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Review article

Effects of baclofen administered to reduce muscle spasm on balance maintenance, gait ability and quality of life in stroke patients

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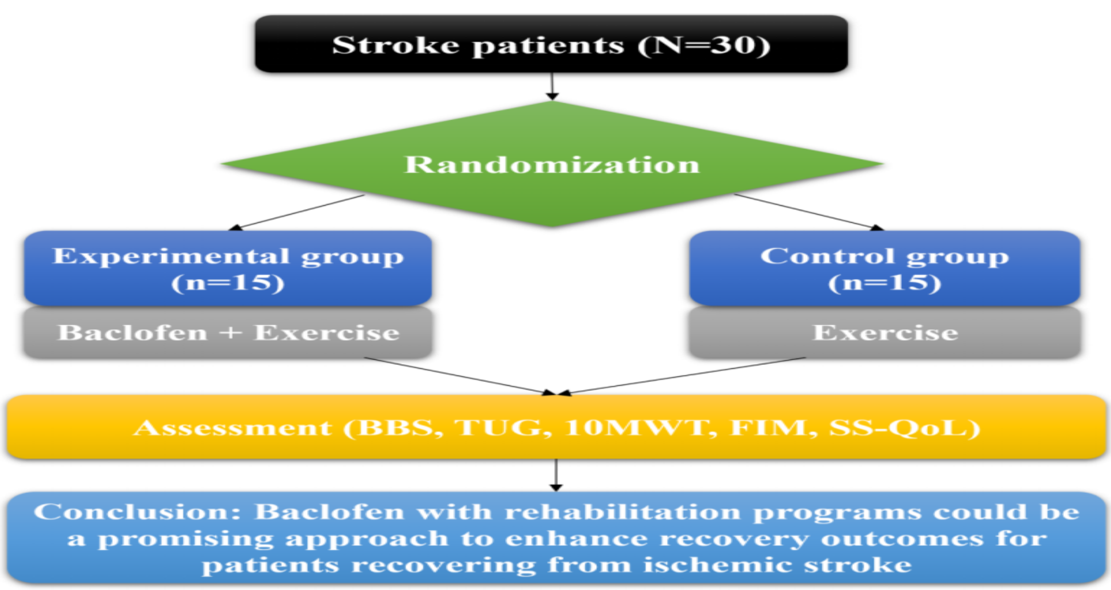
ABSTRACT

This study aimed to investigate the impact of Baclofen on balance, gait, functional independence, and quality of life in ischemic stroke patients. Thirty patients diagnosed with ischemic stroke by a rehabilitation medicine specialist were randomly assigned to either an experimental group that underwent exercise therapy in conjunction with Baclofen or a control group that received conventional exercise therapy without Baclofen. In this study, Berg Balance Scale, Timed Up and Go, and 10-Meter Walk Test were used to evaluate balance and walking ability. Functional Independence Measure was employed to assess functional independence, and Stroke-Specific Quality of Life was used to evaluate the quality of life. The experimental results revealed statistically significant improvements in all evaluation measures for both groups when comparing post-test to pre-test. However, in comparisons between groups, all test items in the experimental group that combined Baclofen with exercise therapy were significantly higher than those in the control group. In conclusion, these results suggest that integrating Baclofen into exercise therapy rehabilitation programs could be a promising approach to enhance recovery outcomes for patients recovering from ischemic stroke.

Keywords: Baclofen, Ischemic stroke, Functional activity, Quality of life

Figure 1: Grapical Abstarct



INTRODUCTION

Stroke, caused by the interruption of blood flow to the brain, can result in a variety of impairments, including cognitive, sensory, and motor deficits. Among these, balance and walking impairments are particularly prevalent and debilitating, affecting up to 75% of stroke survivors [1]. These impairments can lead to decreased mobility, increased risk of falls, and reduced quality of life [2]. A stroke occurs when the blood supply to a part of the brain is either reduced or interrupted, leading to a lack of oxygen and nutrients for the brain tissue. This deprivation ultimately results in the death of brain cells and can cause long-lasting or permanent damage to the affected individual. There are two main types of strokes as ischemic stroke and hemorrhagic stroke [3].

