International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Stem Cell Therapy Used to Treat Diabetes Mellitus or Parkinson Disease

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Abstract

Numerous cell types can be produced from stem cells. The ability of a stem cell to continuously regenerate itself and its tendency to differentiate into a specific adult cell type make it unique. Pluripotent stem cells have the ability to differentiate into any cell in the adult body, while multipotent stem cells are limited to differentiating into a specific subset of cells. A variety of tissues, such as bone marrow, amniotic cells, adipose tissue, umbilical cord, and placental tissue, can yield stem cells. By utilizing stem cells' capacity for regeneration, stem cell-based therapies have become a viable treatment option for a number of neurological conditions by repairing damaged brain tissue and circuitry. In humans, a loss of neurons and glial cells in the brain or spinal cord results in neurological illnesses such Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis (ALS), Alzheimer's disease, multiple sclerosis (MS), stroke, and spinal cord injury.

Keyword: Stem cell, Adult cell, Neurological conditions , Parkinson disease.

Introduction

Stem cell are cells that can self-renew and differentiate into other types of cells. They are found in almost all tissues of the body including bone marrow, blood, umbilical cord blood, and other tissues in the body. Stem cells are a population of immature tissue precursor cells capable of self-renewal and provision of de novo and/or replacement cells for many tissues. Embryonic stem cells can be obtained from the inner cell mass of the embryonal blastocyst. Although it was recently shown that human Embryonic stem cells can differentiate into cardiomyocytes, because of the immunogenicity and rejection, as well as ethical considerations, these cells may be restricted to experimental in vitro studies and their therapeutical potential remains to be determined. Furthermore, these cells can provide an unexpected cause of arrhythmia following an intramoycardial transplant. [1]

Stem cells are used in a therapy known as stem cell therapy, sometimes called regenerative medicine, to replace or mend damaged tissues. Unheard-of potential in modern medicine for curing many debilitating diseases and injuries, stem cell therapy offers a fresh method of approach. For applications in regenerative medicine, stem cells are essential due to their distinctive qualities, which include self-renewal and differentiation into specialized cell types. [2]

Stem cells are defined as cells capable of both cloning themselves and self-renewal, as well as differentiating into various cell types. They exist in everyone, from early human development through to old age. Stem cells are unspecialized and can evolve into the specialized cells that form the different tissues within the human body. Their defining features include the ability to replicate through mitotic division and to transform into a wide variety of specialized cell types. They play a crucial role in the development,

growth, maintenance, and repair of various organs, including the brain, bones, muscles, nerves, blood, skin, and more. [3]

The first bone marrow transplant took place in 1956, marking the beginning of stem cells' use in contemporary regenerative medicine in the 1950s. This discovery cleared the path for the currently available stem cell therapies and provided insight into the possible treatments that could be developed in the future with additional clinical technique development and improvement. Stem cell therapies have shown significant effectiveness when other treatments have failed and are currently recommended for a variety of clinical disorders beyond typical origins to treat inherited blood illnesses. The ability of stem cells to cure paint states and neurodegenerative illnesses like Parkinson's and Alzheimer's disease is one new application for them.[4]

Types of stem cells:

1. **ESCs (Embryonic stem cells):** In stem cell biology, ESCs have traits that set them apart from one another. They are particularly versatile and have a lot of therapeutic potential because to their pluripotency, which is characterized by unique characteristics that allow them to differentiate into any human body cell . Furthermore, ESCs have a remarkable capacity for self-renewal, which helps explain why they remain active and effective for prolonged periods of time . Humans, mice, and nonhuman primates are possible sources of ESC. Prior to implantation, they are separated from the core cell mass of the blastocysts.[5]
2. **ASCs (Adult stem cells):** Because of their unique characteristics and crucial functions in tissue maintenance, ASCs stand out in the field of regenerative biology. Multipotency is the capacity of cells to develop into a limited, diversified range of cellular phenotypes or to exhibit many possible fates. An essential component of maintaining the structural integrity of tissues such as bone, skin, and blood are endogenous stem cells, or ASCs. Particular tissue regions or niches contain them. Blood, stomach, muscle, skin, brain, and heart are among the tissues where ASCs have been found. They have shown effective in treating diseases, although being less powerful than ESCs. They can be taken out of people and harvested, then used in autologous or allogeneic transplantation to regenerate tissue.[6]
3. **Perinatal stem cells:** Perinatal stem cells represent a separate and very promising class of hybrid stem cells. Their use in regenerative medicine, therapeutic treatments for particular disorders, and alloopic transplantation highlight their promise to transform the scene of stem cell-based treatments.[7]
4. **iPSCs (Induced pluripotent stem cells):** Furthermore, iPSCs play a pivotal function in sickness modeling in personalised medication . The ability to generate iPSCs fro people with precise genetic situations has enabled researchers to create in vitro sickness fashions. These fashions are extraordinarily worthwhile gear for know-how sickness mechanisms on the cell degree and allow the exploration of focused therapeutics interventions. iPSC-primarily based totally sickness modeling advances the sector of personalised medication with the aid of using allowing a greater accurate and custom designed method to scientific research, as a result establishing the door for custom designed treatments. Beyond contamination modeling and custom designed treatments, iPSCs have a chief effect on toxicity checks and drug development. The pluripotent characteristics of iPSCs permit the technology of numerous cell phenotypes, offering a bendy platform for comparing the safety and effectiveness of prescribed drugs. iPSC-primarily based totally assays provide a greater thorough know-how of the way prescribed drugs interact with diverse mobile types, which allows become aware of feasible facet effects and directs improvements withinside the introduction of treatments that are

