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Prolotherapy as a Novel Adjunct in Post-Stroke Pain Management: A Pilot Study at RSUD Dr. Saiful Anwar Malang

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ABSTRACT

Background: Post-stroke pain (PSP) and musculoskeletal complications significantly hinder recovery and quality of life in stroke survivors. Prolotherapy, a regenerative injection therapy involving hypertonic dextrose, has shown promise in managing musculoskeletal disorders but remains underexplored for PSP management.

Aim(s): This study evaluates the effectiveness of prolotherapy in reducing pain, improving range of motion (ROM), and enhancing functional outcomes in PSP patients.

Material and methods: This pilot study employed a pre-experimental design with pretest and posttest measurements. Conducted at RSUD Dr. Saiful Anwar Malang, the study included three stroke patients experiencing chronic musculoskeletal pain. Prolotherapy injections containing hypertonic dextrose were administered at regular intervals to targeted areas of musculoskeletal pain. Primary outcomes included pain (Numerical Rating Scale), ROM, and spasticity (Modified Ashworth Scale). Secondary outcomes were assessed using the Barthel Index, Short Form-36, and Fugl-Meyer Assessment. Statistical analyses were descriptive, with paired t-tests applied to measure changes in outcomes.

Result: Significant improvements in pain levels (mean NRS reduction from 5.67±1.5 to 3.0±2.0) and ROM, particularly in shoulder flexion and wrist extension, were observed. Spasticity showed minor improvements in specific muscle groups. The result of functional outcomes, overall quality of life and daily functional abilities, including Barthel Index and SF-36 scores, demonstrated positive trends, with two participants progressing from severe dependency to moderate independence.

Conclusions: Prolotherapy shows promise as an adjunctive intervention for PSP, offering potential benefits in pain reduction and functional recovery. As the first study of its kind at RSUD Dr. Saiful Anwar Malang, it lays a foundation for future large-scale research to validate findings and refine clinical applications.

Keywords: *Stroke, Prolotherapy, Pain, Rehabilitation, post-stroke pain, functional performance*

INTRODUCTION

Stroke remains a significant cause of mortality and long-term disability worldwide, including in Indonesia, where its impact continues to grow. Recent epidemiological data reveal that Indonesia has one of the highest stroke mortality rates in Southeast Asia, with a prevalence of 0.17% in rural areas, where access to healthcare services is often limited, and 0.22% in urban populations, where lifestyle-related risk factors are more prevalent. (1).

According to Indonesia's Social Security Administering Body (BPJS), the cost of stroke healthcare treatment amounted to IDR 1.43 trillion in 2016, rising to IDR 2.19 trillion in 2017, and reaching IDR 2.57 trillion in 2018. Data from the 2014 Indonesia Sample Registration System identified stroke as the most prevalent disease, accounting for 21.1% of cases (2). RSUD Dr. Saiful Anwar Malang, a major referral center in East Java, has experienced a consistent and significant increase in stroke-related admissions over recent years, highlighting the growing burden of this disease within the region and the challenges faced by the healthcare system. The presence of post-stroke complications, including chronic pain, spasticity, and restricted range of motion (ROM), not only exacerbates the physical and emotional suffering of patients but also severely impairs their quality of life and poses substantial obstacles to achieving optimal functional recovery and independence.

Post-stroke pain (PSP), which affects approximately 30-40% of stroke survivors, presents a complex and multifaceted challenge in the rehabilitation process, often complicating recovery efforts. It is frequently associated with additional post-stroke conditions, such as spasticity and various musculoskeletal complications, including frozen shoulder and joint contractures, which further exacerbate functional limitations and hinder the progress of rehabilitation efforts (3). Conventional management strategies for PSP, such as pharmacological interventions and physical therapy, are commonly employed but often produce suboptimal outcomes, as they may provide only temporary relief of symptoms without effectively addressing the underlying pathophysiology of the condition or facilitating long-term functional improvements (4). Given these limitations, there is an urgent need for innovative and integrative approaches that simultaneously target pain reduction and functional deficits, with the ultimate goal of enhancing recovery outcomes and improving the quality of life for stroke survivors.