Ischemic strokes account for approximately 87% of all strokes and occur when an artery supplying blood to the brain becomes blocked [4]. This blockage can result from two primary causes. A thrombotic stroke is caused by a blood clot that forms directly in an artery supplying blood to the brain. This clot typically develops in areas where the artery is already narrowed due to atherosclerosis, a condition characterized by the build-up of fatty deposits on the inner walls of the arteries [5]. The plaque build-up can lead to the formation of a blood clot, ultimately obstructing the flow of blood to the brain. An embolic stroke is caused by a blood clot or other debris that forms elsewhere in the circulatory system and travels through the bloodstream to the brain. In this case, the clot becomes lodged in a narrow artery, blocking blood flow to the brain. Common sources of emboli include the heart, particularly in individuals with atrial fibrillation, and large arteries in the neck, such as the carotid artery [6]. Hemorrhagic strokes account for approximately 13% of all strokes and occur when a blood vessel in the brain ruptures or leaks, causing bleeding in the brain tissue. This bleeding can result in increased pressure on the brain, leading to further damage [7].

The underlying causes of balance and gait impairments following stroke are multifactorial, including muscle weakness, spasticity, sensory deficits, impaired motor control, and cognitive dysfunction [8]. Consequently, rehabilitation programs targeting balance and walking ability must address these complex interactions to optimize functional recovery. Stroke often affects the motor system, specifically the areas responsible for maintaining balance and coordination [9]. Damage to these areas can cause difficulties in postural control and proprioception, leading to a reduced ability to maintain balance. This can manifest in various ways, such as unsteady gait, swaying, and increased risk of falls [10]. The ability to walk is frequently impacted by stroke, as the condition often leads to muscle weakness or paralysis on one side of the body [11]. This asymmetric muscle function can result in a range of gait abnormalities, including reduced walking speed, decreased stride length, and increased energy expenditure. Furthermore, impaired balance and coordination can exacerbate walking difficulties, causing additional challenges in regaining functional mobility [12].

Spasticity is a common complication in patients who have experienced a stroke. It is characterized by increased muscle tone, involuntary muscle contractions, and can be associated with pain or discomfort. This condition can severely limit a patient's ability to perform daily activities and reduce their quality of life [13]. Among the various treatment options, Baclofen has emerged as a particularly effective medication for reducing spasticity in stroke patients. Baclofen is a muscle relaxant and an anti-spastic agent. It works primarily by acting on the GABA (gamma-aminobutyric acid) receptors in the spinal cord and brain. GABA is an inhibitory neurotransmitter, and by activating its receptors, Baclofen helps reduce the excitability of motor neurons, which in turn decreases muscle tone and relieves spasticity [14]. Multiple studies have shown that Baclofen is effective in reducing muscle tone and improving the range of motion in patients with spasticity following a stroke. Patients often experience less stiffness, which can improve mobility, facilitate participation in physical therapy, and enhance the patient's ability to perform activities of daily living [15].

Traditional treatment methods for stroke patients include physical therapy, occupational therapy, and speech therapy. These approaches focus on improving motor function, balance, and walking ability through targeted exercises, gait training, and functional activities. In recent years, there has been a growing interest in utilizing technology to enhance the rehabilitation process, with robot-assisted training emerging as a promising tool [16]. Exercise therapy has been shown to improve motor function and facilitate neural recovery in stroke patients. This approach typically involves the use of exoskeletons or robotic devices that assist in performing repetitive movements, allowing patients to engage in high-intensity, task-specific training [17]. By providing external support and guidance, these devices can help stroke patients regain their balance and walking ability more effectively than traditional therapy alone [18].

