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Stem Cell Therapy On Diabetis Mellitus

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Abstract

Diabetes mellitus, which is a widespread health issue, poses a serious threat to public health. Stem cell therapy, known for its ability to regenerate tissues, has become a hopeful option for managing diabetes. This paper looks at the latest developments, future possibilities, and difficulties in using stem cells to treat diabetes. It focuses on the use of induced pluripotent stem cells and mesenchymal stem cells, the creation of pancreatic islet organoids, and the possibility of personalized medicine. The review also evaluates the effectiveness and safety of stem cell treatments based on clinical trials and explores their use in both type 1 and type 2 diabetes. Although there is a lot of promise, there are still challenges like safety issues, the efficiency of transplantation, ethical questions, and the risk of immune rejection. Finally, the paper talks about future steps, such as combining stem cell therapy with other treatments and moving toward more personalized medicine, which off new hope for managing diabetes

Key words: Diabetes mellitus ,Stem cell therapy, Induced pluripotent stem cells (iPSCs),Embryonic stem cells, (ESCs).

Introduction

Diabetes is a long-term health condition that occurs when the body is unable to properly manage blood sugar levels. Blood sugar, also known as glucose, is the primary energy source for the body's cells. Insulin, a hormone produced by the pancreas, helps transport glucose from the bloodstream into the cells so it can be used for energy. If the body doesn't produce enough insulin or can't use it effectively, glucose remains in the bloodstream, leading to high blood sugar levels.Over time, consistently high blood sugar can result in significant health complications affecting the heart, kidneys, eyes, nerves, and other organs.

There are three main types of diabetes:

Type 1 : Diabetes occurs when the body's immune system mistakenly targets and destroys the insulin-producing cells in the pancreas.

This type usually develops during childhood or young adulthood.

Type 2 :Diabetes happens when the body becomes resistant to insulin or doesn't produce enough of it. It is the most common form of diabetes and is often linked to lifestyle factors such as being overweight and a lack of physical activity.

Stem cells have the ability to become any type of tissue in the human body, making them very useful for future treatments that can help repair or replace damaged tissues. For a cell to be considered a stem cell, it needs to have two main traits. The first is the ability to divide and make new cells that are exactly like the original cell. This is similar to how cancer cells work, but stem cells divide in a controlled and regulated way. The second important trait is that stem cells must be able to develop into a specific type of cell that helps the body function properly.

The term "stem cell" Includes many different types of cells. Usually, they are referred to as embryonic or adult stem cells, depending on when they develop in an animal's life. However, as research has grown, these terms are no longer sufficient. Scientists have found a way to change fully mature adult cells back into embryonic stem cells. Adult stem cells are also sometimes called somatic stem cells.

Stem cell therapy is a promising new treatment for diabetes, especially Type 1 diabetes, where the body's immune system attacks the cells that make insulin in the pancreas.

Stem cells are special because they can turn into many different types of cells in the body. Researchers are looking into how stem cells can be used to replace the damaged or destroyed insulin-producing cells in the pancreas. This treatment aims to not only manage diabetes but also potentially cure it by helping the body make insulin naturally again. Although it is still being studied and tested in clinical trials, stem cell therapy offers new hope for people around the world who have diabetes.Stem cell therapy is a very hopeful new approach for treating sever daibetes. However, there are still many unanswered questions about the type of stem cells used, how the treatment is carried out, and how well the body recovers over time. Many studies done on animals have shown that stem cells might be a good option for treating diabetes. However, because the treatment is complicated and there are ethical and practical issues to consider, only a small number of these approaches have moved on to testing in humans. This review and analysis of existing studies aims to closely examine the safety and effectiveness of different stem cell treatments for both Type 1 and Type 2 diabetes. Safety is defined as having no harmful side effects, while effectiveness is measured by a clear improvement in the body's ability to produce insulin. This study could help guide future research and provide doctors and patients with useful information about the results of stem cell therapy for diabetes.

Pathophysiology Of Diabetes

DM has a complex development process and presents various symptoms, so any way of classifying this condition is somewhat arbitrary, but still helpful. The classification can vary depending on the body's condition when the disease is diagnosed. The current system groups diabetes based on both its cause and how it develops. This helps doctors understand the disease better and choose the best treatment. Under this system, diabetes is divided into four main types: type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), gestational diabetes mellitus (GDM), and diabetes associated with specific conditions, diseases, or disorders.