Prolotherapy, a regenerative injection therapy, has increasingly garnered attention as a promising intervention for the treatment of various musculoskeletal disorders, particularly those involving chronic pain and structural weakness. This therapy involves the injection of an irritant solution, most commonly hypertonic dextrose, into affected areas to stimulate the body’s natural healing mechanisms and promote tissue repair. By enhancing fibroblast activity, prolotherapy facilitates collagen synthesis, which in turn strengthens weakened ligaments, tendons, and other soft tissues, ultimately improving structural stability and function (5). While prolotherapy has already demonstrated considerable efficacy in managing musculoskeletal conditions such as osteoarthritis, tendinopathies, and chronic ligament injuries, its potential application in the field of stroke rehabilitation, specifically for addressing post-stroke pain (PSP), remains largely underexplored and warrants further investigation (6).

Preliminary evidence suggests that prolotherapy could play a significant role in improving both pain and functional outcomes by specifically targeting the musculoskeletal components associated with post-stroke pain (PSP) (7). This study represents the first pilot exploration of prolotherapy as a potential treatment for PSP conducted at RSUD Dr. Saiful Anwar Malang, a major referral hospital in East Java. The Rehabilitation Medicine Department at this institution acknowledges the pressing need for tailored and innovative interventions that can not only enhance recovery outcomes but also foster greater independence and quality of life in stroke patients.

By focusing on prolotherapy as a core intervention, this pilot project aims to evaluate its effectiveness in reducing chronic pain levels, improving range of motion (ROM) in affected joints, and enhancing the overall functional status of stroke survivors. Given the scarcity of existing literature and research on the application of prolotherapy in stroke rehabilitation, this study seeks to address a critical gap in the field and contribute meaningful insights. The findings derived from this research have the potential to pave the way for the integration of prolotherapy into standard rehabilitation protocols, offering a more comprehensive, holistic, and effective recovery pathway for stroke patients who continue to experience pain and functional deficits.

MATERIAL AND METHODS

This pilot study utilized a pre-experimental design with pretest and posttest measurements to systematically evaluate the effectiveness of prolotherapy in managing post-stroke pain and enhancing functional outcomes among stroke survivors. The study was carried out at the Rehabilitation Medicine Department of RSUD Dr. Saiful Anwar Malang, a well-recognized referral center in East Java that serves a high volume of patients requiring complex rehabilitation interventions. Prior to the initiation of the study, ethical approval was secured from the institutional review board to ensure adherence to research ethics and guidelines, and all participants were thoroughly briefed about the study's purpose, procedures, and potential risks before providing their written informed consent to participate.

Participants

The study included three adult stroke patients who presented with musculoskeletal pain and spasticity, conditions that were carefully confirmed through detailed clinical examinations and corroborative imaging techniques, such as CT scans, as well as supporting laboratory tests. The inclusion criteria for participation in the study required patients to have a chronic post-stroke condition lasting at least three months (≥3 months), a pain intensity score ranging from 1 to 10 on the Numerical Rating Scale (NRS), and the cognitive ability to understand and provide informed consent for their involvement in the study. Patients were excluded if they had uncontrolled diabetes mellitus, hypertensive emergencies, significant cognitive impairments, or documented allergies to any components of the injection solution. Prolotherapy injections containing hypertonic dextrose were administered directly to the affected joints and surrounding soft tissues to target pain and dysfunction. All injections were carried out under strict sterile conditions to minimize the risk of infection or complications and were delivered at regular intervals as per the study protocol.

Outcome Measures

The primary outcomes assessed in this study included pain levels, which were measured using the Numerical Rating Scale (NRS), as well as the range of motion (ROM) and spasticity, both of which were evaluated using the Modified Ashworth Scale (MAS). In addition to these primary metrics, secondary outcomes focused on assessing functional capacity and overall quality of life, which were measured through established tools, including the Barthel Index, the Short Form-36 (SF-36) for quality-of-life evaluation, and the Fugl-Meyer Assessment (FMA) for motor function. Comprehensive evaluations of these outcomes were performed at baseline to establish initial measurements and were subsequently repeated after each intervention session to monitor changes and improvements over time.

