STEM CELL THERAPY IN STROKE

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ABSTRACT

Stem cells are emerging as an attractive option because of their intrinsic ability as vectors for drug delivery to diseased tissues. The term stem cells or stem cells was first introduced by a Russian histologist, Alexander Maksimov (1874-1928). The purpose of this study is to describe the research and development of stem cell applications for stroke. This study is a literature study (review article) regarding stem cells (stem cells) in stroke which has been discussed in several scientific journals. From several articles that have been collected in giving stem cells to people with stroke, namely in bone marrow. MSC (Mesenchymal Stem Cell) is a multipotent stem cell from bone marrow and Adult SPM and because of its high applicability. Bone marrow is a rich source of hematopoietic stem cells so it can be applied to stroke patients.

Keyword : Stem Cell, Therapy, Stroke

INTRODUCTION

Stroke is a sudden brain disorder caused by vascular disorders and can cause death (Writtenauer R, 2012). Stroke can cause obstacles in blood flow to the brain so that it can result in the death of brain cells. Stroke is the second leading cause of death in the world after heart disease. Therefore, there is a need for therapy for stroke patients, which are generally still carried out conventionally, including stroke with thrombolytic therapy. Stem cells are emerging as an attractive option because of their intrinsic ability as vectors for drug delivery to diseased tissues. The term stem cells or stem cells was first introduced by a Russian histologist, Alexander Maksimov (1874-1928), at the 1908 congress of hematology held in Berlin.

The World Stroke Organization data states that there are around 13.7 million cases of stroke with a mortality of 5.5 million people every year (Apriandra R, 2019). In Indonesia, stroke is the third most deadly disease after heart disease and cancer. Damaged neuron cells cannot recover by themselves. Steinberg and colleagues from

Stanford University (2008), conducted a study using stem cells. Stem cell culture

One way to do therapy using stem cells (stem cells) to restore brain function after a stroke. This therapy uses stem cells to restore brain function after a stroke was started 21 years ago. Previously, stem cells could be transplanted into animal models in stroke trials, euron stem cells have begun to be given to stroke patients (Martínez-Garza et al. 2016). Stem cell therapy is a research in the field of cells that have the ability to form new tissues so that they can replace damaged cells in various diseases caused by organ damage.

One type of stem cells is SPM. Mesenchymal stem cells can be isolated from bone marrow, fatty tissue, peripheral blood, umbilical cord blood, Wharton's Jelly, and so on. Mesenchymal stem cells are multipotent which are able to proliferate and differentiate into several body cells such as osteoblasts, chondrocytes, adipocytes, and neurons. The purpose of this study is to describe the research and development of stem cell applications for stroke.

Table 1. Title Several Researches About Stem Cells Against Stroke

No	Cell Type	Source of Stem Cells	Delivery Route	Study Results	Reference
1.	Multipotensi SPM	Mesenkim	Bone marrow	In a meta-analysis in cardiology, it was concluded that transplantation of SPM from the adult spinal cord improves left ventricular function, infarct size and remodeling.	Ariyanti Noviantari, *et al*
2.	Multipotensi SPM	Hematopoietik	Bone marrow. Peripheral blood and umbilical cord blood.	Stem cells can be taken from aborted or aborted human fetuses and will be injected into the patient's brain. Stem cells are expected to regenerate brain areas damaged by stroke and improve the patient's mobility.	(Nurcahyo n.d.)
3.	Multipotensi SPM	MSC Alogemik	Bone marrow and isolated from fat	MSC has unique properties in the treatment of chronic ischemic stroke. MSC has the ability to reduce inflammation while eliminating environmental conditions that are toxic to Neural Stem Cells (NSC).	(Hasanah 2021)
4.	Neural stem cell (NSCs)	Allogenik	Intranervous	The trial results suggest that administration of BM-MNCs is safe and feasible for stroke. patient. In another phase I, open label, prospective clinical trial, patients with acute ischemic stroke received one i.v. infusion of allogeneic	(Singh 2020)

