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Stem Cell-based Therapies as a Promising Approach in Alzheimer's Disease

Marzieh Rostaminejad (marzieh.rostaminejad@gmail.com)

Department of Medical Biotechnology, School of Advanced Medical Sciences and Technologies, Shiraz University of Medical Sciences, Shiraz, Iran

Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disease and is the most common cause of dementia in the elderly population. In this disease, the process of neurodegeneration begins with the formation of amyloid plaques in the brain, and progressive neuronal cell death leads to cognitive disorders and memory loss in the patients. AD is currently incurable and present treatment options only reduce the symptoms in patients and cannot prevent the neurodegeneration. So far, many attempts have been made to develop small therapeutic molecules or antibodies to treat AD, but they were mostly inconclusive. To date, stem cell-based therapies have become a promising new approach for regeneration process in neurodegenerative disorders, including AD. Stem cells are undifferentiated cells which have the ability to proliferate, self-renewal, and differentiate into different cell types, including neurons. For this reason, they can be used in the production of various cell types and tissue engineering. Successful results in the production, proliferation and differentiation of stem cells in animal models of AD indicate the therapeutic potential of stem cells in the treatment of neurodegenerative disorders. Accordingly, stem cell therapy may provide an opportunity to treat or delay the progression of AD.

Methods

This review performed by searching "Alzheimer's disease" AND "Stem Cell Therapy" AND "Regenerative Medicine" keywords (Title/Abstract) in PubMed, Scopus, Embase, Google Scholar, and Web of Science databases. All original articles (human and animal) written in English were included in this study.

Results

In recent years, the use of stem cells derived from various sources in preclinical studies has been effective in controlling and treating symptoms in animal models of AD, and clinical trials are currently underway in humans. Mesenchymal stem cells (MSCs), induced pluripotent stem cells (iPSCs), embryonic stem cells (ESCs), and neural stem cells (NSCs) are the most common type of stem cells used in the studies for AD which are mainly transplanted intravenously into the body. MSCs have easy isolation and handling without ethical restrictions. These cells were able to cross the Blood-Brain Barrier (BBB) and migrate to damaged areas of the brain. The results of transplantation of MSCs into AD animal models showed the potential for neuroprotection by modulating neuroinflammation, increasing neurogenesis, and suppressing neuroapoptosis. Therefore, they could be used clinically in patients with AD.

IPSCs are pluripotent stem cells which reprogrammed *in vitro* from adult somatic cells and can differentiate into different cell types, including neurons. Despite their promising applications in AD animal models, these cells are ethically controversial, and have many concerns about genetic mutations in the process of iPSCs generation, tumorigenicity, teratoma formation, and immunogenicity. Therefore, the applications of iPSCs in AD have so far focused more on the development of disease models than on treatment. ESCs are obtained from the inner cell mass of blastocyst. They can be the best cellular source for cell therapy studies if pluripotency can be controlled to desired phenotype. Despite the good results obtained in preclinical studies on AD models, duo to the possibility of teratoma formation, tumorigenicity, poor survival rate after transplantation, and ethical limitations, the studies on these cells has been limited in clinical trials compared to other stem cells. NSCs are present in different areas of the adult central nervous system and are able to differentiate into different cell types, including neurons, oligodendrocytes, and astrocytes. NSCs can also be differentiated from brain tissue of aborted fetal, iPSCs, and ESCs. In animal models of AD, transplanted NSCs were able to differentiate into mature brain cells and improved the brain function and cognitive abilities of mice. NSCs showed lower risks in tumorigenicity and immunogenicity which makes them the potential candidates for neural transplantation in human. However, their ability to generate specific neurons remains unknown, and unwanted differentiation into non-neuronal cells, like glia, has been reported.

Conclusions

The successful results of many preclinical studies indicate the ability of stem cells to treat animal models of AD. However, stem cell-based therapies for AD are in early-phase clinical trials and more evidences are needed to support their efficacy and safety for human studies. Along with their countless benefits, ethical concerns, reprogramming efficiency, tumorigenicity, immunogenicity, and the risk of uncontrolled proliferation and differentiation after transplantation should also be considered before use in a wide range of patients.

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