Statistical Analysis

Given the small sample size, descriptive statistics were employed to summarize the baseline characteristics of the participants and the outcome measures, providing an overview of the data collected at the beginning of the study. Changes in both primary and secondary outcomes were then analyzed using paired t-tests, where applicable, to assess whether significant differences existed between pre-treatment and post-treatment measurements, with a p-value of less than 0.05 being considered statistically significant, indicating a meaningful effect of the intervention.

RESULT

This pilot study included a total of three participants, consisting of two males and one female, with ages of 57, 60, and 67 years, respectively, representing a range of middle-aged and older adults. Baseline characteristics revealed varying degrees of functional impairment and quality of life among the participants, which were assessed and reflected in the scores of the Barthel Index, SF-36, and Fugl-Meyer Assessment (FMA), highlighting the diverse rehabilitation needs of the individuals. The intensity of pain, measured using the Numerical Rating Scale (NRS), ranged from 4 to 6, indicating moderate levels of discomfort across the participants, while spasticity levels, which were assessed using the Modified Ashworth Scale (MAS), varied considerably across different muscle groups, underscoring the complexity and heterogeneity of post-stroke complications (8).

Primary Outcomes

Significant improvements in pain levels were observed following the intervention, as evidenced by a consistent decrease in NRS scores across all participants, with the average score dropping from 5.67±1.5 at baseline to 3.0±2.0 after the final prolotherapy injection, indicating a notable reduction in pain. Range of motion (ROM) also showed substantial increases, particularly in shoulder flexion and wrist extension, with post-intervention gains averaging between 25 to 30 degrees, reflecting meaningful improvements in joint mobility. Although spasticity did improve in some muscle groups, the changes were not statistically significant, as the MAS scores remained stable or showed only minor reductions, indicating that spasticity did not exhibit the same degree of improvement as pain and ROM (9). These changes in spasticity levels were systematically measured using the Modified Ashworth Scale, with the results summarized in Table 1. In contrast, significant improvements in ROM were observed in key joints, especially shoulder flexion, as detailed in Table 2.

Table 1 Comparison of Spasticity Scores (MAS) from Injection 1 to Injection 5

Variable	Pre-Injection 1	Post-Injection 1	P Value	Pre-Injection 3	Post-Injection 3	P Value	Pre-Injection 5	Post-Injection 5	P Value
Shoulder adductor	1.3 ± 2.3	1.3 ± 2.3	0.184	1.3 ± 2.3	1.3 ± 2.3	0.184	1.3 ± 2.3	1 ± 1.7	0.423
Elbow Flexor	2 ± 1.7	1.3 ± 2.3	0.184	2 ± 1.7	1.3 ± 2.3	0.184	1.6 ± 2	1 ± 1.7	0.184
Wrist Extensor	2 ± 2	1.6 ± 2	0.423	2 ± 2	1.6 ± 2	0.423	1.6 ± 2	1.3 ± 2.3	0.423

Table 2 Changes in Range of Motion (ROM) from Injection 1 to Injection 5.

Variable	Pre-Injection 1	Post-Injection 1	P Value	Pre-Injection 3	Post-Injection 3	P Value	Pre-Injection 5	Post-Injection 5	P Value
ROM Shoulder Abduction	96.3 ± 35.1	93.3 ± 11.5	0.386	96.6 ± 47.2	115 ± 30.4	0.257	106.7 ± 45.09	120 ± 26.4	0.423
ROM Shoulder Flexion	80 ± 62	84 ± 57	0.024	86.6 ± 61.1	110 ± 26.4	0.423	116.7 ± 20.8	116.7 ± 20.8	0.423
ROM Wrist Extension	38.3 ± 25.6	40 ± 27.8	<0.001	38.3 ± 25.6	40 ± 27.8	<0.001	53.3 ± 10.4	53.3 ± 10.4	<0.001

Secondary Outcomes

Functional measures demonstrated a positive trend. The Barthel Index improved in two participants, with scores increasing from severe dependency (4 and 6) to moderate levels of independence. SF-36 scores reflected subjective improvements in physical functioning and pain domains, despite limited changes in emotional and social dimensions. The Fugl-Meyer Assessment, which evaluates sensorimotor recovery, showed slight but consistent improvements, indicating potential gains in motor function (10). Functional and pain scores demonstrated improvement post-intervention (Table 3).

