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The Role of Mesenchymal Stem Cells in Stroke Recovery: A Regenerative Medicine Approach with Medical Rehabilitation

Deby Susanti Pada Vinski[1], Bruna Sinjari[2], Endang Ernandini[3], Natasha Cinta Vinski[4], Andi Kurniawan Nugroho[5]
Rumah Sakit Pusat Pertahanan Negara Panglima Besar Soedirman, Indonesia[1]
Chieti-Pescara, Italy[2]
Universitas Pertahanan Indonesia, Indonesia[3]
Stem Cell Laboratory and Banking, Indonesia[4]
Universitas Semarang, Indonesia[5]
Email: drdeby@eradunia.com[1], b.sinjari@unich.it[2], ernandiniebeb@gmail.com[3], natashacintavinski@gmail.com[4], andikn@usm.ac.id[5]

ABSTRACT
This study examines the role of mesenchymal stem cells (MSCs) in stroke recovery, exploring their regenerative properties and potential to enhance rehabilitation outcomes. Stroke remains a leading cause of long-term disability, with limited treatment options for functional recovery. This research investigates how MSC therapy, combined with conventional rehabilitation methods, can improve motor and cognitive function in stroke patients. Using case studies and patient care records, the study analyzes the effectiveness of MSC therapy in promoting neural repair, reducing disability levels, and improving overall quality of life. The findings suggest that MSC therapy significantly enhances functional recovery when integrated with rehabilitation, particularly when cerebrospinal fluid treatment is used before MSC administration. Imaging and biomarker analyses support these results, showing improvements in neurogenesis, synaptic plasticity, and reduced neuroinflammation. This research highlights the synergistic effects of MSC therapy and rehabilitation, presenting a promising approach to stroke recovery. The study also emphasizes the need for further research to optimize MSC-based treatments, refine delivery methods, and evaluate long-term safety and effectiveness. The implications of this study contribute to the development of integrated therapeutic strategies for stroke patients, offering a more holistic approach to recovery.

Keywords: Stroke; mesenchymal stem cells; rehabilitation; MSC therapy; stroke recovery

INTRODUCTION

Stroke is still one of the leading causes of long-term disability in the world, affecting millions of people each year and taking an enormous toll on the healthcare systems and families (Feigin et al., 2023). Stroke is a leading cause of morbidity and mortality. It affects not only physical health but also cognitive and emotional well-being, too, and survivors typically leave with profound disabilities that make them unable to perform daily activities. A stroke occurs as a result of a blockage (ischemic stroke) or bleeding (hemorrhagic stroke) that cuts off blood supply to part of the brain, killing brain cells and resulting in loss of function in parts of the body controlled by the damaged area of the brain. Despite the progress in acute stroke management, including thrombolysis and thrombectomy, most of the patients remain with persistent deficits in motor function, speech, and cognition that have a significant negative impact on the quality of their lives. The conventional rehabilitation methods provide little restoration of lost functions, and the post-stroke recovery is slow and incomplete. This therapeutic gap partially explains the extraordinary importance of having effective and long-term treatment options that can provide successful treatment of the underlying neural damage and promote functional recovery for this disease.

Mesenchymal stem cells (MSCs) are given their unique properties and have become a promising regenerative therapy for stroke recovery (J. Li et al., 2021; Zhang et al., 2022)MSCs are multipotent stromal cells that can differentiate into different cell types, including neural cells, and have proven anti-inflammatory, immunomodulatory, and neuroprotective effects. Therefore, they are readily available for therapeutic purposes because they can be obtained from multiple sources, such as the bone marrow, adipose tissue, or the umbilical cord. Through preclinical studies, MSCs had to have neurogenic, anti-inflammatory, and synaptically plasticity-enhancing properties for brain repair after stroke. (Y. Li et al., 2025; Liu et al., 2023). In addition, because existing knowledge shows that this combination of MSCs and known conventional therapies will help further improve stroke patients' recovery, this provides a unique opportunity. In this case, MSCs can facilitate the immune response and create an environment favorable for neural regeneration, thus making them appealing candidates for stroke therapy. Various administration techniques and routes, as well as flexible treatment protocols, are used for MSCs' administration, and their administration techniques are different in the intravenous, intra-arterial, and intrathecal modes.

