although the primary focus of some studies is pain. A randomized clinical trial, for example, showed that this therapy, also known as segmental neuromyotherapy, promotes an improvement in global arm function and a reduction in hemiplegic shoulder pain, which often accompanies severe spasticity.[27] The theoretical mechanism of action suggests that the blockade works by desensitizing the somatic nervous system, reducing the bombardment of nociceptive impulses (pain) that exacerbate muscle spasm and spasticity, facilitating rehabilitation.[28,29]

Dry needling is emerging as a promising intervention for post-stroke spasticity, demonstrating benefits in improving function and reducing muscle tone. Clinical studies and systematic reviews indicate that the technique can lead to a significant decrease in spasticity, as measured by the Modified Ashworth Scale, and an increase in range of motion (ROM) in affected joints. Additionally, dry needling may contribute to improved general motor function and walking ability when used as part of a rehabilitation program. Although more research is needed to standardize protocols, preliminary results suggest that dry needling, especially when combined with other therapies, is a safe and effective therapeutic option.[30,31]

Functional electrical stimulation (FES) applied to antagonist muscles has been shown to be an effective strategy in the treatment of post-stroke spasticity. This technique benefits patients by promoting reciprocal inhibition, directly reducing muscle tone and the stretch reflex of the spastic muscle.[32,33] Studies indicate that FES of antagonist muscles, such as the tibialis anterior to inhibit the triceps surae significantly improves motor function and performance in daily activities, such as walking and rising from a sitting position.[34]

This study was designed to evaluate the efficacy of a comprehensive treatment protocol using four therapeutic modalities compared with that of sham interventions. Considering the scientific evidence of the mentioned therapies for post-stroke spasticity, the treatment protocol consisted of transcranial electrical stimulation to treat the brain aspects of spasticity, paraspinal block to treat the medullary aspects, spastic muscle needling, and functional electrical stimulation to treat the muscular aspects. Additionally, the effects of the protocol on upper-limb spasticity

OBJECTIVE

The general objective of this study was to evaluate the efficacy of a comprehensive protocol involving four therapeutic modalities (transcranial electrical stimulation, paraspinous block, spastic muscle needling, and functional electrical stimulation) to improve post-stroke upper limb spasticity.

The specific objectives were to evaluate pain improvement and changes in quality of life and functional capacity in patients who were subjected to the comprehensive protocol compared with those in patients who underwent sham interventions.

METHOD

Subjects of both sexes were enrolled in the study based on the following criteria: age > 18 years, diagnosed with an ischemic or hemorrhagic stroke at least six months previously, and presence of single upper limb spasticity. Patients were excluded from the study based on the following criteria: spasticity due to conditions other than stroke, hypersensitivity to lidocaine, cardiac pacemakers, coagulation disturbances, or insufficient perceptual and cognitive capacity to understand the proposed treatment and answer questionnaires.

The study was approved by the local ethics committee in accordance with the Declaration of Helsinki and was carried out between August and December 2023. The study conforms to all CONSORT guidelines and reports the required information accordingly (see Supplementary Checklist). All subjects enrolled in the study read, understood, and signed informed consent forms before inclusion. The project was approved by the local ethics committee - Comissão de Ética Para Análise de Projetos de Pesquisa (CAPPesq) of Diretoria Clínica of the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo - HCFMUSP under registration number 3853, project number 0511/09. This trial was registered in ClinicalTrials.gov - Identifier - NCT0594080535.[35]

Randomization

The study subjects were randomly allocated to two groups: the protocol group (PG) and the sham group (SG). Randomization was performed using a computer-generated list of numbers in random blocks of two, four and six sequences. Randomization was performed by an independent individual who was not involved in the study and who also maintained the randomization list until the end of the study. Sequentially numbered opaque sealed envelopes were used to ensure that the allocations were kept confidential.

