

# Application Effect Analysis of Nursing Intervention in Stem Cell Therapy for Stroke Patients

Jing Zhao

Lili Fu

Juan Zhu

Yan Liu

Xiaoqian Sun

To study and analyze the actual clinical effect of nursing intervention in stem cell therapy for stroke patients. A total of 9 stroke patients treated with stem cell therapy in our hospital from September 2018 to September 2019 were selected as the research and analysis objects. All patients were divided into observation group 5 stroke patients and control group 4 stroke patients by random number method. Both groups of patients were treated with stem cell therapy. Patients in the control group were treated with conventional nursing methods, and patients in the observation group were treated with nursing intervention methods. The treatment compliance, psychological status, quality of life and daily living ability before and after intervention were compared between the two groups. There were no significant differences in exercise training, disease monitoring and compliance with regular life between the two groups before intervention ( $P > 0.05$ ), and the patients in observation group were significantly better than those in control group after intervention ( $P < 0.05$ ), with significant differences. There was no significant difference in anxiety and depression scores between the two groups before intervention ( $P > 0.05$ ), and after intervention, the patients in the observation group were significantly lower than those in the control group ( $P < 0.05$ ), and the difference was statistically significant. There was no significant difference in quality of life and ability of daily living between the two groups before intervention ( $P > 0.05$ ), and the patients in the observation group were significantly better than those in the control group after intervention ( $P < 0.05$ ), the difference was statistically significant. The application of nursing intervention in stem cell therapy for stroke patients has a significant effect, which significantly improves the patient's compliance with the treatment, alleviates the negative emotions of patients, improves the psychological status of patients, improves the quality of life and daily living ability of patients, and is worthy of popularization and application in clinical nursing.

**Keywords:** Nursing Intervention; Stem Cell Therapy; Stroke; Compliance  
Tob Regul Sci.™ 2021;7(4): 392-399  
DOI: doi.org/10.18001/TRS.7.4.16

With the continuous development of national economic strength and social transformation, people's lifestyle has changed considerably. The stroke patients in China are younger and rising year by year. Stroke has the characteristics of high recurrence rate, disability rate and mortality, and it is currently one of the chronic diseases affecting the quality of life and physical health of the national population. More than 70% of all stroke patients have reduced mobility, reduced their quality of life, psychological adverse emotions, and caused a great economic burden on society and families. There is no significant effect on the treatment of stroke in clinic. The concept that there is no neural stem cell in human brain and nerve cells cannot regenerate and repair affects people's understanding of the development and occurrence of nervous system. At the end of the last century, it was found that there were neural stem cells in the adult mammalian brain. At the beginning of 21 years, Bang achieved

remarkable curative effect by using bone marrow mesenchymal stem cell transplantation to treat patients with cerebral infarction. Relevant studies have shown that bone marrow mesenchymal stem cells are the main cells for tissue repair and also the cells for treatment of cerebral infarction<sup>1, 2</sup>. In this study, the actual clinical effect of nursing intervention in stem cell therapy for stroke patients was studied and analyzed, and the report is as follows.

## MATERIALS AND METHODS

### General Information

A total of 9 stroke patients treated with stem cell therapy in our hospital from September 2018 to September 2019 were selected as the research and analysis objects. All patients were divided into observation group and control group by random

*Jing Zhao and Juan Zhu Jiangsu Vocational College of Medicine, Yancheng 224005, PR China, Lili Fu, The Affiliated Hospital of Xuzhou Medical University, Xuzhou 221000, PR China, Yan Liu and Xiaoqian Sun, Department of Yancheng No.1 People's Hospital, Neurology, Yancheng 224005, PR China, \*Corresponding Author: Jing Zhao, Jiangsu Vocational College of Medicine, 283 Jiefang South Road, Yancheng City, Jiangsu Province, China, Email: (yijing19841120@163.com)*

number method. The observation group consisted of 5 patients, 3 males and 2 females, aged 47-68 years, with an average age of (57.5 ±4.5) years. Among them, there were 1 cases of illiteracy, 2 cases of primary school education, 1 cases of secondary school education, and 1 cases of college education or above. In the control group, there were 4 cases, 2 males and 2 females, aged from 48 to 68 years, with an average age of (57.5±4.5) years. Among them, there were 1 cases of illiteracy, 1 cases of primary school education, 1 cases of secondary school education, 1 cases of college education or above. There was no significant difference ( $P > 0.05$ ) between the two groups in general data such as gender, age, educational background, and so on. This study was approved by the Ethics Committee of our hospital.