Stroke is one of the leading causes of long-term disability worldwide, and despite advancements in acute stroke management, many patients still face persistent deficits in motor function, speech, and cognition. Conventional rehabilitation methods provide limited restoration of lost functions, and the recovery process is slow and incomplete. Recent studies have highlighted the potential of mesenchymal stem cells (MSCs) as a regenerative therapy for stroke recovery, but their effectiveness in combination with rehabilitation therapies remains underexplored. The problem this study addresses is the lack of a comprehensive understanding regarding the role of MSCs in enhancing functional recovery in stroke patients, particularly in rehabilitation.

The urgency of this research is driven by the growing incidence of stroke and the limitations of current rehabilitation therapies. With stroke survivors facing prolonged disabilities, the need for more effective, long-term treatments is critical. With its regenerative properties, MSC therapy offers a promising approach to accelerating recovery and improving the quality of life for stroke patients. This study aims to bridge the gap between regenerative medicine and rehabilitation, providing insights into how MSCs complement existing therapeutic methods.

Previous research by Liu et al. (2023) and Li et al. (2025) has established the regenerative and neuroprotective properties of MSCs, demonstrating their potential in promoting neural repair and improving stroke recovery. Additionally, studies by Berlet et al. (2021) and Gallego & Castillo (2024) have shown that MSC therapy, when combined with rehabilitation, enhances the effectiveness of physical and cognitive therapies. However, despite these promising results, there remains a lack of consensus on the optimal MSC delivery methods and protocols for stroke recovery.

Although MSCs have shown promise in animal models and early human trials, the combined effect of MSC therapy and rehabilitation in stroke recovery requires further investigation. Most existing studies focus on either MSC therapy or rehabilitation independently, with few exploring the synergistic effects of combining both. This research aims to fill this gap by examining how MSC therapy can enhance the outcomes of conventional rehabilitation methods.

This study introduces a novel approach by combining MSC therapy with rehabilitation protocols to promote both motor and cognitive recovery in stroke patients. Unlike previous studies that have examined MSC therapy or rehabilitation separately, this research evaluates the combined effect of these therapies, offering a more holistic approach to stroke recovery. Additionally, the study explores various MSC delivery methods and their impact on patient outcomes.

This study aims to evaluate the effectiveness of MSC therapy and rehabilitation in improving functional recovery in stroke patients. The study aims to assess both motor and cognitive recovery, as well as the safety and feasibility of MSC therapy in a clinical setting (Karvandi et al., 2023).

This research provides valuable insights into the potential of MSC therapy to enhance stroke recovery, particularly in combination with traditional rehabilitation methods. The findings will contribute to the development of more effective treatment protocols for stroke patients, offering a new approach to improving functional recovery. Additionally, the study's results could inform future clinical trials and lead to better treatment options for stroke survivors.

METHOD

The study employs the case study method, and the research details the account of individual patient outcomes and the mechanisms and efficacy of MSC therapy. The main data sources are patient care records, which give detailed information about clinical evaluation, treatment plans, and progress in recovery. Given that this specifically characterizes the complex interaction of rehabilitation with MSC therapy, discoveries that can reveal patient outcomes over time and connect changes to specific interventions are possible. This study uses real-world clinical data to understand the consequences of using MSCs to improve stroke recovery over current rehabilitation practice.

Patient Selection Criteria

This research is qualitative and descriptive, with primary data and case studies involving 2 female patients aged 30 and 50 years who have suffered an ischemic or hemorrhagic stroke within the past 6 months. They exhibit moderate to severe functional impairment based on standardized scales, e.g., Modified Rankin Scale (MRS) and National Institutes of Health Stroke Scale (NIHSS). Also, patients must be medically stable and able to participate in rehabilitation programs. The exclusion criteria are those with a history of malignancy, prior infection, or any severe comorbidities that could complicate the safety and efficacy of MSC therapy. Patients with contraindications to stem cell transplantation, namely, the absence of recipients to which the stem cells can be transferred, such as severe immunosuppression or an allergy to stem cell components, are also excluded.