The purpose of this study is to investigate the effects of a combined treatment approach, involving Baclofen and exercise therapy, on balance maintenance, walking ability, and quality of life in stroke patients. Through a series of clinical trials and assessments, this study seeks to elucidate the potential synergistic effects of this combined approach and provide evidence-based recommendations for clinical practice in stroke rehabilitation.

MATERIALS AND METHODS

Subjects

In this study, a total of 30 patients diagnosed with ischemic stroke by a specialist in rehabilitation medicine were selected as subjects. To randomly assign the participants to either the experimental group or the control group, a card-based randomization method was employed. Each patient was asked to select a card marked with either 'A' or 'B.', and those who selected the card with 'A' were assigned to the experimental group, while patients who picked the card with 'B' were assigned to the control group.

All subjects participating in this study provided informed consent after receiving detailed explanations of the experimental procedures. They signed consent forms to confirm their voluntary participation and understanding of the study objectives and potential risks. The study was conducted in accordance with the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of University.

The inclusion and exclusion criteria for the selection of subjects in the study are mentioned below. Inclusion criteria for the study encompass participants aged between 55 and 75 years, diagnosed with a first-time unilateral stroke confirmed by a magnetic resonance imaging scan. Eligible subjects must be within 12 weeks to 12 months post-stroke onset and possess the ability to understand and follow verbal instructions, demonstrated by a score of ≥24 on the mini-mental state examination. Exclusion criteria for the study include severe cognitive deficits that interfere with participation, significant visual, or vestibular impairments affecting balance or walking, a history of multiple strokes or other neurological conditions impacting balance or walking ability, severe musculoskeletal or joint limitations restricting participation or confounding study outcomes, contraindications for robotic-assisted training (e.g., implanted pacemakers, skin conditions), and concurrent participation in another clinical trial that could affect balance or walking ability.

Intervention methods

Pharmacological intervention

In the experimental group, participants were administered an initial dosage of Baclofen (Saol Therapeutics, Roswell, GA, USA), amounting to 5 mg thrice daily. The medical team, equipped with pharmacological expertise, vigilantly monitored the participants for side effects and therapeutic response. The dosage was systematically escalated in increments of 5 mg every three days. This titration was executed until an optimal dose was ascertained, which ameliorated spasticity without inducing severe side effects.

Subsequently, the appropriate amount of Baclofen dosage was determined for each patient individually based on their response and tolerance. It was imperative to personalize the dosage to ensure optimal therapeutic outcomes while minimizing adverse effects. Once the individualized optimal dosage of Baclofen was established for each participant in the experimental group, a structured exercise treatment regimen was initiated. This exercise treatment was carefully timed to be administered post each Baclofen dosage during the experimental period. The rationale behind this scheduling was to harness the maximal reduction in spasticity rendered by Baclofen, and thereby facilitate more effective and efficient exercise therapy sessions.

Exercise therapy

In this study, the exercise therapy applied to the experimental group utilized the robot rehabilitation system (iReGo, Shanghai Jinshi Robot Technology, China), a lower extremity training robot specifically designed for rehabilitation purposes. The system is equipped with pelvic support to ensure patient safety and comfort during the training sessions. The iReGo robot rehabilitation system features a sophisticated motion control algorithm that guides an individual's lower limbs along a predetermined trajectory on an over ground walking track, simulating natural gait patterns and promoting functional improvements.

To further enhance the effectiveness of the training, the iReGo system was customized and adjusted according to each patient's specific needs and rehabilitation goals. The system offers multiple training modes, such as standing, sitting, and walking, which can be tailored to target specific functional deficits or challenge the patient's balance and coordination abilities. Additionally, the iReGo robot rehabilitation system provides real-time feedback on the patient's performance, allowing the therapist to monitor progress and make any necessary adjustments to the training protocol.