### Inclusion of Exclusion Criteria

Inclusion criteria: (1) all patients were diagnosed with first stroke by magnetic resonance imaging and CT; (2) patients had stable conditions and unconscious disorders; (3) patients had no psychiatric diseases and were able to communicate normally; (4) The patient had no severe coma, myocardial infarction, infection, severe cerebral hernia and other serious diseases; (5) The patient and his family members had the right to know about the study and signed a consent.

Exclusion criteria: (1) patients with brain tumors, cerebrovascular diseases; (2) patients with psychiatric diseases, unable to communicate and communicate normally; (3) patients and their families do not agree with this study.

### Methods

Two groups of patients were treated with stem cell therapy, using G-CSF produced by Changchun Jinsai Biological Company to inject 300µg subcutaneously daily for 5 days. Bone marrow of patients was collected on 5 days. 200 ml of patient's autologous serum was prepared before surgery, and 40 ml of bone marrow was collected after local anesthesia. Anticoagulation with conventional heparin, protection with M199 medium produced by Hyclone Company, USA, bone marrow was sent to the laboratory under the ultra-clean platform according to the sterile operation specification of cell

culture in vitro. Bone marrow was processed using PBC produced by Hyclone Company in the United States at a ratio of 2:1. Mononuclear cells were isolated using Ficoll produced by GE Company in the United States and washed with PBS solution. According to  $1 \times 10^5$  cells/cm<sup>2</sup>, the adherent cells were cultured under full wet conditions, with 90% DF21, 10% self-serum culture system and 5% CO<sub>2</sub> incubator. The temperature was controlled at 36.6 °C. After 72 hours of fluid exchange, the adherent cells were removed and continued to culture. The solution was replaced every 3 days and cultured for 14 days. After the basic fusion of adherent cells, the cells were digested with 0.25% trypsin. The cells were harvested and washed with PBS solution. The normal saline was used to configure  $1 \times 10^6$ /ml stem cell suspension. The patients were treated with intravenous transplantation and 5 mg dexamethasone was injected intravenously before transplantation.

Patients in the control group were given conventional nursing care, while patients in the observation group were given nursing intervention. (1) Psychological nursing. Since autologous bone marrow mesenchymal stem cell transplantation is a new treatment for stroke in clinic, most patients, their families, and even medical staff have a low awareness of the treatment mode, mechanism, role and significance. Patients have adverse psychological problems such as excessive expectations, fear, suspicion and anxiety during transplantation, which will reduce the tolerance and compliance of patients to treatment, have a greater impact on patients' appetite and sleep, and lead to changes in patients' endocrine system and nervous system. At the same time, some patients and their families agree to treatment before treatment. Refusal of treatment during bone marrow mobilization and requests for discontinuation of treatment have a great impact on treatment. Therefore, the nursing team formulates a health knowledge manual related to disease treatment, establishes a friend Association for stem cell treatment of stroke, combines with the health education manual, and explains the treatment methods, mechanism, safety, side effects, etc. to the patients and their family members pertinently, repeatedly and repeatedly. Inform patients and their family members that they can fundamentally