Type 1 diabetes (T1D) is an autoimmune condition where genetic and environmental factors work together to cause lymphocytes to attack the pancreatic islets, which leads to the destruction of beta cells that make insulin.As a result, people with T1D need insulin injections for the rest of their lives. It is fairly common, affecting about 1 in every 300 people, and its occurrence is increasing globally at a rate of 3% each year. However, the exact ways in which genes and the environment interact to trigger the disease are still not fully understood. Managing T1D can be challenging for patients, their families, and caregivers. Since there are not enough pediatric endocrinologists available, general pediatricians and other specialists

sometimes have to handle diabetes-related issues. In this review, we cover the progression of the disease, how it affects the body, and current approaches to managing it. We also look at the latest developments in T1D research.

Type 2 diabetes develops when the body does not produce enough insulin to maintain normal blood glucose levels and is unable to use insulin effectively. It mainly involves two issues: insulin resistance and beta-cell malfunction.In detail: The development of insulin resistance occurs when the body's cells stop responding properly to insulin, especially muscle, liver, and fat cells.

This means the cells cannot easily absorb glucose for energy. As a result, blood glucose levels rise.

To counteract this, the pancreas produces more insulin.

Initially, this helps maintain normal blood sugar levels. However, the pancreatic beta cells, which produce insulin, eventually become worn out and cannot produce enough of the hormone. This leads to insulin insufficiency.

Concept of stem cell therapy

Stem cells have two main features that make them special. First, they can make more of themselves, which means they can renew or replace themselves. Second, they can change into different types of cells with specific jobs. Almost every part of the body has stem cells, and they help keep tissues working and repair them when they get hurt. Depending on where they are, stem cells can turn into many types of tissues, such as blood, heart, brain, muscle, bone, and others.

There are different kinds of stem cells.Embryonic stem cells are the most versatile because they can become any cell in a developing baby. Most stem cells in our bodies are more limited and mainly help in keeping their own tissue and organs healthy. Embryonic stem cells come from embryos that are about three to five days old.

These embryos are called blastocysts, and they have around 150 cells. These cells are pluripotent, meaning they can either make more stem cells or become any cell in the body. Because of this, they can be used to repair or replace damaged tissues and organs.

Adult stem cells are found in many parts of the body, like fat and bone marrow.

They are not as flexible as embryonic stem cells when it comes to turning into other cell types. But scientists have found a way to change ordinary adult cells into stem cells using genetic reprogramming. This process turns adult cells into cells that act like embryonic stem cells, and they are called induced pluripotent stem cells (iPSCs). This method could help avoid the immune system rejecting the cells, which is a problem with using embryonic stem cells. However, scientists are still unsure if using these modified cells could cause any harmful effects. In some cases, they have turned regular connective tissue cells into heart cells, and animals with heart failure that received these cells showed better heart function and longer lives.

Researchers have also found stem cells in umbilical cord blood and amniotic fluid Amniotic fluid is the liquid that surrounds a developing baby inside the womb. Scientists have discovered stem cells in samples of this fluid, which can be collected through a process called amniocentesis for testing or treatment purposes. These stem cells can also become specialized cells.

Types of stem cell used in diabetes

1.Induced pluripotent Stem cell

2.Mesenchymal stem cell

3.Embryonic stem cell

1.Induced pluripotent Stem cell: One intriguing strategy being investigated for the treatment of diabetes mellitus, particularly type 1 diabetes, is induced pluripotent stem cell (iPSC) therapy. This treatment uses particular genetic elements to transform adult cells (such as skin or blood cells) into iPSCs, which are then differentiated into insulin-producing pancreatic β-cells. Patients with diabetes can get transplants of these lab-generated β-cells to manage blood glucose levels and restore endogenous insulin production.

Therapy Mechanism: iPSCs offer an infinite supply of patient-specific β-cells, which lowers the chance of immunological rejection. Transplanting iPSC-derived β-like cells has been shown to enhance insulin levels considerably and stabilize blood glucose levels for months in animal studies. Long-term benefits are suggested by the procedure's ability to preserve normoglycemia.