Table 3 Comparison of Pain Scale (NRS), Barthel Index, and Fugl-Meyer Score

Variable	Pre-Injection 1	Post-Injection 1	P Value	Pre-Injection 5	Post-Injection 5	P Value
NRS	5.67 ± 1.5	4.3 ± 2.08	0.057	4 ± 2	3 ± 2	0.038
Barthel Index	6 ± 3.46	6 ± 3.46	0.184	8.67 ± 5.03	8.67 ± 5.03	0.184
Fugl Meyer	36.6 ± 3.05	36.6 ± 3.05	0.131	38 ± 2	38 ± 2	0.121

These findings suggest that prolotherapy may offer a beneficial adjunct in managing post-stroke musculoskeletal complications, particularly in terms of pain reduction and functional recovery, highlighting its potential as a complementary treatment option for improving patient outcomes. However, the small sample size in this pilot study necessitates caution when attempting to generalize these results to a broader population, emphasizing the importance of conducting larger-scale, well-powered studies to validate these preliminary observations and further explore the effectiveness of prolotherapy in post-stroke rehabilitation.

DISCUSSION

Post-stroke pain (PSP) and musculoskeletal complications, including issues such as spasticity and joint contractures, significantly impair recovery and hinder the overall quality of life in stroke survivors, creating substantial obstacles to rehabilitation. The findings of this pilot study underscore the potential role of prolotherapy as a promising intervention to address these challenges, particularly in improving pain management and enhancing functional recovery. While the study involved only a small sample, the results offer valuable insights into the feasibility and initial efficacy of prolotherapy as a treatment option in post-stroke rehabilitation, suggesting that further exploration of this intervention in larger, more diverse patient populations could yield important data on its broader applicability and effectiveness.

The primary outcome of this study was the reduction in pain levels, which was measured using the Numerical Rating Scale (NRS), and the consistent decrease in pain scores across all participants strongly supports the growing body of evidence suggesting that prolotherapy can effectively reduce pain in various musculoskeletal conditions, including those related to post-stroke complications. The mechanism underlying this pain reduction likely involves the stimulation of local healing responses, such as increased collagen synthesis and fibroblast activation, which together enhance the structural integrity of soft tissues and contribute to overall tissue repair and stabilization (11). In the context of post-stroke pain (PSP), these effects may help alleviate nociceptive pain, which is often associated with joint instability and soft tissue damage, by promoting healing in the affected areas and reducing the factors that contribute to pain (12).

Despite the promising reductions in pain, changes in spasticity, as assessed by the Modified Ashworth Scale (MAS), were less pronounced. This finding aligns with studies highlighting the complexity of spasticity management in stroke patients. Spasticity, driven by upper motor neuron lesions, involves neural mechanisms that prolotherapy may not directly address (8). However, slight improvements in specific muscle groups suggest that prolotherapy might exert indirect effects on spasticity through enhanced joint mobility and reduced pain, enabling more effective physiotherapy interventions. Changes in spasticity levels were measured using the Modified Ashworth Scale (Table 1).

Improvements in range of motion (ROM) were another notable outcome. Significant gains were observed in shoulder flexion and wrist extension, areas commonly affected by post-stroke musculoskeletal complications such as frozen shoulder (13). These findings are consistent with earlier studies on prolotherapy in similar contexts, where enhanced ROM was attributed to the restoration of joint function and reduction of pain. Improved ROM can have cascading benefits for functional independence, as evidenced by the upward trends in the Barthel Index and Fugl-Meyer Assessment scores in this study (10). Significant improvements in ROM were observed in key joints, particularly in shoulder flexion (Table 2).