Intervention

This study was conducted in a tertiary hospital located in São Paulo, Brazil. All procedures were performed by two medical doctors who were specialists in physical medicine and rehabilitation and had more than six years of experience in the specific field of interventional pain treatment.

The PG received a combination of four therapeutic modalities twice a week for five weeks:

1. Low-frequency transcranial electrical stimulation[22-26] (2/100 Hz) was applied through 0.3-mm-diameter and 40-mm-long needles placed subcutaneously on the scalp at the projection of Penfield's motor homunculus and the sensory and frontal supplementary motor associative areas (Figure 1). The intensity of the electrical stimulation was adjusted such that the patient could feel it but did not experience discomfort. The total stimulation time was 30 min per session.

2. The paraspinous block[27-29] at the levels of the C5, C6, and C7 vertebrae was concordant with spasticity laterality. The procedure aimed to effectively block the medial branch of the posterior primary rami of the nerve root at the targeted segmental levels[29] using 1 cc of 1% lidocaine injected through a 22 G, 1 1/4" needle connected to a 5-cc syringe.

3. Dry needling[30,31] of spastic upper limb muscles, as identified through a thorough physical examination, using 0.3-mm-diameter and 40-mm-long needles.

4. Muscular functional electrical stimulation (FES) in antagonists[32-34] of the upper limb muscles with spasticity with the following parameters: 20-Hz frequency, 300-µs pulse width, zero-second ramp time, 5-second stimulation time, and 5-second resting time. The FES sessions were 30 minutes in length.

The SG also received the four modalities of intervention, but these modalities were all inactive. To simulate transcranial electrical stimulation and FES, electrodes were placed on the scalp and in the upper extremity muscles and connected to a device similar to a real electric current generator. This device did not transmit any electric current, but had blinking lights and produced sound to provide the subjects with visual and auditory feedback. Retractile needles were used to simulate dry needling and paraspinous blocks. Patients were blinded to the assigned treatment groups.

Patients in both groups received physical therapy instructions on upper limb mobilization and stretching and were encouraged to perform these exercises twice a day at home. After the interventions, patients in both groups received conventional care and were evaluated after undergoing a real or placebo procedure.

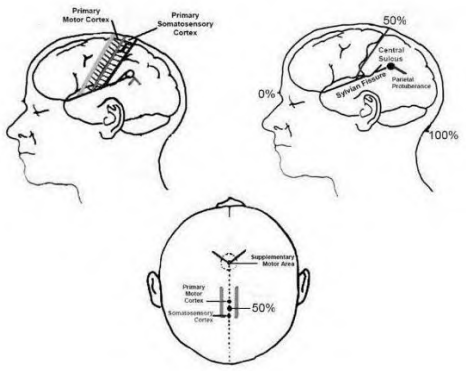

Figure 1. Diagram showing the localization of the needling points using scalp landmarks. With these landmarks, it is possible to localize the primary motor and sensory cortexes, as well as the supplementary motor associative areas

Assessments

Blinded examiners evaluated the patients at baseline, one week post-treatment and three months post-treatment. Baseline epidemiological data were collected before the start of the study and at each of the two study time points after treatment. The Modified Ashworth Scale (MAS)[36] was used to measure spasticity, and shoulder, elbow, and wrist active and passive goniometry were performed to measure range of motion improvement.[37] Additionally, pain, as measured by the Visual Analog Scale (VAS);[38] functionality, as measured by the Functional Independence Measure (FIM);[39] and quality of life, as measured by the Short Form 36 (SF-36)[40] questionnaire, was assessed at the same three time points.

Statistical Analysis

Sample size calculation was conducted based on MAS variation using the Minitab 15.0 software (Minitab Inc., Chicago, IL, USA). Considering a power of 90%, a significance level (alpha) of 0.05, and a mean difference of one point (standard deviation) between

groups in MAS, a sample size of 18 patients per group was calculated.

