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Review Article

Stem Cells a better way for Treatment: Diabetes

Mamta Kumari[1*], Parmanand Pandey[2], Anupam Kr Sachan[1]

[1]Dayanand Dinanath College, Institute of Pharmacy, Kanpur Nagar-209214

[2]Nector Life Sciences, Jharmajari, Baddi-173205 Himanchal Pradesh

A B S T R A C T

Insulin-producing cells derived from the stem cell embryonic stem cell and pluripotent stem cell have been long duration to encourage, but evasive treatment far from clinical interpret into type1 diabetes therapy. Although stem cell therapies provide a great opportune time there is also conceivable risk such as teratoma formation to relate with the treatment. Mesenchyme stem stromal cells have due to their modulator effects on immunity, inflammation, and tissue repair been suggested to be used to either halt beta-cell loss during T1D development or be used to protect and support pancreatic islets when transplanted. This review aims to give an overview of the current knowledge of stem cell therapy outcomes in animal models of type-1diabetes and a proposed road map towards the clinical setting with a special focus on the potential risks and hurdles which need to be considered. From a clinical point of view, transplantation of insulin-producing cells derived from stem cells must be performed without immune suppression to be an attractive treatment option.

Keywords: Stem cell, Cell therapy, Diabetes, Insulin

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***Address for Correspondence:**

Mamta Kumari, Dayanand Dinanath College, Institute of Pharmacy, Kanpur Nagar-209214

INTRODUCTION

Diabetes Mellitus

Diabetes mellitus is characterized by chronic hyperglycemias with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both [1, 2]. Diabetes mellitus is a metabolic complication. There is an increase in the prevalence of type 1diabetes also, but the main cause of the diabetic epidemic is type2 diabetes mellitus, which accounts for more than 90 percent of all diabetes cases 1. According to the World Health Organization WHO reports, India had 32 million diabetic people in the year [3].

It is disturbed the homeostasis level of the body function and lifestyle changes. This disease is characterized by hyperglycemias due to autoimmune destruction of β-cells in the pancreas and insulin resistance, usually due to obesity, with decreased pancreatic insulin production and B-cell failure type metabolic disturbances associated with diabetes. Type of diabetes Figure show in-flowchart [4].

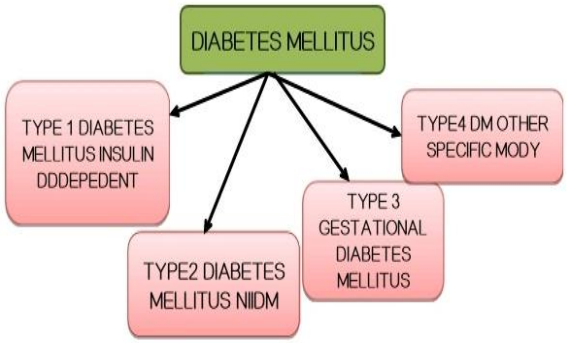


Figure:1

Type of Diabetes Mellitus

Type 1 DM

Insulin-dependent and also known as " Juvenile diabetes " Type 1 diabetes develops when the body's immune system destroys pancreatic beta cells, the only cells in the body that make the hormone insulin that regulates blood glucose, the result of the pancreas failure and to give enough insulin[5].

Type-2 DM

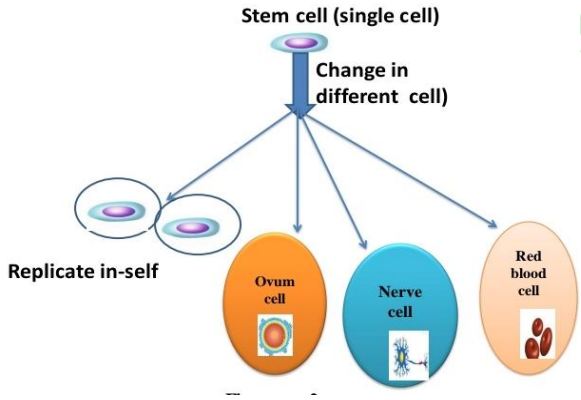
Non –Insulin-dependent diabetes mellitus and also called the adult-onset type of diabetes. It starts with insulin resistance, a situation in Beta-cells of failing to respond to insulin properly finally give the result of Symptoms of excessive body weight and not doing enough exercise[6].

Type-3 Gestational Diabetes

Gestational diabetes mellitus is defined as the occurs of during pregnancy. Pregnant women without a previous history of diabetes develop high blood sugar level. Gestational diabetes mellitus is a common metabolic problem, considered an important issue [7].

The stem cell of the therapeutic role in type 1 diabetes mellitus.