Reprogramming adult somatic cells, such as skin or blood cells, into pluripotent stem cells that can develop into insulin-producing pancreatic β-like cells is the therapeutic mechanism of induced pluripotent stem cell (iPSC) therapy for diabetes. After being transplanted, usually into the liver, these β-like cells engraft, survive, and work to restore endogenous insulin production, returning blood glucose levels to normal in diabetic mice.

iPSCs differentiate into glucose-responsive, functional β-like cells that can secrete insulin in response to variations in blood glucose levels. stable distribution and engraftment of these cells in the transplantation site (liver parenchyma, for example), guaranteeing prolonged insulin production. reduction of the likelihood of graft rejection, particularly when iPSCs are produced from closely matched donors or patient-specific cells, promoting immunological tolerance. Significant increases in circulating insulin and sustained normoglycemia have been shown in animal models, suggesting the possibility of long-term treatment of hyperglycemia.

Applications of iPSCs in producing different cell types for diabetes problems and enabling genome editing to enhance β-cell survival and function provide additional therapeutic benefits. Additionally, this method offers an in vitro platform for diabetes-related medication development and disease modeling. As a promising regenerative medicine approach for the treatment of diabetes, iPSC therapy works mainly by producing patient-specific insulin-producing β-cells that restore insulin secretion and glucose regulation. These cells are supported by their ability to engraft steadily and with minimal immune rejection.

Advantages and Challenges: Gene correction and cell customization for each patient are made possible by this method, which enables individualized therapy. It directs the development of precision drugs and provides insights into the pathophysiology of diabetes. Before it may become a common therapeutic therapy, there are still obstacles to overcome, such as maximizing cell differentiation yield, guaranteeing long-term safety, resolving immunogenicity, and standardizing production procedures. In conclusion, iPSC therapy for diabetes is a novel sector that has the promise to provide long-term cell replacement for insulin independence. However, clinical translation is still in progress as researchers work to overcome significant safety and technical challenges.

2. Mesenchymal Stem cell: Recent clinical trials have demonstrated the safety and prospective efficacy of mesenchymal stem cell (MSC) therapy, a novel approach to the treatment of diabetes. MSCs are adult stem cells with potent regenerative, immunomodulatory, and anti-inflammatory qualities that aid in the regeneration of insulin-producing β-cells and repair injured pancreatic islets. These cells can improve the structure and function of pancreatic islets, move to injured regions, maintain the survival of β-cells, and modulate immunological responses related to diabetes.

Therapeutic Effects: Glycemic management has improved with MSC therapy; HbA1c and fasting blood glucose levels have significantly decreased, and some patients have shown increased endogenous insulin production. Additionally, the treatment can improve insulin resistance and reduce the need for anti-diabetic medications. Numerous clinical investigations have shown no major adverse effects, indicating a good safety profile.

Mesenchymal stem cell (MSC) therapy for diabetes has several key benefits. It helps control blood sugar levels by significantly lowering HbA1c levels by around 32% and fasting blood glucose by about 45%. Many patients need less insulin, and some are able to stop using it altogether. MSCs support the function of pancreatic beta cells and boost the body's own insulin production, which is shown by improved C-peptide levels. These cells also help repair and regenerate damaged islet cells, regulate autoimmune responses that attack beta cells, especially in type 1 diabetes, and reduce insulin resistance through their anti-inflammatory and immune-modulating effects. Moreover, MSC therapy may help prevent or reduce diabetes-related complications like kidney disease, nerve damage, and eye problems. Overall, MSC treatment is generally well-tolerated and has few side effects, making it a promising option for both type 1 and type 2 diabetes.

Potential and Challenges: There are several sources of MSCs being studied, including human umbilical cord and adipose tissue, each of which has unique benefits in terms of cell yield and therapeutic potential. Clinical results are encouraging, but more extensive research is needed to maximize MSC homing, post-transplant survival, and efficacy, as well as to standardize procedures and elucidate long-term advantages and hazards. In conclusion, MSC treatment is a novel and potentially successful approach for improving metabolic outcomes and restoring insulin production in patients with type 1 and type 2 diabetes. Current research is concentrated on optimizing safety and clinical benefit.