SPSS software (version 16.0; IBM Corporation, Armonk, NY, USA) was used for further statistical analysis. All descriptive continuous data are reported in terms of means and standard deviations. For baseline data, t-tests for independent samples were conducted to compare groups with respect to age, body mass index, stroke duration, and goniometry results. The chi-squared test was used to compare sex and spasticity laterality. The nonparametric independent samples Mann-Whitney U-test was used to compare the baseline values of the VAS, MAS, and FIM scores, as well as SF-36 health survey responses, between the groups. The outcome comparison tests used included the paired t-test for goniometry and Wilcoxon signed rank test for the VAS, FIM, MAS, and SF-36 health surveys.

RESULTS

Initially, the sample size calculation was performed based on a 1-point variation on the Modified Ashworth Scale (MAS), using a power of 90% and a significance level of 5%. Therefore, it was estimated that 36 participants (18 per group) would be needed to detect a significant difference between the groups. However, during recruitment and follow-up, four patients were lost, resulting in a final sample of 32 patients (21 men and 11 women), with ages ranging from 44 to 83 years (mean 57.81 years).

The baseline characteristics of the study population are presented in Table 1, and, in general, these characteristics were well balanced between the two groups. No side effects were reported during the study period. Losses occurred due to: Two patients died from external causes, unrelated to the intervention or the study; one patient withdrew due to logistical difficulties accessing the study site; one patient was withdrawn for health reasons, as he had to remain bedridden and was unable to continue participating (Figure 2). Patients were recruited between July 2023 and October 2023, and treatments and follow-ups took place between October 2023 and January 2024. With the final sample of 32 patients (16 per group), statistical power was recalculated and estimated at 78.1%, slightly lower than the initially planned power of 90%. Despite this reduction, the study still maintains sufficient power to detect significant differences in the main outcomes between the groups.

Modified Ashworth Scale

In the PG, a statistically significant improvement in MAS score was found. The intervention improved wrist extension one week post-treatment (p= 0.007), forearm supination (p= 0.034), and wrist extension (p= 0.034) three months post-treatment.

In the sham group, there was a significant difference in wrist extension one week post-treatment (p= 0.016), forearm supination (p= 0.038), and wrist extension (p= 0.007) three months post-treatment. There were no differences in the other parameters between the groups (Table 2).

Functinal Independence Measure

In the PG, statistically significant improvements in FIM scores were found. The mean increases in FIM score from baseline was 8.03 points at one week post-treatment (p= 0.02) and 5.28 points at three months post-treatment (p= 0.03). In the SG, no statistically significant difference in FIM score was found at any of the study time points.

Visual Analogue Scale

The VAS scores improved in both groups at one week post-treatment and three months post-treatment compared with baseline. In the PG, the mean VAS score reduced by 3.52 points (p<0.001) at one week post-treatment and by 3.47 points (p= 0.001) at three months post-treatment. In the SG, the mean VAS scores were reduced by 3.51 (p<0.001) and 3.23 (p= 0.001) points at one week and three months post-treatment, respectively.