each more secure and greater effective. In conclusion, iPSCs provide a innovative method to stem mobile investigation, as a result of their pluripotent traits and the beginning of grownup mobile reprogramming .[8]

Source of stem cell:

Bone marrow as a source for stem cell : Stem cells are required with the aid of using self-renewing tissues to replace broken and getting older cells due to everyday biological processes. Both myeloid and lymphoid lineage cells derived from hematopoietic stem cells are especially short-lived mobileular kinds and require a non-stop supply of newly differentiated substitute cells. Hematopoietic stem cells (HSC's) are people who are living withinside the bone marrow and offer a supply for the a couple of kinds of blood cells required for normal physiological and immunological functions. These cells inhabit a physiological area of interest which permits them to undergo the procedure of uneven department. When stem cells divide asymmetrically the progeny of the department consists of one same daughter mobileular however additionally outcomes withinside the production of a differentiated daughter mobileular. Differentiation of these daughter mobileular into specialised mobileular kinds is guided with the aid of using certain Microenvironments, extrinsic cues, and boom elements that the mobileular comes in touch with. This mechanism permits for bone marrow stem mobileular numbers to live especially constant regardless of sustained proliferation and differentiation of progeny taking place[9]

Amniotic cells as a source for stem cell : In current years, hADSCs, consisting of human amniotic epithelial stem cells (hAESCs) and human amniotic mesenchymal stem cells (hAMSCs) were appealing mobileular reassets for scientific trials and scientific research, and have been proven to have blessings over different stem cells types. These blessings encompass low immunogenicity And excessive histocompatibility, no tumorigenicity, immunomodulatory effects, and vast paracrine effects. Also, numerous research have evaluated the proangiogenic capacity of hADSCs. Interestingly, they located that hAMSCs had been proven to enhance blood perfusion and capillary structure while transplanted into ischemic limbs of mice, suggesting that hAMSCs stimulate neovascularization. Additionally, every other gain is that hADSCs are less difficult to acquire in comparison to different stem mobileular reassets, together with bone marrow stem cells (BMSCs)[10]

Adipose tissue as a source for stem cell : Though now common, scientists are considering other sources of mesenchymal stem cells (MSCs) given challenges with collection techniques and the possibility of low mobileular yields and are therefore still looking for other sources of mesenchymal stem cells (MSCs) using adipoyarnic tissue. One source under examination is human adipose tissue. A varied collection of adipocyte precursors is created inside a cell group named the stromal vascular fraction (SVF) following the enzymatic decomposition of adipose tissue. The stromal vascular fraction contains adipose-derived stem cells (ADSCs).[11]

Umbilical cord as a source for stem cell : Numerous sources, such as umbilical cord blood, umbilical cord perivascular cells, umbilical vein endothelial cells, umbilical cord lining, chorion, and amnion, can yield umbilical cord stem cells. Since 1988, umbilical cord blood has been utilized as a source of hematopoietic stem cells because it can be extracted with little danger to the donor. Stem cells produced from umbilical cords are far more accessible than those derived from bone marrow. Given that over 100 million people are born each year worldwide, there are many opportunities to use umbilical cord blood as a source of stem cells[12]

Placental tissue as a source for stem cell : Placental tissue consists of epithelial cells able of differentiating into a broad spectrum of tissue types, including those connected to fat, muscle, liver, bone, heart, blood vessels, pancreas, lungs, and the nervous system, as well as stem cells. Different lineages related to particular regions of the placenta provide the basis for placental cells' capacity to become these many tissues. Hematopoietic cells come from the chorion, allantois, and yolk sac, whereas mesenchymal lineages come from the chorion and amnion, for example. Human fetal placental cells can be helpfully grouped into four distinct categories: amniotic epithelial cells, amniotic mesenchymal stromal cells, chorionic mesenchymal stromal cells, and chorionic trophoblast cells.[13]

Diabetes mellitus

Diabetes mellitus is a group of disease characterized by high blood glucose resulting from defects in insulin production, insulin action or both.