Design of study

For the experimental group, after the administration of the individually tailored dosage of Baclofen, participants engaged in exercise therapy using the iReGo system. Each treatment session was conducted three times per week for a duration of six weeks and lasted for 45 minutes. Within each session, participants underwent 30 minutes of robot-assisted walking and 15 minutes of balance exercises. Real-time visual feedback was provided to the participants throughout the session, as per the iReGo system protocol. The combination of Baclofen and RAT aimed to maximize the benefits of reducing spasticity and improving motor function.

The control group underwent conventional therapy, which included gait and balance training. The frequency and duration of the conventional therapy were kept identical to the experimental group, i.e., 45 minutes per session, three times per week for six weeks. However, the control group did not receive Baclofen, and the therapy was solely focused on physical exercises.

Both groups were evaluated for balance, walking ability, functional independence, and quality of life before the first intervention session and after the completion of the last intervention session. These assessments were diligently conducted by an experienced physical therapist with over 10 years of clinical experience in stroke rehabilitation.

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Assessment methods

In this study, the Berg balance scale (BBS) and timed up and go (TUG) test were utilized to evaluate the participants' ability to maintain balance following a stroke. The BBS is a widely used clinical assessment tool for evaluating static and dynamic balance in individuals with various neurological conditions, including stroke. It consists of 14 tasks that challenge an individual's balance abilities, such as standing on one leg, turning 360 degrees, and reaching forward. Each task is scored on a scale of 0 to 4, with a maximum total score of 56. Higher scores indicate better balance performance.

In this study, 10-meter walk test (10MWT) was used to evaluate walking ability. The 10MWT is a reliable and valid measure of walking speed in individuals with neurological conditions, including stroke. The participant is instructed to walk at a comfortable pace for 10 meters, and the time taken to cover this distance is recorded. Walking speed is calculated by dividing the distance by the time taken, with higher speeds indicating better walking ability.

The functional independence measure (FIM) used in this study is a comprehensive assessment tool designed to evaluate an individual's functional independence in performing activities of daily living (ADLs) and instrumental activities of daily living (IADLs). It is commonly utilized in various clinical settings, including stroke rehabilitation. The FIM comprises 18 items that cover six domains: self-care, sphincter control, transfers, locomotion, communication, and social cognition. The FIM provides valuable information on the individual's functional abilities and can be used to monitor progress and evaluate the effectiveness of rehabilitation.

The Stroke-Specific Quality of Life Scale (SS-QoL) is a comprehensive, self-reported assessment tool designed to measure health-related quality of life in individuals who have experienced a stroke. The SS-QoL was developed to capture various dimensions of the stroke survivor's experience and to evaluate the impact of stroke on their overall well-being. The SS-QoL consists of 49 items that cover 12 domains and each item is rated on a 5-point Likert scale, ranging from 1 (strongly disagree) to 5 (strongly agree). The scores for each domain can be calculated separately, and a total score can also be computed by summing the scores across all domains.

Statistical analysis method

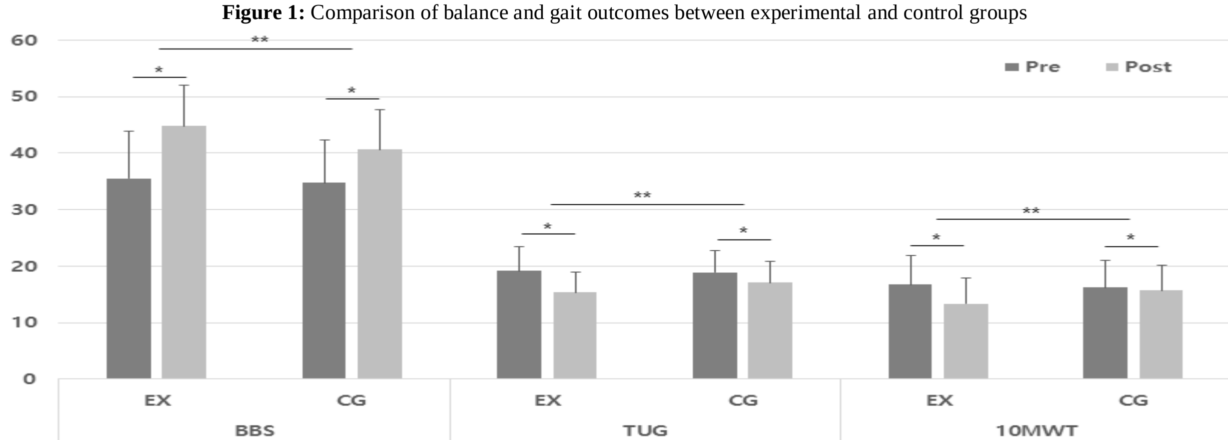
This study utilized the SPSS program (version 18.0 for Windows) for statistical analysis. Descriptive statistics were utilized to compute the mean and standard deviation of the measured values. To compare pre-test and post-test within the group, a paired-sample t-test was used. Additionally, an independent t-test was conducted to determine differences between groups. The significance level was set to less than 0.05.