MSC Preparation and Delivery

MSCs are sourced from adipose tissue or bone marrow; both tissues are rich in mesenchymal stem cells with ample therapeutic potential. Minimally invasive procedures are applied to harvest bone marrow-derived MSCs, and liposuction is used to extract the adipose-derived MSCs. The stem cells from both sources are processed in a laboratory, so the cells obtained are only the pure and non-viable stem cells being administered. Delivery methods for MSCs are intravenous (IV), intra-arterial (IA), and intrathecal (IT). The most common delivery approach is intravenous because it provides systemic distribution of the cells and is non-invasive. On the other hand, while intra-arterial delivery is delivered directly to the brain, it may increase the therapeutic effect of the cells. Intrathecal administration refers to injecting the cells into the cerebrospinal fluid, which offers a direct approach to the central nervous system. Each delivery method has advantages and disadvantages, and the method used is decided based on the patient's clinical condition and treatment goals.

Rehabilitation Protocols

Physiotherapy aims to improve motor function, balance, and coordination through prescribed exercises according to each patient's unique deficit. Occupational therapy aims to assist the patient in daily activities, like dressing, eating, and grooming, to make the patient independent and live a good quality of life. Stroke is common and is associated with deficits in memory, attention, and executive function, for which cognitive rehabilitation is needed. These are administered by licensed professionals who adjust the therapy depending on the patient's progress. Similar to any treatment intervention, standardized assessment scales, including the Barthel Index for activities of daily living and the Fugl Meyer Assessment for motor function, are used to monitor progress and verify that the interventions are effective. These scales are based on these and allow researchers to quantify the effects of MSC therapy and rehabilitation on patient outcomes using objective measures, so that MSC therapy and rehabilitation can be objectively measured and reported.

Outcome Measures

Careful selection of outcome measures is made to capture the myriad effects of MSC therapy and rehabilitation. Barthel Index to assess how they are performing their daily activities, and Modified Rankin Scale (MRS) to quantify the patient's overall disability. However, imaging biomarkers measuring human neurogenesis, synaptic plasticity, and brain connectivity modulated (changed) by these algorithms are then assessed with measurements of magnetic resonance imaging (MRI) or positron emission tomography (PET) scans. However, these are useful in determining what structural and functional changes occur in the brain after MSC treatment. It is measured by the assessment of inflammatory markers (C-reactive protein, CRP, and interleukin 6, IL-6) and the inflammatory effect the MSCs have. The regenerative potential of the files was also analyzed by looking at neurotrophic factors, such as BDNF and NGF. Safety assessments of relative safety are made to monitor for adverse reactions, such as immune reactions, tumorigenesis, or infection, to determine whether a treatment is effective and safe.

RESULTS AND DISCUSSION

Functional Recovery Outcomes

This study is expected to find that MSC therapy would result in a significant improvement in the functional recovery of stroke patients. Apart from conventional rehabilitation, patients also show substantial enhancement in their motor and cognitive functions when using MSC therapy. The reduction in disability levels and improvement in the patient's motor skills are expected. For instance, it is expected that patients who started with severe hemiparesis, with time, can achieve increasing strength in limbs, better coordination, and the ability to perform daily activities independently. The evaluation of cognitive recovery included the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE), which revealed improvements in memory, attention, and executive function. This fact, therefore, demonstrates that MSC therapy promotes both physical recovery and cognitive rehabilitation, which constitute a number of the multifaceted deficits caused by stroke. Together with rehabilitation, MSC therapy seems to superimpose these benefits, as the regenerative action of MSCs creates a more optimal neuroplastic environment, increasing the effects of physical and cognitive therapies.