Diabetes mellitus (DM) is a significant metabolic disorder that poses a serious health risk. It is caused by either insufficient insulin production in type 1 diabetes mellitus (T1DM) or the body's inability to effectively use this hormone, as in type 2 diabetes (T2D). As of 2014, over 400 million individuals were affected by DM, a significant increase from 108 million in 1980. If the current pattern persists, this number may rise to over 600 million by 2045. Of these cases, T1DM represents about 10%. The development of T1DM is associated with the autoimmune destruction of insulin-secreting β-cells in the pancreatic islets. Evidence for the autoimmune origins of T1DM includes the presence of lymphocyte infiltration in and around the islets and the detection of autoantibodies against various islet autoantigens.[14]

Stem cell therapy for diabetes Mellitus:

Stem-cell treatments often get a lot of attention since they promise to revolutionize healthcare by giving self-sustaining cures that might obviate the need of pharmaceuticals and devices. Still uncertain is the timing and feasibility of such a change, though. Published on September 25, 2024, a phase 1 clinical trial describes the first human trial of autologous transplant using chemically induced pluripotent stem cell derived islets to treat type 1 diabetes. The study included a 25-year-old lady who, 75 days after the transplant, was free of insulin and who maintained this independence over the coming year while her HbA1c level decreased from 7.57% to 5.37% by day 120. Especially given that only about 20% of adults with type 1 diabetes now reach the American Diabetes Association's HbA1c goal, this change is quite important. The patient had already been on immunosuppressants because of a previous liver transplant, but it is important to point out the constraints of the study: this complicates any inferences about autoimmune reactions. Furthermore not known still are the long-term consequences of this transplant beyond one year.[15]

The Seven Pillars of Credibility" as essential criteria in the evaluation of claims of success in the use of stem cell and/or gene therapy for diabetes[16]

1. Cure of hyperglycemia
2. Response to glucose tolerance test
3. Evidence of appropriate C-peptide secretion
4. Weight gain
5. Prompt return of diabetes when the transfecting gene and/or insulin producing cells are removed
6. No islet regeneration of stereptozotocin-treated animals and no re-generation of pancreas in pancreatectomized animals

7. Presence of insulin storage granules in the treated cells

Source of stem cell for diabetics:

- **Pluripotent stem cells:**

Human pluripotent stem cells (hPSCs) include embryonic stem cells (hESCs) that are derived from the inner cell mass of the embryo and human induced pluripotent stem cells (hiPSCs) that are generated by somatic cell reprogramming. hESCs show unlimited replicative properties and have the potential to diferentiate into any adult cell type. hiPSCs have the same ability to expand and diferentiate as ESCs.[17]

Mechanisms:

Step 1: Production of iPSC

Adenoviral infection with
OCT4, SOX2,c-MYC, KLF4

Fibroblasts → **iPS cell**

Step 2: Production of Insulin Expressing Cells

Activin A, EGF
FGF, OCT4, KLF4

iPS cell. → **Insulin Expressing Cells**

- **Mesenchymal stem/stromal cells (MSCs)**

General functions

MSCs are widely available from many tissues and can be readily expanded in vitro. Naive MSCs can home to injured tissues thereby expediting their repair. These cells are immune evasive due to the lack of expression of HLA class II antigens and the costimulatory molecules CD40, CD80, and CD86. Furthermore, MSCs exert an immunomodulatory function by releasing soluble factors as well as via cell-to-cell contact when activated by proinfammatory cytokines[18]