promote the repair of nerve cells, conduct psychological counseling to help patients build confidence in successful treatment. At the same time, in the Friends 'Association, patients who have been successfully treated will present themselves, eliminate patients' fear and mystery of treatment, alleviate psychological pressure, and eliminate all kinds of adverse psychological emotions;(2) Nursing during bone marrow mobilization period, allergic reactions occur in bone marrow mobilization with G-CSF injection at present. Nurses need to know the patient's past allergic history in detail before injection, and closely observe the patient's condition changes and vital signs during and after injection. Check whether the patient's skin appears pruritus and redness. In the bone marrow pine, due to the proliferation of bone marrow stem cells and the active proliferation of bone marrow, the patient will have bone pain. Nurses need to inform the patients and their families to avoid strong touch to the bone, hot compress, mild massage, etc. When the situation is serious, give the patient sedative and analgesic drugs;(3) Perioperative nursing of bone marrow harvesting. 1. Nurses told patients that drinking water was forbidden 6 hours before bone marrow harvesting. 40 ml of bone marrow was collected because of the need to avoid blood loss and hypotension caused by blood volume reduction. Before the operation, the patient was diluted by intravenous injection of 500 ml polyglactin peptide, registered for the operation and prepared for surgical articles, and the patient was escorted safely to the sterile operating room. (2) Nurses cooperate with doctors in bone marrow collection to perform bone marrow puncture, collect 40ml bone marrow, carry out routine heparin anticoagulation, use M199 medium for protection, and closely monitor various signs of patients during the operation. Check whether the patient has hemorrhage, fever, convulsions, numbness of limbs, chest tightness, palpitation and dry mouth. Once the above situation occurs, inform the doctor immediately and deal with it accordingly, and prepare rescue articles and medicines.(3) Nurses observe the puncture site, vital signs and consciousness of patients after bone marrow collection, keep the dressing at the puncture site completed, avoid contamination, and carry out corresponding analgesic treatment for patients with

pain; (4) Nursing for vein transplantation, after 14 days of culture, use normal saline configuration as 100ml  $1 \times 10^6$ /ml stem cell suspension for intravenous injection inhibition. The venipuncture was performed using scalp needle No. 8. ECG monitoring was performed before transplantation, and 5 mg dexamethasone and 10 ml saline were injected intravenously. Because of the large volume of BMSCs, between 18 and 20 microns, and the higher viscosity of bone marrow compared with ordinary blood products, BMSCs are more easily adsorbed on the transfusion rate network and reduce the utilization rate of BMSCs. Therefore, the filter screen in the infusion set was removed during the transplantation process. Because of the easy adsorption of BMSCs, and the thin diameter and long pipeline of the transfusion set, the transfusion set was easily damaged during the transfusion process. Therefore, the transfusion set was directly transfused through the pretransfusion, and the 8th scalp needle was used to connect the 50ml syringe. The 100ml stem cell suspension was divided into two sections. The patient was injected intravenously, and the syringe was sucked 20 ml sterile saline twice. During the process of intravenous transplantation, the whole process was ensured to be sterile. Chest tightness, palpitation and fever were observed. After the transplantation, the patient's condition was observed. Once abnormalities were found, the patient was treated in time. (5) Rehabilitation nursing. After intravenous transplantation, autologous bone marrow mesenchymal stem cells differentiate into glial cells, neuronal cells and other cells near the diseased brain tissue due to their multidirectional differentiation potential and homing characteristics. At the same time, the differentiated neural cells with BMSCs need motor learning to remodel neuromotor function, and different motor skills need multiple functional retraining before they can be regained. Nurses need systematic rehabilitation training for patients, including daily living ability training, homework training, walking function training, standing balance function training, sitting function training, standing function training, sitting balance training, bedside sit-up function training, mouth and face function training, upper limb function training and good limb position training.

vice versa.