3: Embryonic stem cell: Embryonic stem cell therapy for diabetes involves using pluripotent stem cells taken from early embryos. These cells can develop into insulin-producing cells in the pancreas, known as beta cells. In diabetes, these cells are either lost or not working properly, so replacing them with healthy ones can help the body regulate blood sugar levels. The stem cells have the ability to create many functioning beta cells that can make insulin when blood glucose levels rise, which helps bring blood sugar back to a normal range. Using pluripotent stem cells from early embryos that can develop into insulin-producing pancreatic β-cells to replace those lost or malfunctioning in diabetes is the main goal of embryonic stem cell (ESC) treatment. In order to restore glycemic control, ESCs can produce a significant number of functioning β-cells that can produce insulin in response to blood glucose.

Therapy Mechanism: In the lab, ESCs go through certain steps to turn into mature beta cells that act like the ones in the pancreas. When these cells are placed into the body, they can settle in and produce insulin, which can lower or even stop the need for insulin injections. In addition to replacing damaged cells, this therapy might also help the immune system and support the growth of blood vessels in the pancreas.

Embryonic stem cell therapy for diabetes seeks to restore or replenish damaged or non-functional insulin-producing β-cells by guiding embryonic stem cells to develop into fully mature, glucose-sensitive β-cells ,which are then transplanted into patients. This approach mimics the natural function of islets: the transplanted cells detect blood glucose levels and release insulin, aiding in the regulation of blood sugar, and may ultimately reduce or eliminate the requirement for external insulin administration.

Differentiation into β-like cells: In vitro, embryonic stem cells are guided through developmental stages to become cells that resemble pancreatic β-cells and can produce insulin in response to glucose. Engraftment and function: Transplanted β-like cells (often into sites like the liver via the portal vein) aim to integrate with the host vasculature and secrete insulin in a regulated manner to restore endogenous insulin production.

Immune considerations: Immune rejection and the requirement for immunomodulation or encapsulation techniques, such as immunosuppression or the use of histocompatible/donated cells in controlled environments, are major obstacles with allogeneic stem cell therapy. Safety issues: Potential hazards include the development of tumors (such as teratomas) if undifferentiated cells continue to exist, which calls for thorough purification and quality assurance prior to clinical application.

Current status and challenges: Evidence base: Although findings vary and bigger, carefully monitored trials are required to establish consistent efficacy and long-term safety, early-stage and small-scale studies report improvements in glycemic control and decreased insulin requirements in some patients. Ethical and regulatory considerations: Advances in gene-editing techniques and alternative pluripotent sources, such as induced pluripotent stem cells, are adding to the ongoing controversies around embryonic sources. Practical challenges: Ensuring permanent engraftment, minimizing immune rejection, reducing teratoma dangers, and scaling the generation of fully differentiated, functionally stable β-cells continue to be top research goals.

By creating β-like cells from embryonic pluripotent cells and transplanting them to restore endogenous insulin secretion, embryonic stem cell therapy for diabetes aims to regenerate insulin-producing capacity. However, clinical adoption requires strong evidence of safety, efficacy, and ethical/regulatory alignment.

Other Stem cells:

1. Pancreatic stem cell

2.Umbilical cord blood Stem cell

3.Thymic regulatory T cell

1.Pancreatic stem cell: Pancreatic stem cells are specialized progenitor cells present in or derived from the pancreas that have the potential to differentiate into various pancreatic cell types, including insulin-producing β-cells. They are considered an important resource for diabetes treatment because they can support regeneration of damaged or lost β-cells, restoring endogenous insulin secretion and improving glycemic control. These stem/progenitor cells are often located near pancreatic ducts and can give rise to new islets through a process called islet neogenesis. Besides ductal stem cells, acinar cells may also transdifferentiate into insulin-producing cells under certain conditions. Recent research has focused on improving efficiency and safety in generating pancreatic progenitor cells from pluripotent stem cells or directly from patient tissues to overcome limitations of donor islet availability and immune compatibility. These approaches aim to create patient-specific or immunologically compatible pancreatic β-cells for transplantation, potentially reducing or eliminating the need for lifelong insulin injections and immunosuppression. In summary, pancreatic stem cells represent a critical natural or engineered source capable of regenerating insulin-producing cells for diabetes therapy, with ongoing research striving to enhance their therapeutic potential and clinical applicability.