Mechanisms

Step 1: Production of definitive endoderm

Nodal, Activin A, FGF,
Retinoic Acid, IDEL, IDE2

Blastocyst → **Embryoid body**
Endoderm

Step 2: Production of Insulin Expressing Cells

Indolactam V, KGF,
Retinoic Acid, Cyclopamine

Embryoid body, → **Insulin Expressing**
Endoderm → **Cells**

Treatment of Diabetes Mellitus

Diabetes' migration rate is quickly increasing; forecasts show that by 2030, 366 million people will be affected. Today, roughly 7.7% of Iran's people—two million or more—suffer from diabetes. Around 2000, diabetes was projected to cost Iran some 306,440 years. Strict diets, daily insulin shots, and constant blood sugar monitoring greatly change patients' quality of life. Furthermore damaging other organs is the financial burden diabetes imposes on the national healthcare budget. Islet cell transplantation of the pancreas is one therapy for diabetes; however, the shortage of donor organs and the small possibility of patients becoming insulin-independent from it pose obstacles. [19]

Research is still underway regarding stem cell treatment. Diabetes treatment studies are looking at the following kinds of stem cells:

Embryonic stem cells : Soria et al. documented in 2000 the generation of insulin-producing cells from mouse embryonic stem cells. Further research has yielded promising results, and translation factors like pdx1 and pax4 as well as nestin-positive cells, changed culturing conditions have extended the lifespan of these cells.[20]

Mesenchymal stem cell: According to several clinical and laboratory studies, mesenchymal stem cells under particular cultural circumstances could regulate immune response by modifying B cells, T cells, natural killer cells, and cytokines like TGFβ and interleukin 10.They also have the potential to become insulin-producing cells. Mesenchymal cells from several sources—including those from bone marrow, adipose tissue, umbilical cord, and pancreas—have in vitro differentiation potential. Study of animals using mesenchymal cells obtained from umbilical cord and bone marrow showed improved blood glucose levels. A study on mesenchymal cell therapy for type 1 diabetes is now being run at the Endocrine and Metabolism Research Institute of Tehran University of Medical Sciences. [21]

Other cells: including skin fibroblasts, human neural progenitor cells, hepatic oval cells, and placental stem cells, might also have the ability to differentiate into insulin-producing cells under particular circumstances [22]

Stem cell therapy has also helped to control a number of diabetes-related problems including diabetic foot. Promising results have been seen with fetal CD133+ cells, autologous bone marrow stem cells, autologous biografts, mesenchymal stem cells, and autologous peripheral blood mononuclear cells.[23]

Neurological disorder: Improvements in healthcare, technology, and accessibility have led to longer average lifespans in the last hundred years. But this improved life expectancy has also raised the dangers of age -linked neurodegenerative illnesses and neurological conditions. As the elderly population keeps growing, McGovern Institute projects an increase in frequency of these illnesses in 2018. Patients, their families, and society at large suffer great financial and social toll from neurological disabilities. Most neurological disorders lack cures, and current treatments primarily aim to manage symptoms and slow disease progression . Patients often endure years of diminished quality of life, resulting in stress for both themselves and their families, all while facing escalating healthcare costs.[24]

Furthermore, compared to other age classes, seniors are much more likely to suffer from these diseases. Neurological conditions are estimated to affect 12 million Americans over the next three decades. New and efficient treatments therefore urgently need to be developed and found that could be useful in several neurological diseases over times[25,26]

Types of neurological disease: The brain, spinal cord, and nerves are all Impacted by neurological illnesses, which can cause a variety of symptoms like pain, seizures, movement problems, and cognitive loss. Typical neurological conditions include :[27]

Parkinson’s disease.
Alzheimer’s disease
Multiple sclerosis (MS)
Stroke
amyotrophic lateral sclerosis. (ALS)

Parkinson disease: Parkinson’s disease is characterized by a novel deficiency of dopaminergic neurons in the substantia nigra, which is the primary cause of both motor and non-motor symptoms. With stem

cells developing into dopamine-generating neurons and alleviating some symptoms, stem mobile therapy for Parkinson's disease has shown encouraging results in preclinical and early clinical trials.[28]

Parkinson's disease (PD) is characterised with the aid of using an extensive lack of dopamine neurons (DA) withinside the substantia nigr pars compacta and their terminals withinside the striatum and impacts extra than 500,000 humans withinside the United States. Lang and Lozano, 1998a,b, Although the etiologic of idiopathic PD isn't known, numerous predisposing elements for the dopaminergic depletion related to the disease had been suggested, together with programmed mobileular death, viral infection, and environmental toxins. As an effective remedy for PD, sufferers had been given L-dihydroxyphenyl alanine (L-DOPA), a precursor of dopamine, but long-time period management of L-DOPA therefore produces grave aspect.[29,30]

Benefits of stem cell therapy for Parkinson's disease:

Current studies has proven that stem mobileular remedy may want to probably result in upgrades in numerous signs and symptoms related to the condition, such as:[31]

- **Tremors:** Stem cells can be capable of update or restore misplaced or broken dopamine-generating cells withinside the brain, that may assist to lessen tremors.
- **Bradykinesia (slowness of movement):** Stem cells might also additionally enhance the feature of the dopamine-generating cells withinside the brain, that may assist enhance bradykinesia.
- **Rigidity:** Stem cells might also additionally lessen infection and oxidative strain withinside the brain, that may assist lessen rigidity.
- **Dyskinesia (bizarre movements):** Stem cells might also additionally enhance the feature of the dopamine-generating cells withinside the brain, that may assist lessen dyskinesia.
- **Postural instability:** Stem cells can be capable of enhance the feature of the dopamine-generating cells withinside the brain, that may assist to lessen postural instability.

Parkinson's disease treatment with mesenchymal stem cells: Stem cell therapy may benefit Parkinson's Disease by replacing and repairing damaged dopamine-producing nerve cells within the brain. One study published in the journal "Stem Cells Translational Medicine" in 2016 reported the results of phase I clinical trial in which MSCs derived from bone marrow were transplanted into the brains of 12 patients with Parkinson's disease[32]

Mesenchymal Stem Cell Therapies for Neurodegenerative Diseases: First, MSCs were proven to secrete neurotrophic boom elements, which include glial cell-derived neurotrophic factor (GDNF), vascular endothelial boom factor, and brain-derived neurotrophic factor (BDNF),which may be similarly better below unique tradition conditions. Neurotrophic boom elements were proven to enhance neuronal survival in some of preclinical fashions of neuron harm, which include ALS, PD, and MSA transgenic animals and nerve harm fashions.[33]

Second, MSCs strongly modulate the immune gadget and might useful resource wound healing, and this mechanism has been exploited in problems consisting of graft as opposed to host ailment and Crohn's ailment. From a neurodegenerative perspective, it has turn out to be an increasing number of identified that neuroinflammation performs a giant pathomechanistic role."[33]

Treatment of Parkinson disease : Stem cell therapy is a enormously new and experimental remedy technique for Parkinson's ailment, and it differs from conventional remedy alternatives in numerous ways:[34]

Medications: Stem cell therapy goals to update or restore misplaced or broken dopamine-generating cells withinside the mind, while conventional drug treatments for Parkinson's, together with Levodopa remedy

and dopamine agonists, purpose to boom dopamine degrees withinside the mind or mimic the consequences of dopamine.

Surgery: Stem cell therapy includes transplanting stem cells into the body, while conventional surgical operation for Parkinson's ailment, together with deep mind stimulation , includes the implantation of electrodes into the mind to supply electric impulses to particular regions of the mind which can be stricken by the ailment.

Rehabilitation remedy: Traditional rehabilitation treatment options together with speech, occupational, and bodily remedy can increase stem cell therapy consequences. Studies have proven that an lively way of life and rehab can enhance stem cell therapy outcomes.

Effectiveness: The effectiveness of stem cell therapy for Parkinson's ailment remains being studied, and greater studies is wanted to verify the outcomes of preclinical and medical studies, while conventional remedy alternatives for Parkinson's ailment were used for plenty years, and their effectiveness is nicely established.

Risks: Stem cell therapy is considered safe when proper procedures are followed; however, it's still regarded as experimental and more research is needed to determine this treatment's long-term effectiveness. Traditional treatment options for Parkinson's disease may have potential risks, but these risks have been sufficiently studied.

Conclusion

New additions to pharmaceutical medications are stem cell drugs. They are generated from stem cells. More than ten stem cell medications have adapted from 2012 to the present have received regulatory clearance in several nations for medical uses. These products might have mesenchymal stem cells or live hematopoietic stem cells. A developing body of evidence points strongly to these secreted molecules coordinate several protective mechanisms, including cell survival remodeling, proliferation, and neoovascularization. Although stem cell therapy is still in the early stages of study and has not been shown to be a definitive treatment for either condition, it offers hope for both diabetes and Parkinson's disease. Stem cell therapy seeks to replace destroyed insulin-producing cells for diabetes; for Parkinson's, stem cell-based treatments have advanced greatly in recent years, with encouraging outcomes from early clinical studies and preclinical research. Parkinson disease seeks to replace dying dopamine-producing neurons. Although hopeful, more studies and clinical trials are needed to completely evaluate the long-term advantages and hazards as well as maximize the efficacy of these treatments

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