RESULTS AND DISCUSSION

Balance maintenance and walking ability

Table 1 presents the within-group analyses for BBS, TUG, and 10MWT, including means and standard deviations for pre-test and post-test scores, as well as t and p-values. For the BBD measure, both groups showed a significant improvement. The exercise group had a mean score of 35.56 before the intervention, which increased to 44.81 after the intervention. The control group had a mean score of 34.78 before the intervention, which increased to 40.62 after the intervention. The t-value was 8.24 for the exercise group and 6.27 for the control group, both of which were significant with p-values less than 0.001. The TUG measure also showed a significant improvement in both groups. The exercise group had a mean score of 19.21 before the intervention, which decreased to 15.33 after the intervention. The control group had a mean score of 18.93 before the intervention, which decreased to 17.12 after the intervention. The t-value was 7.14 for the exercise group and 3.22 for the control group, both of which were significant with p-values less than 0.05. The 10MWT measure showed a significant improvement only in the exercise group. The exercise group had a mean score of 16.72 before the intervention, which decreased to 13.41 after the intervention. The control group had a mean score of 16.19 before the intervention, which decreased to 15.73 after the intervention. The t-value was 6.86 for the exercise group and 2.38 for the control group, with a significant p-value of less than 0.05 only for the exercise group.

Figure 1: Comparison of balance and gait outcomes between experimental and control groups



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*EX: experimental group; CG: control group; BBS: Berg balance scale; TUG: timed up and go test; 10MWT: 10- meter walk test; *<0.05: paired t test within groups; **<0.05: independent t test between groups*

Table 1: Comparison of balance maintenance and gait ability between groups using pre-test and post-test

Measure	Group	Pre	Post	t	p
BBS	EX	35.56 ± 8.41	44.81 ± 7.13	8.24	<0.001
	CG	34.78 ± 7.62	40.62 ± 7.04	6.27	<0.001
TUG	EX	19.21 ± 4.31	15.33 ± 3.64	7.14	<0.001
	CG	18.93 ± 3.89	17.12 ± 3.71	3.22	0.002
10MWT	EX	16.72 ± 5.11	13.41 ± 4.53	6.86	<0.001
	CG	16.19 ± 4.83	15.73 ± 4.41	2.38	0.022

EX: experimental group; CG: control group; BBS: Berg balance scale; TUG: timed up and go test; 10MWT: 10- meter walk test

In the independent sample t-test conducted to determine the

Functional independence and quality of life

For the FIM measure, the experimental group showed a significant increase in scores from pre-test (80.42 ± 14.32) to post-test (95.24 ± 12.75), with a t value of 7.89 and a p value of <0.001. The control group also showed a significant increase in FIM scores, from pre-test (79.86 ± 13.81) to post-test (89.12 ± 13.22), with a t value of 5.08 and a p value of <0.001. Regarding the SS-QoL measure, the experimental group demonstrated a significant improvement in scores from pre-test (127.51 ± 22.41) to post-test (150.38 ± 25.36), with a t value of 20.33 and a p value of <0.001. The control group also showed a significant increase in SS-QoL scores, from pre-test (125.93 ± 21.63) to post-test (139.68 ± 24.41), with a t value of 11.12 and a p value of <0.001. In summary, the results indicate that both the experimental and control groups showed significant improvements in FIM and SS-QoL scores from pre-test to post-test (Table 2).