2.umbilical cord blood Stem cell: Umbilical cord blood stem cell therapy for diabetes mainly uses mesenchymal stem cells (MSCs) taken from umbilical cord blood. These cells have shown great promise in helping control blood sugar levels and repair the pancreas. They also have a special ability to reduce the body's immune response, which is helpful in type 1 diabetes. Additionally, these stem cells can turn into insulin-producing cells, which helps the body make its own insulin again.

In treatment, giving these MSCs through an infusion has led to better results in people with type 2 diabetes, like lower HbA1c levels and more time spent in a healthy glucose range.

Some studies with type 1 diabetes patients also found that they needed less insulin and had a better quality of life.

One of the big advantages of using umbilical cord blood cells is that they carry a low risk of causing rejection in the body, are not likely to form tumors, and don’t need much immunosuppression, which makes them a safe option for treatment.

They might also help in treating complications of diabetes, such as nerve and kidney damage.

Overall, umbilical cord blood stem cell therapy is a promising and safe way to treat diabetes by using the MSCs’ ability to change into different cell types, control the immune system, and repair damaged tissues.

However, more large-scale studies are needed to create standard treatment plans and prove long-term effectiveness

3.thymic regulatory T cell: An developing immunotherapeutic strategy for diabetes, namely type 1 diabetes (T1D), is thymic regulatory T cell (Treg) therapy, which attempts to block the autoimmune destruction of pancreatic insulin-producing beta cells and restore immunological tolerance. According to research, T1D is caused by a breakdown in immunological tolerance in which autoreactive T cells target beta cells. This process is facilitated by reduced Treg activity.

In T1D, tregs are essential for preserving immunological tolerance and averting autoimmune reactions. Reduced or dysfunctional Tregs contribute to the pathogenesis of the disease. Dendritic cells can be conditioned to support the differentiation and growth of functional Tregs by thymic stromal lymphopoietin (TSLP), a substance generated from the thymus. By restoring immunological tolerance, TSLP therapy or TSLP-conditioned dendritic cell transplantation prevented the development of diabetes in non-obese diabetic (NOD) animal models. To improve Treg survival and function in T1D patients, clinical trials are testing ex vivo growth and reinfusion of autologous polyclonal Tregs in conjunction with low-dose interleukin-2 (IL-2). The goal of this combination is to specifically increase Tregs in order to inhibit autoreactive T cells and maintain beta cell activity.

Genetic engineering techniques to increase therapeutic specificity and efficacy include CAR Tregs (chimeric antigen receptor Tregs) that are specific for beta cell antigens. Although maintaining Treg stability, antigen specificity, and optimum trafficking to the pancreas are still difficult to achieve, thymic Treg medications offer a promising immunomodulatory approach to stop or slow the course of T1D by reestablishing immunological tolerance and homeostasis.

Thymic Treg therapy for diabetes aims to use and rebuild the body's own ability to control the immune system, which helps stop the immune system from attacking the cells that make insulin. Methods include using substances related to the thymus, like TSLP, growing large numbers of Tregs in the lab with IL-2, and improving Tregs through advanced techniques. All these approaches try to balance the immune system to keep the pancreas working and help people with type 1 diabetes feel better.

Method of stem cell delivery

1.Systemic (Intravenous) Delivery:

Description: Stem cells are given through a vein, letting them travel through the blood.

Advantages: It's a straightforward and gentle method.

Limitations: Only a few cells make it to the intended area; most get caught in organs like the lungs or liver.

Used in: Situations where tissue damage or inflammation affects a wide area, such as diabetes or autoimmune diseases.

2. Local (Direct) Injection:

Description: Stem cells are put directly into the affected tissue or organ.

Advantages: More cells reach the exact spot they're needed.

Limitations: Needs accurate placement and may involve surgery.

Used in: Cases of localized injury, like delivering stem cells to the pancreas for diabetes or to the heart after a heart attack.

3.Intra-arterial Delivery:

Description: Stem cells are put directly into an artery that supplies the target organ.