				human cord blood cells in a 3–10 day window.	
5.	MSCs	Allogenic	Bone marrow	In addition, behavioral outcomes are often restricted to the mNSS scoring system, which is a crude measure of outcomes and may not capture the post-stroke motor recovery induced by MSCs	(Zheng 2018).
6.	Human neuronal	Allogenic	Bone marrow	Pros and cons of different donor cell types and routes of cell delivery, including intravascular delivery, in ischemic stroke. Intravascular cell delivery and an up-to-date comprehensive list of ongoing clinical trials in ischemic stroke.	(Vivek and Misra 2012).
7.	Eksogen	Lungs	Brain	One of the alternative treatment which will be able to recover stroke patients and reduce the morbidity and mortality of stroke cases, namely stem cell therapy neuronal.	(Sihanto and Rindha 2019).
8.	Endogen dan eksogen	Allogenic	Bone marrow	Stem cell transplant in neurological disorders including stroke, namely to replace or improve function biologics of damaged neuron cells in order to maintain or restore brain function. New neuron cells can be generated from stem cell transplantation. Besides, the adult brain will triggered to make new neuron cells in response to damage so it will improve the healing quality of stroke patients.	Tangkuman F. Venki, et al.
9.	Eksosom	MSCs	Brain	From the results of several preclinical studies conducted, it was found that MSCs have the potential to be developed as a next-generation cell-based drug delivery system, which is promising in the treatment of glioblastoma, sensorineural hearing loss, colorectal cancer, epilepsy, ischemic stroke and Intervertebral Disc Degeneration (IDD).	(Suparno 2022).
10.	Endotelial	Miokard	Bone marrow	Stem cells have the ability to regenerate other cells in two ways mechanisms namely, cell differentiation and secretion of cytokines and growth factors. Most stem cells Mostly used in the	(Amin 2013)

				treatment of myocardial infarction are bone marrow derivatives. These cells have a high level of applicability, do not require in vitro expansion, and most importantly capable of differentiating into various cell types	

METHODS

This study is a literature study (review article) regarding stem cells (stem cell) disease in stroke which has been discussed in several scientific journals. The collection of this study is by collecting references via the internet in the form of Google Scolars with the keywords "stem cell, and stroke" and then conducting a review of related literature. Related articles reviewed include stem cells, stroke and stem cell therapy in stroke.

RESULTS

Stem cells are defined as undifferentiated cells, so they have the potential to multiply and grow into certain cells. There is terminology in explaining the characteristics of stem cells (Du et al, 2009):

1. Pluripotent stem cells, have the potential to develop into cells derived from the three germ layers, for example embryonic stem cells.
2. Totipotent stem cells, have the ability to differentiate into all cells and tissues that make up the embryo and support fetal development, such as a zygote or a fertilized ovum.
3. Unipotent stem cells, have the ability to differentiate into one type of cell, such as epidermal stem cells.

Several clinical trials were conducted on the use of stem cells (stem cells) in stroke patients. Therapy using peak cells is a new window for treating diseases of the central nervous system (Hosseini et al. 2015). Stroke is a cerebrovascular disease which is characterized by the death of brain tissue (cerebral infarction) due to blockage, narrowing or rupture of blood vessels, causing reduced blood flow to the brain. So that it can cause blood cell death because there is a blockage in the blood vessels to the brain (ischemic stroke) there is a rupture of a blood vessel to the brain (hemorrhagic stroke) that occurs through the process of apoptosis, excitotoxicity and inflammation (Harukuni I, Bhardwaj A, 2017).

Stem cells are able to travel to damaged tissue and combine with other cells in that tissue. Stem cells can develop into certain cells with special functions from the tissues or organs that occupy them (transdifferentiation). Therefore, stem cells can repair or create new healthy tissue (regeneration) in damaged organs.

From several articles that have been collected in giving stem cells to people with stroke, namely in bone marrow. MSC (Mesenchymal Stem Cell) is a multipotent stem cell from bone marrow and Adult SPM and because of its high applicability, Stem Cells (ASCs) consist of Hematopoietic Stem Cells. SPM mesenchyme can be isolated from bone marrow, fat tissue, umbilical cord and peripheral blood. Mesenchyme is multipotent which is able to work and differentiate into cells that make up the body such as osteoblasts, chondrocytes, adipocytes and neurons (Halim 2010).

In the transplantation of stem cells can be: Autologous transplantation (using the patient's own stem cells). Allogeneic transplantation (using stem cells from a matched donor, who are related to each other or are genetically identical). Types of stem cell transplantation from the source, namely from the bone marrow (bone marrow transplantation). Bone marrow is a spongy tissue found in the sternum, spine and ribs. Bone marrow is a rich source of hematopoietic stem cells so it can be applied to stroke patients.

SUMMARY

Based on the results of the study of several theories above, it can be concluded that: Stem cells can be applied to stroke patients by conducting cell therapy. There are two types of cells in the human body, namely somatic cells and sexual cells. Not only stroke, this therapy can be given to people with heart disease and diabetes.

Most of the locations for stem cell administration are in the bone marrow, namely MSCs which are multipotential to proliferate into adult neuron cells that can inhibit inflammation in stroke patients.

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