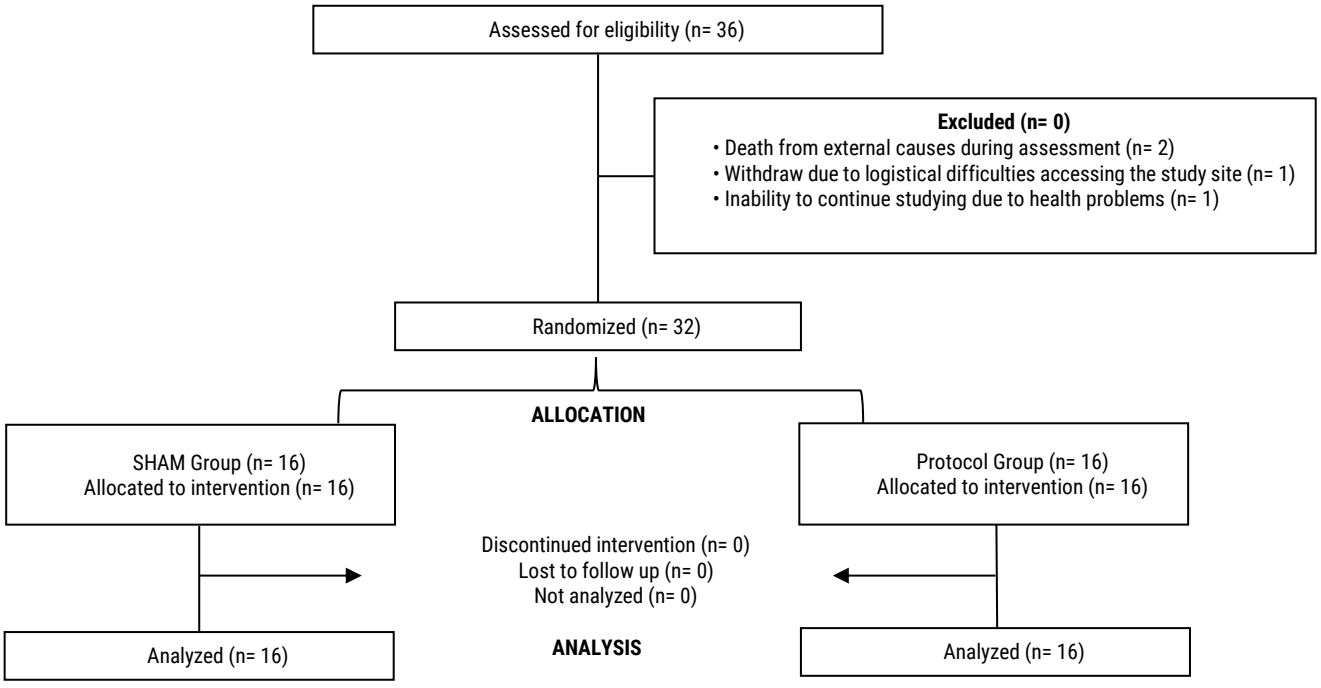

Figure 2. Participant flow diagram

Table 1. Characteristics of the Study Subjects at Baseline

	Protocol group	Sham group	p value
Age*	59.63 (±8.35)	56 (± 5.81)	NS
Gender	18.75% female	50% female	NS
	81.25% male	50% male	
Body Mass Index	25.84 (±4.73)	27.39 (± 3.89)	NS
Stroke Duration+	41.56 (± 75.57)	34.27 (± 52.21)	NS
Hemiplegia Laterality	35.25% right	43.75% right	NS
	68.75% left	56.25% left	
FIM	112.42 (± 17.29)	121.25 (± 5.88)	NS
VAS	5.73 (± 1.37)	6.17 (± 1.62)	NS
SF-36 Physical Functioning	34.68 (± 26.36)	46.87 (± 26.38)	NS
SF-36 Physical Role Functioning	37.5 (± 44.72)	29.69 (± 40.02)	NS
SF-36 Bodily Pain	36.37 (± 18.66)	33.06 (± 19.22)	NS
SF-36 General Health Perceptions	67.5 (± 22.12)	64.31 (± 16.18)	NS
SF-36 Vitality	52.5 (± 22.43)	50.31 (± 16.68)	NS
SF-36 Social Role Functioning	46.87 (± 31.79)	50.78 (± 27.94)	NS
SF-36 Emotional Role Functioning	45.83 (± 45.33)	20.83 (± 26.26)	NS
SF-36 Mental Health	69.75 (± 24.17)	55.25 (± 22.45)	NS
Active movement goniometry ‡ for:			
Shoulder flexion	59.31 (± 51.67)	98.13 (± 41.66)	.027
Shoulder extension	29.44 (± 16.92)	35.63 (± 12.34)	NS
Shoulder abduction	55.94 (± 39.09)	91.69 (± 38.78)	.014
Shoulder adduction	13.81 (± 13.61)	18.5 (± 12.12)	NS
Shoulder internal rotation	20.81 (± 16.65)	40.25 (± 31.23)	.036
Shoulder external rotation	33.75 (± 34.36)	50.88 (± 33.34)	NS
Elbow flexion	105.5 (± 34.53)	115.69 (± 33.52)	NS
Elbow extension	18.88 (± 27.39)	18.69 (± 30.74)	NS
Forearm supination	26.94 (± 40.6)	56.5 (± 26.24)	NS
Forearm pronation	64.63 (± 34.41)	72.75 (± 28.27)	NS
Wrist flexion	51 (± 27.63)	54.31 (± 18.54)	NS
Wrist extension	36.5 (± 25.08)	39.13 (± 23.51)	NS
Passive movement goniometry ‡ for:			
Shoulder flexion	115.5 (± 16.29)	132.38 (± 23.84)	.026
Shoulder extension	44.44 (± 9.88)	46.94 (± 11.11)	NS
Shoulder abduction	106.88 (± 23.6)	119.75 (± 27.46)	NS
Shoulder adduction	26.44 (± 12.94)	29.38 (± 11.75)	NS