Advantages: More cells reach the right place efficiently.

Limitations: There's a risk of blood clots or blocking blood vessels.

Used in: Treating neurological and heart-related conditions.

4.Intraperitoneal Delivery:

Description: Cells are injected into the abdominal cavity.

Advantages: Easy to do and covers a large area for absorption.

Limitations: Not very targeted; cells might not reach the exact tissue needed.

Used in: Research studies and models for diseases that affect the whole body.

5.Scaffold-Based Delivery:

Description: Stem cells are placed on special materials like scaffolds or hydrogels before being placed into the body.

Advantages: The material helps support the cells and helps them grow and connect better.

Limitations: The process is more complicated and costly.

Used in: Building tissues and using regenerative medicine.

6.Encapsulation Techniques:

Description: Stem cells are put inside special materials that let nutrients pass through but keep them safe from the immune system.

Advantages: The cells can get nutrients while staying protected from the body's defenses.

Used in: Treating diabetes by using encapsulated pancreatic cells.

Preclinical and clinical studies

Types of Stem Cells Used in Preclinical studies

1. Embryonic stem cell: developed into pancreatic β-like cells, which react to glucose by producing insulin.

2. Induced pluripotent Stem cell: Reprogrammed from adult cells to lower the danger of immunological rejection and ethical concerns.

3. Mesenchymal stem cell: Located in adipose tissue, bone marrow, and the umbilical cord, it protects the remaining β-cells and reduces inflammation.

4. Hematopoietic and pancreatic progenitor cell: help the pancreatic tissue to regenerate.

Animal model used

1.Streptozotocine induced diabetes rats mice:

Type: Model generated by chemicals.

How it works: High blood glucose and insulin insufficiency result from the selective destruction of pancreatic β-cells by streptozotocin (STZ).

For: Research on type 1 diabetes.

The goal is to determine whether transplanted stem cells can normalize glucose levels and restore insulin secretion. For instance, transplanting ESC or iPSC-derived β-like cells into STZ-diabetic mice can reduce blood glucose levels.

2.Alloxan – Induced diabetes model:

Type: Model induced by chemicals.

How it works: Alloxan causes oxidative stress to β-cells, which results in insulin insufficiency.

Used for: Early-stage drug or cell testing and type 1 diabetes.

Benefit: Easy and economical. Limitation: Glucose levels may vary; less stable than the STZ model.

3.Non obese diabetes mouse:

Type: Autoimmune/genetic model.

How it works: Similar to human Type 1 diabetes, these mice acquire autoimmune destruction of β-cells on their own.

Used for: Assessing the immunomodulatory properties of MSCs and other stem cells. For instance, in NOD mice, MSCs protect β-cells and lessen immunological assault.

4.High fat diet mice:

Type: Type 2 diabetes model induced by diet.

How it operates Animals that are fed a high-fat diet develop moderate hyperglycemia, insulin resistance, and obesity.

Used for: Assessing the combined impact of metabolic control and stem cells. For instance, in HFD-fed mice, MSCs enhance insulin sensitivity and lower inflammation.

5.Large animal model (pig ,fog ,non – human primates):

Use: Prior to human trials, large-scale transplanting and safety are tested following rodent studies.

Benefits: Human-like physiology. For instance, functional insulin production is demonstrated when human iPSC-derived pancreatic cells are transplanted into diabetic pigs.

Clinical studies

In preclinical animal trials, stem cell therapy has demonstrated encouraging outcomes for the treatment of diabetes. Numerous clinical trials have been carried out globally to verify its efficacy and safety in humans. Restoring insulin-producing β-cells, enhancing glucose regulation, and lowering the need for insulin injections in diabetic patients are the goals of these investigations.

Types of Stem Cells Used in Clinical Studies.

1.Mesenchymal Stem Cells (MSCs): derived from adipose tissue, bone marrow, or the umbilical cord. possess immune-modulating and anti-inflammatory properties. enhance insulin sensitivity and safeguard current β-cells.

2.Embryonic Stem Cells (ESCs): differentiated into β-like cells that produce insulin. used in Type 1 Diabetes early human trials.

