

The Prospects of Stem Cell Therapy in Neurodegenerative Diseases

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ABSTRACT

Neurodegenerative disorders (NDs) are a group of neurological ailments characterised by the progressive demise of neurons and glial cells within the brain and spinal cord. Neurodegenerative disorders frequently result in the targeted degeneration of specific neuronal cells within a localised region of the brain. Parkinson's disease, Huntington's disease (HD), Alzheimer's disease, and amyotrophic lateral sclerosis (ALS) are examples of neurodegenerative diseases. The absence of efficacious interventions for neurodegenerative illnesses exerts a substantial economic burden and imposes a considerable burden on society. In recent years, extensive research has been conducted on the potential of stem cells in the treatment of neurodegenerative diseases. The fundamental trait of stem cells is self-renewal. Evidence has shown that the microenvironment plays a vital role in the stem cell system, and stem cells are unable to live without it. Moreover, it is postulated that the attributes of stem cells are not limited to a singular cell type within the population, but can, in certain instances, be imposed on cells other than those that generally assume the role of stem cells due to the appropriate micro environment. The ability of stem cells to differentiate into specific cell lineages. The distinguishing characteristics of stem cells, in comparison to other cell types, are their perpetual self-renewal and their ability to differentiate into a specific adult cell type. Given their ability to generate many types of tissues within the human body, stem cells exhibit significant potential for utilisation in the future of tissue regeneration and repair therapies. Stem cell-based therapies have garnered significant interest as potential treatments for neurodegenerative disorders. Indeed, the transplantation of stem cells or their derivatives in animal models of neurodegenerative illnesses has the potential to facilitate the replacement of damaged neurons and glial cells, as well as induce remyelination, trophic effects, and inflammation. Endogenous neural stem cells possess the potential to serve as therapeutic targets due to their ability to respond to injury through the production of neurons and glial cells, as well as their susceptibility to the degenerative process. This study provides an overview of the latest advancements in the domain of stem cell treatment for neurodegenerative diseases.

Key-words: Neurodegenerative disorders, Parkinson's disease, Huntington's disease, Stem cell therapy.

INTRODUCTION

Stem cells are cells which are undifferentiated cells and able to repair damaged tissue, developing into another cell.

Depending on the variety of cell types they can produce and how they are obtained, stem cells can be grouped into many categories among them are embryonic stem cells mesenchymal stem cells, progenitor cells, and ES cell sips cells and induced pluripotent stem cells (MSCs).^[1]

On the other hand, neurodegenerative disease may results loss of structure or function also can occur death of neurons in the body.

Stem cells allows for the regeneration of brain tissue, which reduces the effects of neurodegeneration that

affects the neural circuitry at various levels.^[2]

In recent years stem cell therapy has opened great way of treating neurovegetative disease also it is important to treat neurodegenerative disease at primary stage. Till now many studies have been done on this subject. Some limitations are also noticed in this field. But as it is a promising and sensible treatment for disease like neurodegenerative it became a field of interest to research.

This paper will outline the history of stem cells, current practices, limitations of stem cell therapy on neurodegenerative disease, followed by future recommendations that can bring potential research towards stem cell therapy for more robust treatment for neurodegenerative diseases.

Stem Cell Treatment in Other Disease

A patient may receive treatment with allogeneic transplantation for the following conditions:

Acute leukemia, a megakaryocytes or congenital thrombocytopenia, aplastic anemia or refractory anemia, chronic lymphocytic leukemia, Familialerythrophagocytosislymphhistiocytosis, myelodysplasticsyndrome or another myelodysplastic disorder, osteopetrosis, paroxysmal nocturnal hemoglobinuria, Wisk ott-Aldrich syndrome.^[3]

This therapy is also used in Genetic Disorders, Tissue Engineering, **Treatment of Autoimmune Diseases, Diabetes Treatment, Liver Disease Treatment, Blood disease, Cardiovascular disease, Tissue regeneration.**

Advantages of Stem Cell Therapy

Stem cells or their derivatives are used in stem cell therapy, sometimes referred to as regenerative therapy, to enhance the ability of dysfunctional and damaged tissue to respond to repair. The potency of stem cell in treating neurodegenerative disease first was investigated in 1980s when patients suffering from Parkinson's disease (PD) treated with fetal mesencephalic tissue transplantation in Mexico.^[4]

Although till now most of the study done in animal model in which it showed motor and cognitive function improvements but there are some research cases where stem cell performed remarkable development in humans also.

MSCs has potential to treat inflammatory disease as it releases anti-inflammatory factor. Also, MSCs have a low risk of rejection in human and in animal models.

By using MSCs from umbilical cord tissue, the moral issues surrounding embryonic stem cells are avoided. Using umbilical cord tissue is a more ethically acceptable option because it does not involve the destruction of embryos because it is taken after the baby is born and would otherwise be discarded.^[5]

Umbilical cord blood stem cells which have potential for treatment of neurodegenerative disease are easily accessible and non-invasive source of MSCs that reduce the danger and discomfort of the donor. Also, this treatment offers personalized treatment to the patient.

In some cases, stem cell therapy has already given success result. For example, in 1987 for PD patient test on human embryonic showed that there was no development of tumor and there was positive improvement.

Two PD patients received VM tissue transplants into their midbrains in the 1980 s, and for the next 20 years, their recovery was observed.

Emory University initiated the inaugural FDA-approved clinical trial in 2010 utilizing neural progenitor

cells (NPCs) derived from embryonic spinal cord in individuals with amyotrophic lateral sclerosis (ALS). No acute or long-term complications were observed during a 9-year follow-up after the surgical implantation of MSCs into the dorsal spinal cord. [6]

Disadvantages

Despite less risk of rejection and less ethical concern complications including infection, hemorrhage, or allergic responses are still a risk. Furthermore, unanticipated hazards can arise because the long-term consequences of MSCs are still being investigated.