Shoulder internal rotation	51.5 (± 29.2)	60.38 (± 28.68)	NS
Shoulder external rotation	62.56 (± 21.28)	77 (± 20.26)	NS
Elbow flexion	137.69 (± 7.45)	138.63 (± 7.24)	NS
Elbow extension	18.38 (± 40.68)	4.69 (± 8.53)	NS
Forearm supination	68.06 (± 27.63)	81 (± 9.96)	NS
Forearm pronation	88.13 (± 5.14)	86.38 (± 10.02)	NS
Wrist flexion	79.63 (± 14.55)	77.63 (± 9.99)	NS
Wrist extension	46 (± 26.47)	58.13 (± 14.68)	NS
AME for †:			
Shoulder flexion	1.72 (± 0.93)	1.38 (± 0.76)	NS
Shoulder extension	1.25 (± 0.84)	1.16 (± 0.7)	NS
Shoulder abduction	1.75 (± 0.82)	1.44 (± 0.75)	NS
Elbow flexion	1.19 (± 0.6)	0.81 (± 0.51)	NS
Elbow extension	1.31 (± 0.93)	1.25 (± 0.86)	NS
Forearm supination	1.84 (± 1.03)	1.34 (± 0.7)	NS
Forearm pronation	0.16 (± 0.44)	0.06 (± 0.25)	NS
Wrist flexion	0.62 (± 0.81)	0.72 (± 0.79)	NS
Wrist extension	2.03 (± 0.94)	1.69 (± 1.12)	NS

*NS, not significant; FIM, Functional Independence Measure; VAS, Visual Analog Scale; AME, Ashworth Modified Scale; *Measured in years; +Measured in months; ‡Measured in degrees; †Mean AME values assumed the six categories as 0, 1, 1.5, 2, 3, and 4*

Table 2. Modified Ashworth Scale Results for the Two Study Groups

Movement evaluated	Protocol Group			Sham Group		
	Baseline AME	1 week follow up (p value)	3 months follow up (p value)	Baseline AME	1 week follow up (p value)	3 months follow up (p value)
Shoulder flexion	1.72 ± 0.93	NS	NS	1.38 ± 0.76	NS	NS
Shoulder extension	1.25 ± 0.84	NS	NS	1.16 ± 0.7	NS	NS
Shoulder abduction	1.75 ± 0.82	NS	NS	1.44 ± 0.75	NS	NS
Elbow flexion	1.19 ± 0.6	NS	NS	0.81 ± 0.51	NS	NS
Elbow extension	1.31 ± 0.93	NS	NS	1.25 ± 0.86	NS	NS
Forearm supination	1.84 ± 1.03	NS	1.56 ± 1.08 (0.034)	1.34 ± 0.7	NS	1.12 ± 0.56 (0.038)
Forearm pronation	0.16 ± 0.44	NS	NS	0.06 ± 0.25	NS	NS
Wrist flexion	0.62 ± 0.81	NS	NS	0.72 ± 0.79	NS	NS
Wrist extension	2.03 ± 0.94	1.37 ± 0.45 (0.007)	1.59 ± 1.07 (0.034)	1.69 ± 1.12	1.28 ± 1.12 (0.016)	1.19 ± 0.95 (0.007)

NS: not significant.