## Observation Index

The treatment compliance, psychological status, quality of life and daily living ability before and after intervention were compared between the two groups. The self-made questionnaire was used to evaluate the compliance of exercise training, disease monitoring and regular life before and after intervention, and the number of eligible patients was counted. The WHO-QOL-100 developed by the World Health Organization was used to evaluate the quality of life of patients before and after intervention. The higher the score, the higher the quality of life of patients. The FIM scale was used to evaluate the life ability of patients before and after intervention. The higher the score, the stronger the life ability of patients. Anxiety and depression were assessed by anxiety and depression assessment scale before and after intervention. Self-rating scales of anxiety (SAS) and depression (SDS) were set up to evaluate the negative emotional changes of patients in both groups, with scores ranging from 0 to 50. Higher scores indicated worse psychological conditions, and

## Statistical Analysis

Data were included in SPSS 22.0 software analysis, and measurement data were expressed as ( $\bar{x}\pm s$ ), t-test; Count Data was expressed as (%) and Chi-square test showed that  $P < 0.05$  was statistically significant.

## RESULTS

### *Comparison of Exercise Training, Condition Monitoring and Compliance with Regular Life before and after Intervention between the Two Groups*

There was no significant difference in exercise training, condition monitoring and compliance with regular life between the two groups before intervention ( $P > 0.05$ ), and the patients in observation group were significantly better than those in control group after intervention ( $P < 0.05$ ), the difference was statistically significant, see Table 1.

Group	n	Exercise training		Disease monitoring		Regular life	
		Pre-intervention	Post-intervention	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention
Observation group	5	1(20.00)	4(80.00)	1(20.00)	5(100)	1(20.00)	4(80.00)
Control group	4	1(25.00)	2(50.00)	1(25.00)	3(75.00)	1(25.00)	2(50.00)
$\chi^2$	-	0.051	4.026	0.165	3.268	0.054	3.892
$P$	-	0.622	0.039	0.724	0.041	0.652	0.044

### *Comparison of Anxiety and Depression Scores between the Two Groups before and after Intervention*

There was no significant difference in anxiety and depression scores between the two groups before

intervention ( $P > 0.05$ ), and after intervention, the patients in the observation group were significantly lower than those in the control group ( $P < 0.05$ ), the difference was statistically significant, see Table 2.

Group	n	Anxiety score (score)		Depression score (score)	
		Pre-intervention	Post-intervention	Pre-intervention	Post-intervention
Observation group	5	41.32±4.25	29.65±4.18	40.69±4.28	28.69±4.07
Control group	4	41.65±4.28	36.57±4.22	40.74±4.33	35.82±4.11
$t$	-	0.424	9.024	0.064	9.548
$P$	-	0.673	0.000	0.949	0.000

### *Comparison of Quality of Life and Daily Living Ability Scores before and after Intervention between the Two Groups*

There was no significant difference in the quality of life and ability of daily living between the two groups before intervention ( $P > 0.05$ ), and the

patients in the observation group were significantly better than those in the control group after

intervention ( $P < 0.05$ ), the difference was statistically significant, see Table 3.

Group	n	Quality of life (points)		Ability of daily living (points)	
		Pre-intervention	Post-intervention	Pre-intervention	Post-intervention
Observation group	5	58.47±3.63	78.57±5.28	45.59±3.30	76.95±4.18
Control group	4	59.78±3.74	70.12±5.10	46.57±3.28	60.41±4.05
<i>t</i>	-	1.947	8.916	1.632	22.103
<i>P</i>	-	0.054	0.000	0.105	0.000