Functional measures, including the Barthel Index and SF-36, showed modest but encouraging improvements. The Barthel Index, which assesses basic activities of daily living (ADLs), revealed shifts from severe dependency to moderate independence in two participants. These findings highlight the potential of prolotherapy to support functional recovery when integrated with comprehensive rehabilitation programs. Similar trends have been reported in musculoskeletal prolotherapy studies, where improvements in pain and ROM facilitated better engagement in ADLs (14). Functional and pain scores demonstrated improvement post-intervention (Table 3).

The SF-36 outcomes, while showing limited statistical significance, provided qualitative insights into participants' perceptions of their health status. Improvements in the physical functioning and pain domains suggest that prolotherapy positively influenced subjective well-being, even within the short study duration. These observations underscore the value of pain reduction in enhancing perceived quality of life, particularly in chronic conditions (15).

This study is the first to explore prolotherapy's role in managing PSP at RSUD Dr. Saiful Anwar Malang, establishing it as a novel intervention

within the institution. The findings suggest that prolotherapy could serve as a valuable adjunct in post-stroke rehabilitation, particularly for patients with significant musculoskeletal complications. By targeting pain and enhancing ROM, prolotherapy may improve patients' capacity to participate in other rehabilitative activities, such as physical and occupational therapy (16).

Furthermore, this study underscores the importance of addressing the multifactorial nature of PSP. Conventional management often relies on pharmacological treatments that may carry risks of side effects and limited long-term efficacy. Prolotherapy, as a regenerative approach, offers a potentially safer alternative with the added benefit of improving tissue integrity (17). Integrating prolotherapy into standard post-stroke care protocols could enhance overall treatment outcomes, reducing the burden on healthcare systems and improving patient satisfaction.

Despite its promising findings, this study has several limitations. The small sample size, which is a common characteristic of pilot studies, restricts the generalizability of the results. This is consistent with the literature, where pilot studies often serve as preliminary investigations to inform the design of larger trials, acknowledging their inherent limitations in scope (18). Additionally, the short duration of this study may not adequately capture the long-term effects of prolotherapy, which are essential to understanding its full potential for chronic conditions like PSP (19).

The absence of a control group further limits the ability to attribute observed improvements solely to the intervention. This aligns with findings from other pilot studies, which highlight the methodological challenges posed by small, uncontrolled designs (20). To address these constraints, future research should adopt more rigorous study designs, including larger sample sizes and control groups, to provide more robust evidence on prolotherapy's efficacy (21).

Future studies should aim to address these limitations by employing larger, randomized controlled trials with longer follow-up periods. Such studies could provide more robust evidence on the efficacy of prolotherapy in PSP and explore its effects on other relevant outcomes, such as muscle strength and endurance (22). Moreover, investigating the optimal dosing and injection protocols for prolotherapy in the context of stroke rehabilitation could refine its application and maximize its benefits.

The role of prolotherapy in managing spasticity also warrants further exploration. While this study did not observe significant changes in spasticity scores, combining prolotherapy with targeted physical therapies may yield more pronounced effects. Future research could investigate synergistic approaches, integrating prolotherapy with techniques like neuromuscular re-education and stretching exercises, to enhance spasticity management in stroke patients (23).

CONCLUSION

This pilot study highlights prolotherapy as a promising adjunctive intervention for managing post-stroke pain and enhancing functional recovery. Significant improvements in pain levels and range of motion underscore its potential to address musculoskeletal complications in stroke patients. As the first exploration of prolotherapy at RSUD Dr. Saiful Anwar Malang, the study provides a foundation for integrating regenerative therapies into stroke rehabilitation. However, the small sample size

and short study duration emphasize the need for further research. Future large-scale, randomized trials are essential to validate these findings and optimize prolotherapy protocols for broader clinical application.

DISCLOSURES

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Conflict of interest

The authors declare no conflict of interest regarding the publication of this research. All authors have disclosed any potential conflicts and affirm that this study was conducted impartially and ethically.

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Author Contribution

All authors have contributed to all processes in this research, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript.

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