SF-36 Health Survey

In both groups, improvements in the Bodily Pain category of the SF-36 questionnaire were found at one week and three months post-treatment. At one week, this category score improved by 74.74% (p= 0.002) in the PG and 70.32% (p= 0.001) in the SG. At three months, the score improved by 78.69% (p= 0.004) in the PG and by 48.77% (p= 0.006) in the SG compared with the baseline values. The scores for the categories of Social Role Functioning and Emotional Role Functioning significantly improved at the one-week follow-up. In the PG, social and emotional role functioning improved by 70% (p= 0.004) and 77.27% (p= 0.01), respectively. In the SG, social and emotional role functioning improved by 41.54% (p= 0.045) and 140% (p= 0.018), respectively. At three months, both categories also showed statistically significant improvements in both groups: Social Role Functioning, 73.33% (p= 0.003) in the PG and 45.15% (p= 0.032) in the SG; and Emotional Role Functioning, 81.82% (p= 0.007) in the PG and 190% (p= 0.009) in the SG. The score for the category of Physical Role Functioning significantly improved at the one-week follow-up in the PG (83.33%, p= 0.033) and SG (84.21%, p= 0.046), and at the three-month follow-up in the PG (108.33%, p= 0.009) and SG (97.74%, p= 0.008). At the three-month follow-up, only the PG improved significantly, with a 19.54% (p= 0.004) improvement in the General Health Perceptions category, a 32.14% (p= 0.001) improvement in the vitality category, 14.34% (p= 0.028) improvement in the Mental Health category, and 58.56% (p= 0.006) improvement in the Physical Functioning category. Table 3 summarizes the results of the SF-36 health survey.

Table 3. The SF-36 Health Survey

	Protocol Group				Sham Group			
	1-week follow-up	p value	3-month follow-up	p value	1-week follow-up	p value	3-month follow-up	p value
Physical Functioning	NS		58.56	0.006	NS		NS	
Physical Role Functioning	83.33	0.033	108.33	0.009	84.21	0.046	97.74	0.008
Bodily Pain	74.74	0.002	78.69	0.004	70.32	0.001	48.77	0.006
General Health Perceptions	NS		19.54	0.004	NS		NS	
Vitality	NS		32.14	0.001	NS		NS	
Social Role Functioning	70	0.004	73.33	0.003	41.54	0.045	45.15	0.032
Emotional Role Functioning	77.27	0.01	81.82	0.007	140	0.018	190	0.009
Mental Health	NS		14.34	0.028	NS		NS	

NS: not significant

Goniometry

The goniometric results are listed in Table 4. One week post-treatment, the intervention improved the active movement of shoulder flexion and internal rotation of the shoulder. Three months post-treatment, the intervention improved the active movement of shoulder extension, shoulder abduction, and elbow extension.

The sham group showed improvement in the active movement of shoulder abduction one week post-treatment. In addition, this group showed improvements in passive movement of shoulder abduction and internal rotation. There were no differences in other goniometric parameters between the groups.