Table 2: Comparison of functional independence and quality of life between groups using pre-test and post-test

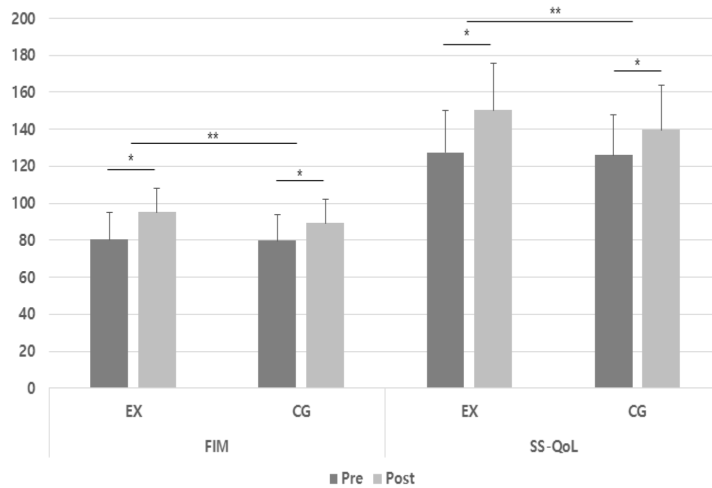
Measure	Group	Pre	Post	t	p
FIM	EX	80.42 ± 14.32	95.24 ± 12.75	7.89	<0.001
	CG	79.86 ± 13.81	89.12 ± 13.22	5.08	<0.001
SS-QoL	EX	127.51 ± 22.41	150.38 ± 25.36	20.33	<0.001
	CG	125.93 ± 21.63	139.68 ± 24.41	11.12	<0.001

EX: experimental group; CG: control group; FIM: functional independence measure; SS-QoL: stroke-specific quality of life scale

In the independent sample t-test conducted to determine the differences in treatment effects between the groups (Figure 2), the FIM revealed a statistically significant difference between the two groups. The mean difference was 6.12, the 95% confidence interval was (2.74, 9.50), the t-value was 4.06, and the p-value was <0.001. For the SS-QoL measure, there was also a statistically significant difference between the groups. The mean difference between the groups was 10.70, the 95% confidence interval was (4.36, 17.04), the t-value was 12.86, and the p-value was <0.001. In summary, the experimental group that received robot-assisted training demonstrated statistically significant improvements in functional independence and quality of life compared to the control group.

differences in treatment effects between the groups (Figure 1), the BBS showed a statistically significant difference between the two groups. The mean difference was 4.19, the 95% confidence interval was (2.12, 6.26), the t-value was 4.33, and the p-value was <0.001. For the TUG test, there was also a statistically significant difference between the groups. The mean difference between the groups was -1.79 seconds, the 95% confidence interval was (-2.93, -0.65), the t-value was -3.47, and the p-value was 0.001. Finally, in the 10MWT, a statistically significant difference between the groups was observed. The mean difference between the groups was -2.32 seconds, the 95% confidence interval was (-3.54, -1.10), the t-value was -4.52, and the p-value was <0.001.

Figure 2: Comparison of functional independence and quality of life between experimental and control groups



*EX: experimental group; CG: control group; BBS: Berg balance scale; TUG: timed up and go test; 10MWT: 10- meter walk test; *<0.05: paired t test within groups; **<0.05: independent t test between groups*

A variety of therapeutic approaches have been employed to improve balance and walking ability in stroke patients. These include conventional physical therapy techniques, such as strength training, balance exercises, and gait training [19], as well as innovative approaches, like robot-assisted therapy and virtual reality-based interventions [20]. Evidence suggests that a combination of these methods, tailored to the specific needs and abilities of each patient, can result in significant improvements in balance and walking ability.