3.Induced Pluripotent Stem Cells (iPSCs): β-cells are created by reprogramming adult somatic cells. Minimize immunological rejection risk and ethical dilemmas.

4.Hematopoietic Stem Cells (HSCs): used in certain research to prevent autoimmune destruction in Type 1 Diabetes and reset the immune system.

Challenges and Limitations of Stem Cell Therapy

Challenges of stem cell:

1. Differentiating stem cells into fully functional β-cells that produce insulin is difficult.
2. Restricted engraftment and survival of transplanted pancreatic cells.
3. Immune rejection of β-cells or transplanted stem cells.
4. Risk of developing a teratoma or tumor following transplantation.
5. Sustaining long-term glycemic control and insulin secretion.
6. Absence of consistent sources and procedures for stem cells.

7. The use of embryonic stem cells raises ethical concerns.
8. Stem cell isolation, culture, and transplantation are expensive.
9. Targeted delivery of stem cells to pancreatic tissue is challenging.
10. Differences in the quality of stem cells from various sources or donors.
11. Difficulties in producing clinical-grade stem cells on a big scale.
12. Uneven outcomes due to unpredictable differentiation efficiency.
13. Monitoring transplanted cells within the body is challenging.
14. Some people require immunosuppressive medication for the rest of their lives.
15. Little knowledge of the precise regenerating processes.
16. Clinical application approval and regulatory obstacles.
17. Replicating the milieu necessary for β-cell development is challenging.
18. Even using autologous stem cells may result in immunological sensitization.
19. Insufficient infrastructure and skilled personnel for stem cell therapy.
20. Research and acceptance are impacted by ethical and public issues.

Limitations of stem cell:

- Pancreatic islet cells do not fully regenerate
- B-cells produced from transplanted stem cells have a short lifespan.
- Some patients receiving treatment have insufficient insulin production.
- High relapse rate, necessitating further therapies.
- Absence of long-term safety information from human experiments.
- Long-term impacts on organ systems and metabolism are unclear.
- Inconsistent treatment results among patients.
- Restricted accessibility because to the high expense of treatment.
- Risk of inflammation or infection after transplantation.
- Immunosuppression is required, which raises the possibility of problems.
- Animal models are insufficient to accurately forecast human behavior.
- Low effectiveness in the processes of cell maturation and differentiation.
- Legal and ethical limitations on specific sources of stem cells.
- Transitioning from research to clinical use is slow.
- Regulating differentiation to prevent undesirable cell types is difficult.
- The function of transplanted cells is limited by poor vascularization.
- Possible genetic instability in stem cells grown in culture.
- Integration with the host tissue is uncertain.
- Limited ability to replicate experimental findings across labs.
- Global regulatory agreement on stem cell-based treatments is lacking.

Role of pharmacist in stem cell therapy

1.Research and Development: Pharmacists take engage in preclinical and clinical stem cell research, especially when it comes to improving stem cell formulations, storage conditions, and delivery techniques (such as injectable stem cell suspensions or encapsulated beta cells).

2.Quality Control and Good Manufacturing Practices (GMP): Pharmacists make sure that stem cell preparations adhere to legal requirements for quality, purity, and safety. They support adherence to the principles of Good Manufacturing Practice (GMP) and Good Laboratory Practice (GLP).

3.Regulatory and Ethical Oversight: Pharmacists help ensure safety and transparency in research and clinical usage by supporting documentation, protocol submission, and adherence to ethical and regulatory frameworks for stem cell-based therapies.

4.Clinical Role and Patient Care: Pharmacists and doctors work together in clinical settings to manage patients receiving stem cell therapy, making sure that the right dosage is administered and that any side effects or drug-cell interactions are monitored.

5.Pharmacovigilance and Safety Monitoring: Pharmacists contribute to long-term safety data and therapeutic optimization by tracking and reporting any adverse effects or immunological reactions following treatment.

6.Education and Counseling: Pharmacists help patients make educated decisions and follow treatment regimens by educating them about the possible advantages, dangers, and reasonable expectations of stem cell therapy for diabetes.

7.Future Role in Personalized Medicine: Pharmacists are anticipated to be more involved in personalized therapy, such as stem cell-derived insulin-producing cells customized for each patient, as regenerative medicine improves.

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