Table 4. The goniometry results

	Movement Evaluated	1 week		3 months	
		PG gain (p-value)	SG gain (p-value)	PG gain (p-value)	SG gain (p-value)
Active	Shoulder flexion	9.13° ± 12.69 (0.012)	NS	NS	NS
	Shoulder extension	NS	NS	6.75° ± 8.32 (0.005)	NS
	Shoulder abduction	NS	13.37° ± 24.71 (0.047)	16.94° ± 17.8 (0.002)	NS
	Shoulder adduction	NS	NS	NS	NS
	Shoulder IR	8.06° ± 14.39 (0.041)	NS	10.83° ± 14.56 (0.01)	NS
	Shoulder ER	NS	NS	NS	NS
	Elbow flexion	NS	NS	NS	NS
	Elbow extension	NS	NS	5.25° ± 9.42 (0.042)	NS
	Wrist flexion	NS	NS	NS	NS
	Wrist extension	NS	NS	NS	NS
Passive	Shoulder flexion	NS	NS	NS	NS
	Shoulder extension	NS	NS	NS	NS
	Shoulder abduction	NS	14.12° ± 26.32 (0.049)	NS	NS
	Shoulder adduction	NS	NS	NS	NS
	Shoulder IR	NS	8.06° ± 14.68 (0.044)	NS	NS
	Shoulder ER	NS	NS	NS	NS
	Elbow flexion	NS	NS	NS	NS
	Elbow extension	NS	NS	NS	NS
	Wrist flexion	NS	NS	NS	NS
	Wrist extension	NS	NS	NS	NS

NS: not significant; IR: internal rotation; ER: external rotation

DISCUSSION

In post-stroke care, upper-extremity functional rehabilitation is a significant challenge for health professionals. A lack of consensus regarding the best physical therapeutic modality[21,41] was the primary motivation for the present study. No published studies have evaluated the efficacy of the combined interventions. Only a few studies have assessed separate physical modalities, and these studies have applied heterogeneous methods to quantify spasticity, pain, quality of life, and functional capacity. Therefore, because the present study evaluated a different protocol than the previous studies, the results are more difficult to compare.

Upper limb spasticity was measured using MAS and goniometry.[36,37] The MAS scores showed minimal improvement in both the groups with respect to forearm supination and wrist extension. This result could be explained by the fact that the MAS is a categorical six-point scale that may fail to detect subtle variations that still represent an improvement. Goniometry is a more precise detection method for evaluating smaller changes. This method showed significant improvements in the PG and SG. Interestingly, in the PG, improvements in goniometry only occurred in active movements of shoulder flexion, internal rotation, extension, abduction, internal rotation, and elbow extension.

One important aspect of the study results was the sustained improvement in FIM scores. An improvement in FIM scores is one of the factors that leads to an improvement in quality of life.[39,42] This study supports this assumption based on the SF-36 quality of life questionnaire results. Physical Function, General Health Perception, Vitality, and Mental Health improved only in the PG group.

Spasticity, as evaluated by MAS, has been previously studied in post-stroke patients with upper limb spasticity receiving muscular electrical stimulation[43,44] or transcranial electrical stimulation.[45] Among these studies, improvements in the MAS score have been inconsistent owing to a lack of statistical significance, uncontrolled co-interventions, or extremely brief effects. Our study also failed to detect meaningful improvements in MAS scores in the treated patients. Using goniometry, we observed improvements in both groups, similar to previously reported results of trials that studied muscular electrical stimulation.[46,47] However, the significant goniometry improvement for active movements differentiates our study from previous reports. This result may be due to the central neuromodulatory effect of the treatment protocol, which results in the enhancement of neural control of the upper limbs.[48,49] Furthermore, active range of motion, compared with passive motion, is more physiologically relevant and beneficial to functionality, as corroborated by improvements in the functional independence measure scale in our study.

Previous publications on muscular electrical stimulation documented FIM improvements in patients with post-stroke upper limb spasticity.[44,46,50] In the present study, the addition of three other treatment modalities, transcranial electrical stimulation, paraspinal block, and spastic muscle needling, tripled the magnitude of FIM improvement. To date, no published studies have evaluated FIM as an outcome measurement in post-stroke upper-limb spasticity during a long-term follow-up period. However, our study demonstrated a sustained FIM improvement of 5.3 points three months post-treatment.