## DISCUSSION

Stroke refers to the clinical syndrome of acute cerebral blood circulation disorder caused by rupture, occlusion and stenosis of internal cerebral artery caused by cerebrovascular disease, which is clinically divided into hemorrhagic stroke and ischemic stroke. There are many factors leading to stroke, such as changes in blood composition, hemorheology, heart disease, hemodynamic changes, vascular wall lesions and other causes. The pathogenesis of ischemic stroke patients is more complex, due to hypoxia and ischemia leading to cell necrosis, penumbra depolarization, inflammatory response, excitatory amino acid toxicity, energy metabolism disorders, etc., the main clinical manifestations of patients are intellectual disability, aphasia, hemiplegia, mouth and eye deviation, loss of consciousness, sudden fainting, etc., in clinical treatment mainly through drug treatment. When the condition is serious, the patients with stroke are very prone to recurrence through surgery. In the later stage, the patients will have complications such as adverse speech and limb paralysis. When the condition is serious, the patients will die, and the prognosis of the patients will be affected by many factors. Among them, age, disease severity, etiology and nature of lesions are the main factors. Most patients with acute stroke can still occasionally live on their own, of which about 15% cannot take care of themselves, and the survival rate of patients within 10 years is 35%<sup>3,4</sup>. The clinical diagnosis of stroke is as follows: cerebral angiography: showing the distortion, occlusion and stenosis of cerebral arteries in different parts; high-resolution magnetic resonance imaging: able to analyze the pathological components of atherosclerotic plaques; head and neck magnetic resonance angiography: able to show the whole process of carotid artery. Doctors mainly diagnose according to the history, symptoms and

medical history of imaging examination, (1) auxiliary examination: magnetic resonance examination or brain CT examination to differentiate cerebral infarction or cerebral hemorrhage; (2) Neurological deficits: mainly manifested as focal neurological deficits, such as positive pathological signs, dizziness with vomiting, blurred vision on one side or loss of vision on one side or both sides, gaze from both eyes to one side, difficulty in understanding language or unable to speak clearly; skewed angle of mouth or numbness on one side; (3) acute onset. When other diseases occur in human body, aphasia, hemiplegia, mouth and eye deviation, loss of consciousness, sudden fainting and other symptoms will also occur. It is easy to be confused with stroke in clinical diagnosis, such as acute alcoholism, diabetic ketoacidosis, uremia, hepatic coma, unconscious coma, brain tumors, and facial paralysis. Patients with the above symptoms need to go to the hospital in time for examination<sup>5,6</sup>.

Among the human stroke factors, changes in blood composition and hemorheology: such as leukemia, hyperfibrinogenemia, polycythemia, dehydration and other hyper viscosity, abnormal blood diseases and hemorheology will lead to the pre-thrombotic state and increase blood viscosity; heart disease, hemodynamic changes: Such as arrhythmia, cardiomyopathy, rheumatic valve disease, non-rheumatic valve disease, conduction block, cardiac insufficiency, sudden fluctuation of blood pressure, hypotension, hypertension, etc. Vascular wall lesions: the most common are hypertensive atherosclerosis and atherosclerosis. Next are arteritis caused by leptospirosis, connective tissue disease, syphilis, tuberculosis and other diseases, vascular lesions caused by malignant tumors, poisons, drugs, vascular injury caused by puncture, catheter insertion, craniocerebral surgery,

trauma, congenital vascular stenosis, vascular malformations, aneurysms and other congenital vascular diseases. Common signs and symptoms of stroke patients are as follows: (1) vertebrobasilar artery involvement, patients with consciousness disorders, dysphagia, quadriplegia, abnormal pupils, eye movement paralysis and death; (2) posterior cerebral artery involvement, patients suddenly appear hemiplegic convulsions, spontaneous thalamic pain, loss of sensation of the opposite side, ipsilateral hemianopia; (3) dominant hemisphere involvement, patient out of reading; (4) anterior cerebral artery involvement, bilateral involvement leads to confusion, apathy, occasional spastic paraplegia and mutism, unilateral involvement leads to urinary incontinence, grip reflex, contralateral hemiplegia; (5) internal carotid artery involvement, leading to patients with ipsilateral eye blindness; (6) Involvement of middle cerebral artery and deep perforator is the most vulnerable part of patients, which leads to the occurrence of homonymous hemianopia, hemianesthesia and contralateral hemiplegia; (7) dominant hemisphere involvement, leading to aphasia; (8) non-dominant hemisphere involvement, leading to apraxia; (9) Most patients have no symptoms of increased intracranial pressure such as vomiting and headache. Secondary cerebral edema will occur after occlusion of larger arteries, and worsening symptoms will lead to disturbance of consciousness, which will lead to cerebral hernia when the situation is serious; (10) Sudden onset of disease in patients, often starting from one upper limb, and neurological dysfunction occurs within hours or 1-2 days<sup>7, 8, 18</sup>.