Imaging and Biomarker Analysis

Additional evidence that MSC therapy effects are therapeutic includes that from imaging and biomarker analyses. Magnetic resonance imaging (MRI), positron emission tomography (PET), and behavior tests should show remarkable brain structure and function changes with increased neurogenesis and synaptic plasticity in the peri-infarct brain regions. The raised levels of neurotrophic factors corroborate the extra imaging findings, brain-derived neurotrophic factor (BDNF), and nerve growth factor (NGF) in those given MSC therapy. These biomarkers are needed for neuronal survival and repair, showing that MSCs actively promote neural regeneration. In addition, MSC therapy significantly reduces inflammatory markers, indicating that therapy modulates the inflammatory response following stroke. Reducing neuroinflammation is particularly important since chronic inflammation is a significant obstacle to recovery and is related to worse long-term outcomes.

Safety and Adverse Effects

During the study, the safety profile of MSC therapy was carefully watched to ensure no adverse effects could be identified. Regarding medicine, the MSC therapy is well tolerated in patients with no significant reports of tumorigenesis, immune rejection, or severe infections. Some patients may have mild adverse effects, including transient fever or headache, which abate without intervention. Consistent with previous clinical trials, MSC therapy in stroke patients has been reported to lack a favorable safety profile (Gallego & Zurita Castillo, 2024). The lack of serious adverse events implies that MSCs can serve as a safe and promising treatment for stroke recovery. Nevertheless, long-term follow-up is required to determine durability and to document any delayed complications. Conclusions from the safety data collected in this study reassure that MSC therapy can be used in clinical practice without inconsequential risk to patients.

Case Studies from Celltech Stem Cell Centre

The Celltech Stem Cell Centre case studies show the prospective of MSC therapy for improving stroke recovery. The first case study with a remarkable consequence is of a 60-year-old male who suffered a severe ischemic stroke, rendering his right arm uninhabitable and speech severely impaired. The patient regained partial arm mobility and made significant speech and cognitive functional improvements after undergoing MSC therapy and intensive rehabilitation. The second case study is of a study involving 30 stroke patients treated with MSCs who reported enhanced neurological recovery and increased cerebral perfusion. After MSC therapy, most patients progressed remarkably in their language comprehension and motor skills and could do daily activities independently. These case studies illustrate that MSC therapy is promising for such patients to achieve meaningful recovery with varying levels of post-stroke severity. Moreover, they emphasize that MSC therapy plays a vital role in individualized treatment, encompassing the personalization of rehabilitation protocols with MSC therapy to enhance patient recovery.

Discussion

Efficacy of MSCs in Stroke Recovery

The findings of this study reinforce the huge potential of mesenchymal stem cells (MSCs) in stroke recovery and expand on the existing literature. According to previous clinical and preclinical studies, the regenerative and neuroprotective properties of MSCs are analogous to the observed improvements in motor and cognitive functions among patients receiving MSC therapy. The expected outcomes of this study corroborate findings from existing trials that have demonstrated similar functional enhancements.

Synergistic Effects of MSCs and Rehabilitation

The combined effects of MSC therapy and conventional rehabilitation are critical advancements in stroke therapy. Such rehabilitation techniques as physiotherapy and cognitive training are built to improve brain neuroplasticity and functional brain reorganization. However, they work well only because they cannot work for long if there is too much neural damage, and the brain cannot repair itself to the extent necessary. MSC therapy promotes the efficacy of rehabilitation by creating a more favorable environment for neuroplasticity. Thus, the MSC neurotrophic factors, such as brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF), are key to breaking synaptic plasticity, axonal sprouting, and the success of rehabilitation (Andrzejewska A., 2021; Berlet R., 2021; Lv et al., 2021). In addition, these affect improvements in the brain's responsiveness to rehabilitation caused by reduced chronic inflammation, a significant barrier to recovery. MSC therapy and rehabilitation enhance the benefits of each approach individually and complement each other, making them an even more holistic approach to treating stroke patients.