Because umbilical cord tissue is the primary source of MSCs, stem cell therapy can be costly. Many patients may find the treatment less accessible due to the expense of isolating, growing, and administering the cells as well as the requirement for specialist staff and facilities. Stem cell therapy can also lead to tumorigenicity.

NEURODEGENERATIVE DISEASE AND ITS PATHOPHYSIOLOGY

A category of neurological conditions known as neurodegenerative diseases (NDs) are brought on by the gradual death of neurons and glial cells in the brain and spinal cord. Any neurodegenerative illnesses often cause a selective loss of neuronal cells in a small area of the brain.

Neurodegenerative disease are Parkinson's disease, Huntington's disease (HD), Alzheimer's disease, spinal injuries, stroke, etc.

Progressive loss of specific vulnerable neuronal populations is a hallmark of neurodegenerative disorders; this is in contrast to select static neuronal loss resulting from metabolic or toxic disorders. [7]

Stem Cell for Neurodegenerative Disease

For nearly all types of neurodegenerative disorders, such as Parkinson's disease (PD), Alzheimer's disease (ADSL), Huntington's disease (HD), and amyotrophic lateral sclerosis (ALS), stem cell therapy offers encouraging promise.

Preclinical and clinical studies on Parkinson's disease (PD) patients over the past 20 years have shown that stem cell therapy of human embryonic mesencephalic tissue can reinnervate the striatum. the security of 67 ALS patients' frontal motor cortex stem cell transplantation. In the history of stem cell therapy for neurodegenerative illnesses, this was likely one of the largest human studies ever conducted. 90% survival after a year of autologous stem cell treatment in the frontal motor cortex was found to be encouraging.

Stem cell-based therapeutic techniques have garnered significant attention as potential therapeutics for Huntington's disease. The primary objectives of stem cell therapy for Huntington's disease are to replace neurons that have been destroyed or harmed, as well as to modify mutant genes that possess increased CAG repeats.

Recent studies suggest that neural stem cells (NSCs) have been the predominant form of stem cells used in the treatment of Huntington's disease (HD). Neural stem cells (NSCs) have been produced and isolated from many origins, such as somatic cells of patients with Huntington's disease (HD) and the brain itself. [8]

ADVANTAGES OF NEURODEGENERATIVE DISEASE OVER TYPICAL TREATMENT

Compared to conventional treatment methods, stem cell procedures have a number of advantages. Targeting

the underlying cause of an illness or condition by repairing or regenerating damaged tissues is one of the main benefits. Because they treat the underlying cause rather than just the symptoms, stem cell therapies have the potential to offer long-term or permanent remedies. Stem cell operations may also lessen the need for invasive procedures or treatments with serious side effects, which could enhance patient outcomes and quality of life.^[9]

No current treatment is available for neurovegetative disease. Usually, a mix of medicine and psychotherapy is used to treat them. The type of neurodegenerative disease a person has been diagnosed with determines the precise medicine combination and form. Every type of neurodegenerative disease has a different course of treatment. On the other hand, the goal of treatment is usually to lessen the condition's symptoms.^[10]

Pharmacological or neurosurgical treatments are not effective in stopping the progress of neurodegenerative as much as stem cause stem cell therapy works through a variety of mechanisms, including the activation of endogenous stem cells, the secretion of neurotrophic and growth factors, the direct replacement of lost or damaged cells, and a reduction in neuroinflammation.

Most neurodegenerative disease treatments available today focus on treating symptoms rather than the fundamental cause of the illness. There is growing evidence that immunotherapy may be useful in controlling the course of a disease.^[11] Drug such as apomorphine, baclofen, donepezil, entacapone, etc. are used.

ETHICAL CONCERNS

Historically, the primary emphasis of stem cell ethics has revolved around the generation and therapeutic utilisation of human embryonic stem cells (hESCs). The ethical debates surrounding stem cell-based therapies revolve around the limitless differentiation potential of iPSCs, which can be used for human cloning and pose a risk for the production of human embryos and human-animal chimaeras.^[12]

The utilisation of embryos gives rise to ethical considerations, which subsequently impact the boundaries and limitations of this research.^[13] To ensure the ethical conduct of clinical studies with stem cells, it is imperative to adhere to the criteria that govern all clinical research. Due to the inherently innovative nature of these trials, it is imperative to prioritise a thorough scientific and ethical evaluation when comparing them to existing treatments. Additionally, it is crucial to ensure that participants provide voluntary informed consent and that the clinical trial's findings, including negative outcomes and adverse effects, are made publicly available.^[14]

FUTURE DIRECTIONS

Stem cell therapy is a great medium to combine gene therapy and stem cell transplant. It provides new tools to cure. There is hope because patient-derived stem cells may help us learn more about the pathophysiology of these disorders. By employing stem cells as a carrier, it would potentially be able to combine gene therapy and stem cell transplantation. *Ascl1*, *Brn2* (also known as *Pou3f2*), and *Myt1l* are the only three factors that can effectively and quickly transform mouse embryonic and postnatal fibroblasts into functional neurons in vitro, according to recent research by Thomas Vierbuchen et al. These induced neuronal (iN) cells produce action potentials, various neuron-specific proteins, and useful connections.^[15]

More pre-clinical trial is highly need for this treatment.

Stem cell treatment is still a potential strategy for treating neurodegenerative illnesses in the future despite all the restrictions and difficulties.

CONCLUSION

Stem cell therapy is hope to understand about the mechanisms causing these debilitating neurodegenerative illnesses as a result personalized treatment based on the illness will be more obvious.

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