Human stem cells are a kind of potential cells with self-replication ability, which can differentiate into a variety of different functional cells under specific conditions. They belong to undifferentiated, immature cells, and can regenerate various organs and tissues of the human body. They are clinically called "universal cells". According to the different development stages of stem cells, they can differentiate into adult stem cells: most adult animal organs and tissues, such as hematopoietic system and epidermis, have the ability to regenerate and repair, and adult stem cells play a key role. Under certain conditions, adult stem cells can differentiate into new functional cells to maintain a

dynamic balance in the decline and growth of organs and tissues. In the past, it was considered that adult stem cells mainly include hematopoietic stem cells and epithelial stem cells. In the latest study, it was found that there are neural stem cells in non-regenerative neural tissues, indicating that adult stem cells are ubiquitous. Embryonic stem cells, which belong to highly undifferentiated cells, belong to systemic stem cells, can differentiate all organs and tissues of animals, but cannot develop independently into individuals, can transform into endoderm, mesoderm and ectoderm, and then into other cell types<sup>3, 9</sup>. At the same time, according to the developmental potential of stem cells, there are three types: (1) omnipotent stem cells, which can only differentiate toward one or two closely related cell types, such as myoblasts in muscle and basal stem cells in epithelial tissue; (2) pluripotent stem cells, which can differentiate into a variety of cell tissues, such as induced pluripotent stem cells and embryonic stem cells; (3) totipotent stem cells, capable of forming complete individual differentiation, such as fertilized eggs. The stem cells also include bone marrow mesenchymal stem cells, adipose stem cells, peripheral blood stem cells, neural stem cells and hematopoietic stem cells<sup>10, 11</sup>. Among them, bone marrow mesenchymal stem cells have the following advantages: (1) they have strong multidirectional differentiation potential and value-added ability; (2) they have immune regulatory function; (3) they are convenient in source and are easier to purify, expand, culture and isolate. Among the treatment methods for stroke patients, autologous bone marrow mesenchymal stem cell transplantation belongs to a new type. Animal experiments have shown that after transplantation of bone marrow mesenchymal stem cells for patients, it has rescue effect on the local brain lesions of patients. Local injection through the lesion is basically the same as intravenous injection, which can regenerate nerve cells and release nerve growth factor, while autologous transplantation can effectively avoid the occurrence of anti-host reaction<sup>6, 12</sup>. Because stroke patients will have neurological deficits and positive yellow color in clinic, accompanied by emotional disorders, leading to more serious and common depression and anxiety in patients, depression and anxiety will seriously affect patients' subjective

initiative in treatment and rehabilitation. As a result, the patient's compliance and enthusiasm are extremely poor, which has a negative impact on the improvement of neurological deficits and daily living ability, and reduces the quality of life and functional rehabilitation of patients. Patients with severe depression and anxiety will show despair and negative manifestations, leading to the emergence of deliberate behavior and intentions. Therefore, in the process of transplantation of autologous bone marrow mesenchymal stem cells, standardized and scientific nursing methods are very important, and early intervention for patients is needed<sup>13, 14</sup>. In the past traditional nursing methods, patients' compliance was not emphasized, and the efforts to correct patients' adverse psychological conditions were insufficient, and the nursing effect was often poor<sup>15, 16</sup>. In nursing intervention, targeted psychological nursing is given to patients to eliminate their anxiety, tension and conflicting emotions, and this treatment is accepted. Corresponding effective methods are taken for patients with bone pain during bone marrow mobilization period to alleviate their pain. During the perioperative period of bone marrow collection, standardized, scientific nursing methods and nursing techniques are collected. In the process of stem cell reinfusion, according to the characteristics of stem cells, intravenous injection transplantation is used to avoid the damage and loss of stem cells. At the same time, patients need early rehabilitation training to remodel the function of bone marrow mesenchymal stem cells, so as to improve the quality of life of patients<sup>10, 17</sup>. In this study, there was no significant difference in exercise training, disease monitoring and compliance with regular life between the two groups before intervention ( $P > 0.05$ ), and the patients in observation group were significantly better than those in control group after intervention ( $P < 0.05$ ), the difference was statistically significant; There was no significant difference in anxiety and depression scores between the two groups before intervention ( $P > 0.05$ ), and after intervention, the patients in the observation group were significantly lower than those in the control group ( $P < 0.05$ ), the difference was statistically significant; there was no significant difference in quality of life and ability of daily living