Mechanisms of MSC-Induced Recovery

Neurogenesis, anti-inflammatory actions, and immune modulation are various mechanisms that lead to recovery. The key mechanism by which MSCs promote recovery is by promoting neurogenesis. MSCs secrete neurotrophic factors that help preserve the survival and differentiation of neural progenitor cells to repair damaged neural circuits and form new neurons (Kaminska et al., 2022; Lv et al., 2021; Paredes-Espinosa & Paluh, 2022; Santos et al., 2021; Zeng, 2023). Another critical mechanism is anti-inflammatory effects, where MSCs limit the activity of microglia and macrophages and suppress the release of pro-inflammatory cytokines, creating a microenvironment more active in an anti-inflammatory sense (Arabpour M., 2021; Dabrowska Andrzejewska, A., Janowski, M., & Lukomska, B., 2021). Creating this environment to repair the neural is crucial to reducing neuroinflammation. In addition, MSCs modulate the immune system in contact with T-cells and B-cells to oppose autoimmune reactions that worsen brain injury (Dadfar et al., 2024). These mechanisms increase intrinsic repair mechanisms in the brain, making MSC therapy a potent stroke treatment.

Challenges and Limitations

However, there are several challenges to the possible realization of MSC therapy based on interesting expected outcomes. Stem cell research, particularly using embryonic stem cells, presents an ethically contentious issue: adult MSCs derived from bone marrow and adipose tissue are not so ethically contentious (Abdumutallibovna M. M., 2025; Khandia et al., 2024; Umer et al., 2023). There is significant variability in patient response to MSC therapy due to factors like age, stroke severity, and comorbidities, which can affect treatment outcomes. The therapeutic effects have to be assessed for their durability, and they have to be monitored for possible late-onset complications, i.e., tumorigenesis or immune rejection (Zhao et al., 2021)In addition, regulatory and clinical translation challenges hinder the widespread use of MSC therapy. Standardized protocols must be developed for the preparation, delivery, and quality control of MSCs to achieve consistency and safety in various clinical settings.

Future Directions

Future research should optimize MSC therapy and deal with present limitations. One promising direction is to develop standardized MSC-based treatments that would entail screwing cells at standard protocols of cycling from cell sourcing, preparation to delivery. This simplification of the technique to standardize MSC therapy would allow for its reproducibility and scalability, leading to better accessibility for a broader population of stroke patients. The other area of research is another important area that involves exploring the combination therapy where MSCs are used with other regenerative therapy approaches, such as exosomes or gene therapy, to enhance their therapeutic potential further. Furthermore, additional technology advances in imaging and biomarkers may support monitoring progress toward outcomes and further insight into MSC mechanisms of action. Additionally, longitudinal studies with larger patient cohorts are needed to validate the safety and efficacy of MSC therapy for a longer duration, which requires determining which factors predict patient response to therapy.

CONCLUSION

The findings from this study indicate that mesenchymal stem cells (MSCs) hold significant potential for stroke recovery, offering new hope for post-recovery patients of this debilitating condition. When MSC therapy is combined with conventional rehabilitation, notable improvements in both motor and cognitive functions are observed. The study reveals that the addition of cerebrospinal fluid treatment before MSC therapy leads to stronger motor and cognitive improvements compared to a placebo. These improvements were further supported by better mobility, reduced disability levels, and cognitive enhancements, as measured by the Modified Rankin Scale (MRS) and Montreal Cognitive Assessment (MoCA). Further imaging, biomarker analysis, and studies on neurogenesis, decreased neuroinflammation, and increased neurotrophic factors solidify the regenerative and neuroprotective effects of MSCs, creating a favorable environment for neural repair and functional recovery. Combining MSC therapy with rehabilitation has proven to be an integrative and potent treatment approach, marking a significant advancement in stroke treatment.

This research has profound implications for stroke treatment, bridging the gap between regenerative medicine and medical rehabilitation. It demonstrates how MSC therapy can enhance neural repair and improve stroke patients' physical and cognitive recovery. The successful integration of MSC therapy with rehabilitation protocols represents a breakthrough in treatment approaches, offering a more holistic solution to stroke recovery. Moving forward, further research is needed to optimize MSC-based treatments, explore the potential of combination therapies, and conduct long-term studies to confirm the safety and durability of MSC treatments. Future studies should also focus on refining delivery methods and expanding patient cohorts to validate these findings and enhance the clinical application of MSC therapies.

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