The present study investigated the combination effects on balance, walking ability, functional independence, and quality of life in individual post-stroke. Our findings indicate that the experimental group, which received Baclofen with exercise therapy, demonstrated statistically significant improvements in balance maintenance, walking ability, functional independence, and quality of life compared to the control group that received conventional therapy.

These results are consistent with previous research highlighting the potential benefits of combining pharmacological intervention with exercise therapy, specifically Baclofen, in stroke rehabilitation. The previous study assessed the effects of Baclofen, stretching exercises, and their combination on children with spastic cerebral palsy. The findings indicated that the combination of Baclofen and stretching exercises led to significant improvements in fluid and calorie intake [21]. Another study investigated the combined effects of mild forced treadmill exercise and Baclofen, a GABAB receptor agonist, on movement and cognitive impairments in mammals due to lesions in the basal ganglia's GABAergic neurons. Morris water maze and open field tests were used to evaluate spatial learning and motor activity. The study found that neither mild exercise nor Baclofen on its own significantly impacted spatial learning or motor activity. However, when combined, they were effective in alleviating impairments in spatial learning and motor activity in animals with striatum lesions.

This suggests the potential benefits of combining GABAB receptor agonist treatment with exercise training in improving memory and motor function impairments caused by striatum lesions [22,23].

In this study, consistent with prior research, the group that combined pharmacological intervention with exercise therapy exhibited numerous improvements compared to the control group. These outcomes are believed to stem from the maximization of the exercise therapy's benefits, which were built upon the reduction of spasticity achieved through pharmacological therapy. Furthermore, the synergistic effect of the pharmacological intervention and exercise therapy could be attributed to several factors. The pharmacological therapy, particularly the administration of anti-spasticity medications such as Baclofen, likely created a more conducive physiological environment for motor relearning by reducing muscle tone and spasticity. This, in turn, might have enhanced the efficacy of the exercise therapy.

In the context of exercise therapy, the regimen probably provided repetitive, structured, and task-specific movements, which are essential for promoting neuroplasticity - the brain's ability to reorganize itself by forming new neural connections. This reorganization is vital for recovery after a neurological injury like a stroke. Additionally, exercise therapy could have improved cardiovascular fitness and muscle strength, further contributing to functional gains. It's also worth noting that exercise can have psychosocial benefits, including the enhancement of mood and self-esteem, which could indirectly affect physical function by increasing motivation and engagement in the therapy.

Importantly, the precise combination and timing of pharmacological intervention and exercise therapy may be critical in achieving optimal outcomes. Individualized treatment plans that consider the patient's specific needs, the severity of spasticity, and the stage of rehabilitation can potentially maximize the benefits of this combined approach. In conclusion, this study adds to the growing body of evidence supporting the combined use of pharmacological interventions and exercise therapy in the management of spasticity and motor function in neurological conditions. Future research should continue to explore the mechanisms underlying these synergistic effects and optimize treatment protocols for individual patients. Additionally, long-term studies are needed to understand the sustainability of the improvements observed with this combined approach.

However, it is essential to acknowledge the limitations of the present study and the need for further research in this area. The sample size was relatively small, and the follow-up period was limited, which may impact the generalization of the findings. Future research should explore the long-term effects of combination treatment on balance, walking ability, and quality of life in larger and more diverse stroke populations.

CONCLUSION

Maintaining balance and walking abilities is critical for stroke survivors as it facilitates independence and enhances quality of life. This study specifically investigated the synergistic effects of combining pharmacological intervention with exercise therapy on post-stroke patients. The findings suggest that the combination of Baclofen and exercise therapy significantly improved balance, walking ability, functional independence, and quality of life compared to conventional therapy alone. These improvements are likely due to the reduction in spasticity through pharmacological intervention, creating a conducive environment for motor relearning and, consequently, maximizing the benefits of exercise therapy.

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