The stem cell is defined as the completely bone marrow to store the blood cell after bone marrow ability of the might of improving the stem cell patient. Stem therapy of this behind of restore the aberrant immune system of the destroying this process is auto reactive T- cell and the replacing with auto reactive[8]. Stem cells are clonogenic cells that have two remarkable features, the ability to differentiate into multiple mature cell type's multipotency and to simultaneously replenish the stem cell pool self-renewal that allows them to sustain tissue development and maintenance[21, 25].



The term Mesenchyme cell gained acceptance to refer to these newly identified precursor cells. Multipotent of the Mesenchyme cell isolation and expansion the in vitro the Mesenchyme stem cell, that is Mesenchyme stem cell is hierarchy progress through the differential manner give rise to the phenotypic ally and bone marrow organ tissue plan[27,31].

Stem cells can differentiate into many cells

- ***Adult Stem Cell***- Stem cells obtained from the organ tissue of an organism after birth in contrast to fetal stem cells.
- ***Embryonic Stem Cell***- It is obtained by the inner ell mass up to the first step of blastocyst. But have the importance of differentiating into any cell of the body.
- ***Fetal Stem Cell***-A stem cell-derived from fetal tissue, including the placenta.
- ***In Vitro and In Vivo***- it is obtained externally and internally in the body laboratory method.
- ***Mesenchyme Stem Cells***-Stem cells present in the human bone marrow and umbilical cord that it is present in the human bone marrow and umbilical cord.
- ***Multipotent stem cells***-Blood forming hematopoietic stem cells are single multipotent cells that can produce all cell types that are normal components of the blood.
- ***Oligopotent***-Stem cells differentiate into a few cells such as lymphoid stem cells.
- ***Pluripotent*** -it is the ability to the stimulant of different types of cells that generate from the germ layers endoderm and ectoderm but cannot developed the embryonic on its own.
- ***Somatic stem cell***- an undifferentiated cell found among differentiated cells in a tissue or organ, which can renew itself and can differentiate to yield the major specialized cell types of the tissue or organ.
- ***Totipotent***- Capable of giving rise to all tissues and organs, including the placenta.
- ***Unipotent***- cells can produce only one cell type, their own, but have the property of self-renewal. They have the lowest differentiation potential.

Mesenchyme stem cell for pancreatic beta-cell

Pluripotent cells can be induced to undergo specific stages of differentiation by exposure to defined combinations of growth factors and small molecules to activate and inhibit signaling pathways to mimic normal human pancreatic development. TD1 being an autoimmune disorder often demands the transplantation of the damaged islet cells, which brings with it the risk of graft rejection. Mesenchyme Stem Cells MSCs exert natural immunosuppressive and protective effects through cell-cell contacts and by secreting soluble factors. Mesenchyme stem stromal cells have due to their modulators effects on immunity, inflammation, and tissue repair been suggested to be used to either halt beta-cell loss during T1D development or be used to protect and support pancreatic islets when transplanted[28].

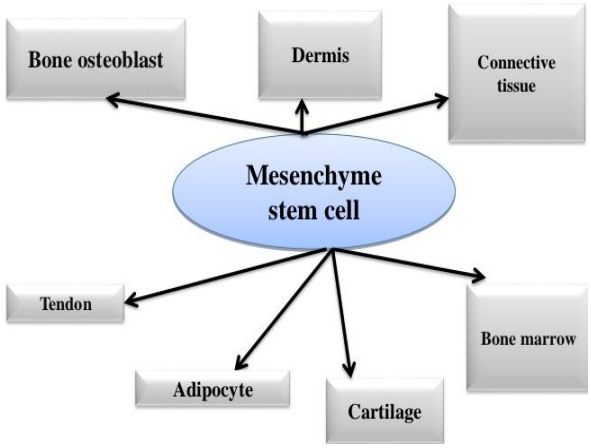


Figure no. 3

Fig.3 Mesenchyme stem cell phenotypes. Mesenchyme stem cells are theoretically capable of differentiating through a series of separate and unique lineage transitions into a variety of end-stage phenotypes as shown.

The function of MSC how to producing the insulin-producing cell

MSCs can differentiate into functional IPCs Insulin Producing Cells in vitro when cultured under specific conditions. Intra-peritoneal injections of IPCs derived from the differentiation of MSCs exhibit better control of T1D than that exhibited by undifferentiated MSCs.[38]

Firstly embryonic stem cell has the limb which gives stimulates the cartilage and bone marrow in vivo can be manoeuvre in the vitro. The second thing the cells have a linear improvement of abstracted, single steps whether it be the chondrogenic pathway [9].