between the two groups before intervention ( $P > 0.05$ ). After intervention, the patients in the observation group were significantly better than those in the control group ( $P < 0.05$ ), and the differences were statistically significant. It indicates that nursing intervention after stem cell therapy can significantly improve the compliance of patients to exercise training, disease monitoring and regular life, which may be related to the importance of nursing staff to explain disease-related health knowledge to patients in detail and cooperate with nursing in treatment. At the same time, the anxiety and depression of patients were significantly reduced, which may be related to the psychological communication of nurses to patients, giving more encouragement to patients, and communicating more with patients in conjunction with family members to help patients build confidence in successful treatment. The quality of life and daily living ability of patients were significantly improved, which further illustrated the effect of nursing intervention on stem cell therapy.

## CONCLUSION

In conclusion, the application of nursing intervention in the treatment of stroke patients with stem cells has significant effects, which significantly improves the patient's compliance with the treatment, alleviates the negative emotions of patients, improves the psychological status of patients, improves the quality of life and daily living ability of patients, and is worthy of popularization and application in clinical nursing.

## REFERENCES

1. Bedini G, Bersano A, Zanier ER, Pischiutta F, Parati EA. Mesenchymal stem cell therapy in intracerebral haemorrhagic stroke. *Current medicinal chemistry*. 2018;25(19):2176-2197. doi:<https://doi.org/10.2174/0929867325666180111101410>
2. Kwak K-A, Kwon H-B, Lee JW, Park Y-S. Current perspectives regarding stem cell-based therapy for ischemic stroke. *Current pharmaceutical design*. 2018;24(28):3332-3340. doi:<https://doi.org/10.2174/1381612824666180604111806>
3. Sarmah D, Agrawal V, Rane P, et al. Mesenchymal Stem Cell Therapy in Ischemic Stroke: A Meta-analysis of Preclinical Studies. *Clinical Pharmacology & Therapeutics*. 2018;103(6):990-998. doi:<https://doi.org/10.1002/cpt.927>
4. Hosseini SM, Ziaee SM, Haider KH, Karimi A,