Currently, there are no published reports evaluating transcranial

electrical stimulation, paraspinal block, muscle needling, or muscular electrical stimulation using the SF-36 quality of life questionnaire as an outcome. Some studies on the use of botulinum toxin type A to treat post-stroke upper limb spasticity have reported improvements in the categories of social role functioning, physical role functioning, and Physical Functioning.[51-53] The scores for these three categories also improved significantly in our study; however, social and physical role functioning improved in both groups.

One factor that can explain the significant improvements in SG is the successful placebo effect achieved by the simulated interventions. Sham devices can produce an enhanced placebo effect, primarily when dealing with pain, resulting in improvements as high as 50%.[54] This was exactly what we observed in the present study regarding the pain outcomes. Both measurements of pain, that is, the Bodily Pain category of the SF-36 and the VAS score, showed significant improvements in both groups at one week and three months post-treatment. In a previous clinical trial[55] studying paraspinous blocks for upper limb pain treatment in post-stroke patients, VAS scores were reduced (approximately 3) in the active treatment group, which was similar to our results. However, pain reduction in the control groups differed greatly between the trials. Although the paraspinous block trial reported that pain reduction was not significant in control patients who received only physiotherapy without any sham procedure, our study showed a pain reduction of 3 points on the VAS in patients who underwent simulated interventions.

Because significant improvements were observed in both PG and SG, it is not possible to state that the proposed protocol is more effective than sham interventions for treating upper limb pain in post-stroke patients. Physiotherapy orientation may explain the improvements observed in both groups, as strengthening and stretching exercises are interventions that have proven effective in the treatment of post-stroke upper limb spasticity.[41]

Of all the outcome measurement methods, the FIM is the most socially relevant. The FIM is universally used to describe function in relation to measuring “burden of care” or “the type and amount of assistance required for a person with a disability to perform basic life activities”.[56] Therefore, the sustained improvement of PG may be the most important result of the study, as it impacts not only the patient but also the entire network of personnel involved in the patient’s daily care.

As a pioneering study, our study approximates a real-life rehabilitation scenario in which complex conditions, such as post-stroke upper-limb spasticity, are rarely treated with monotherapy. Additionally, most publications studying transcranial electrical stimulation, paraspinal block, muscle needling, or muscular electrical stimulation only assessed the immediate follow-up outcomes. In contrast, our study illustrates how patients evolve during real-life treatments. Another strength of our study was the meticulous design of the sham interventions. With reliable simulated interventions, it is possible to estimate the placebo effect more clearly and rule out overestimation of real treatment.

The relatively small sample size may be a limitation of the present study. Notably, with a comprehensive treatment protocol that included four different therapeutic modalities, the study design was not designed to differentiate which specific modality was responsible for a specific improvement. The results of this first-of-its-kind proof-of-principle study are relevant for promoting future research to answer new questions such as "What is the exact contribution of each treatment modality?" What are the mechanisms underlying these observed effects?"

CONCLUSION

In conclusion, the comprehensive protocol is a valid treatment for post-stroke upper-limb spasticity, improving functionality, quality of life, and spasticity. Further studies with larger sample sizes and longer study periods should be conducted to better understand and improve the protocol.

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AUTHOR CONTRIBUTIONS

Pimentel DC and Amadera JED were responsible for group coordination, research planning and data collection, as well as data analysis, writing of the article and assisting other authors when necessary. Chen J and Pimentel TSC was responsible for writing the text, statistical analysis, review of results, review of the discussion text and conclusion of the scientific article. El Abd O and Arakaki CRL were responsible for assisting in article revision and writing of the text. Iuamoto LR, Azevedo RS and Hsing WT were responsible for general supervision of the scientific article from its conception, writing, data collection, discussion among authors at each stage of the project and review of article writing. All authors have read and approved the final manuscript.

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