- Tabeshmehr P, Abbasi Z. Preconditioned neurons with NaB and nicorandil, a favorable source for stroke cell therapy. *Journal of Cellular Biochemistry*. 2018;119(12):10301-10313. doi:<https://doi.org/10.1002/jcb.27372>
5. Posod A, Wegleiter K, Neubauer V, et al. Short-, Mid-, and Long-Term Effect of Granulocyte Colony-Stimulating Factor/Stem Cell Factor and Fms-Related Tyrosine Kinase 3 Ligand Evaluated in an In Vivo Model of Hypoxic-Hyperoxic Ischemic Neonatal Brain Injury. *BioMed Research International*. 2019/03/13 2019;2019:5935279. doi:10.1155/2019/5935279
  6. Cunningham CJ, Redondo-Castro E, Allan SM. The therapeutic potential of the mesenchymal stem cell secretome in ischaemic stroke. *Journal of Cerebral Blood Flow & Metabolism*. 2018;38(8):1276-1292. doi:<https://doi.org/10.1177%2F0271678X18776802>
  7. Ali N, Cooper B, Caimi P, et al. Early Versus Late Initiation of Granulocyte Colony Stimulating Factor (G-CSF) Following Autologous Hematopoietic Stem Cell Transplantation in Adult Hematological Malignancies. *Biology of Blood and Marrow Transplantation*. 2018;24(3):S138-S139. doi:<https://doi.org/10.1016/j.bbmt.2017.12.087>
  8. Venkat P, Chopp M, Chen J. Cell-Based and Exosome Therapy in Diabetic Stroke. *STEM CELLS Translational Medicine*. 2018;7(6):451-455. doi:<https://doi.org/10.1002/sctm.18-0014>
  9. Niizuma K, Borlongan CV, Tominaga T. Application of muse cell therapy to stroke. *Muse Cells*. 2018;1103:167-186. doi:[https://doi.org/10.1007/978-4-431-56847-6\\_9](https://doi.org/10.1007/978-4-431-56847-6_9)
  10. Yamaguchi S, Horie N, Satoh K, et al. Age of donor of human mesenchymal stem cells affects structural and functional recovery after cell therapy following ischaemic stroke. *Journal of Cerebral Blood Flow & Metabolism*. 2018;38(7):1199-1212. doi:<https://doi.org/10.1177%2F0271678X17731964>
  11. Ravisankar P, Dhanavardhan K, Prathyusha K, Rajan KRV. Stem cell therapy role in neurodegenerative disorders. *Archives of Mental Health*. 2018;19(1):3-8. doi:[https://doi.org/10.4103/AMH.AMH\\_10\\_18](https://doi.org/10.4103/AMH.AMH_10_18)
  12. Zheng H, Zhang B, Chhatbar PY, et al. Mesenchymal Stem Cell Therapy in Stroke: A Systematic Review of Literature in Pre-Clinical and Clinical Research. *Cell Transplantation*. 2018;27(12):1723-1730. doi:<https://doi.org/10.1177%2F0963689718806846>
  13. Kuroda S, Koh M, Hori E, Hayakawa Y, Akai T. Muse Cell: A New Paradigm for Cell Therapy and Regenerative Homeostasis in Ischemic Stroke. In: Dezawa M, ed. *Muse Cells: Endogenous Reparative Pluripotent Stem Cells*. Springer Japan; 2018:187-198.
  14. Russo E, Nguyen H, Lippert T, Tuazon J, Borlongan CV, Napoli E. Mitochondrial targeting as a novel therapy for stroke. *Brain Circ*. Jul-Sep 2018;4(3):84-94. doi:[https://dx.doi.org/10.4103%2Fbc.bc\\_14\\_18](https://dx.doi.org/10.4103%2Fbc.bc_14_18)
  15. Glicksman MA. Induced Pluripotent Stem Cells: The Most Versatile Source for Stem Cell Therapy. *Clinical Therapeutics*. 2018/07/01/ 2018;40(7):1060-1065. doi:<https://doi.org/10.1016/j.clinthera.2018.06.004>
  16. Detante O, Muir K, Jolkkonen J. Cell Therapy in Stroke—Cautious Steps Towards a Clinical Treatment. *Translational Stroke Research*. 2018/08/01 2018;9(4):321-332. doi:<https://doi.org/10.1007/s12975-017-0587-6>
  17. Watanabe TK. A Review of Stem Cell Therapy for Acquired Brain Injuries and Neurodegenerative Central Nervous System Diseases. *PM&R*. 2018/09/01/ 2018;10(9, Supplement 2):S151-S156. doi:<https://doi.org/10.1016/j.pmrj.2018.07.008>
  18. Agus Dwi Susanto<sup>1</sup>, Regina Annisa Harahap<sup>1</sup>, Budhi Antariksa<sup>1</sup>, Muhammad Abbas Basalamah<sup>2</sup> FN. The Prevalence and Related Risk Factors of Obstructive Sleep Apnea in Heart Failure Patients at the Indonesian Referral Hospital for Respiratory Diseases. *J Nat Sci Biol Med*. 2020;11(2):164-168. doi:10.4103/jnsbm.JNSBM