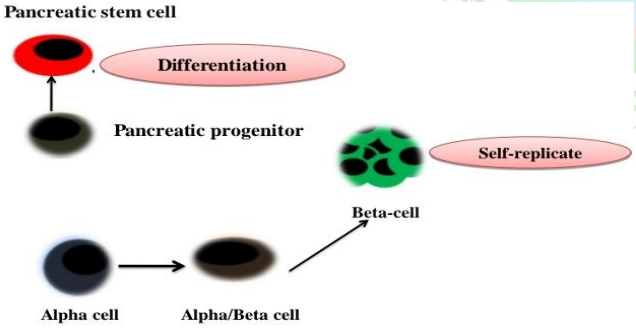


Figure: 4

The Mesenchyme stem cell is derived from adipose tissue. The MSc cell that is generating a new cell that is multipotent. It is also derived from the original embryonic stem cell. MSc has maintained the Skelton muscle tissue that is homeostasis of maintained[30].

The term Mesenchyme cell gained acceptance to refer to these newly identified precursor cells. Multipotent of the Mesenchyme cell isolation and expansion the in vitro the Mesenchyme stem cell,that is Mesenchyme stem cell is hierarchy progress through the differential manner give rise to the phenotypicallyand and bone marrow organ tissue[53].

Type 2 diabetes inhibited the osteogenesis process. BMSC is the Pre-cursor cells for the osteoblast cells which help in the process of estrogens. It was found that the bmal1 gene regulates type 2 diabetes bone remodelling[54]. Suppression of BMAL1 expression was found in DIABETIC-BMSC. While the expression of other genes in Diabetic-BMSC such as beta-catenin and T cell factor decreased and expression of GSK3 beta, NLK was increased. It was found that over-expression of the BMAL1 gene induces the beta-catenin signalling pathway by inhibiting the suppressive effect of gsk beta on wnt/beta-catenin signaling[16]. So this way over expression of the BMAL1 gene may induce estrogens in diabetic –BMSC patients.

Brain and muscle aryl hydrocarbon receptor nuclear trans locator-like protein 1 BMAL1 is a central positive regulator of the core molecular clock and is expressed in the suprachiasmatic nucleus and peripheral tissue such as bone and stem cells[17].

The role of BMAL1 in T2DM-induced suppression of BMSCs osteogenesis. Over-expressed BMAL1 could recover BMSCs osteogenesis in T2DM partially by decreasing GSK-3b expression to activate Wnt/b-catenin pathway. BMAL1 may have potential use in repairing diabetic bone metabolic disorders[17].

In-vitro reprogramming of rat bone marrow-derived by the MS_C producing insulin cell by genetically of the manipulating by negatively and positively.

Reprogramming of BMSC Bone marrow stem cell into a linage of pancreatic islet beta cells required over expression of Pdx1 pancreas and duodenal transcription factor 1 and Ngn3 neurogenin3[21]. After transfection with Pdx1 and Ngn3, they have found that 23 to 25 differential expressed genes those involved in the development and differentiation of islet beta-cell verified with bioinformatics RNA dataset and further validated by rtPCR Real-time PCR. So this way by reprogramming of BMS_C they have to generate surrogate functional insulin-secreting cells.

Islets cell replacement therapy of type 1 diabetes in case autoimmunity to be a bet cell is under the control. However, the islets of the crucial role are limited by a shortage of pancreas donors[22].

According to intravenous administration of mesenchymal stem cells isolated from Wharton's jelly a gelatinous substance derived from canal decreased glucose level after 7 days of injection in STZ induced type 1 diabetic rats[22]. These cells also recover the damage done by STZ and show similar morphology as islet cells. So transplantation of mesenchyme stem cells was an effective method for the treatment of T1DM.

How far away is a cellular replacement therapy for type 1 diabetes mellitus in stem cells as a potential treatment for T1DM first before the need for a new treatment is used in the human being, challenges the transplantation of isolated cells of a non-marginal mass of the insulin-producing cells for the human use [31].

Ammonites stem cell are also used to treatment of T1DM

Amniotic stem cells are also used to treat T1DM the cells are isolated from the neonatal amniotic membrane, having two types of stem cells one is amniotic epithelial cell and

the other is amontic mesenchymal stem cell. Embryonic stem cells a type of pluripotent cell can differentiate in any cell type except the umbilical cord. Amonte epithelial cells were used because it expresses similar characteristic as pluripotent stem cells confirmed by phenotyping study of cell surface marker[24].

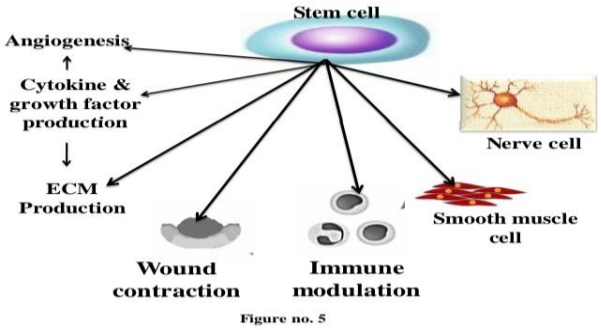


Figure no. 5

AT-MSCs were shown to improve graft rejection due to their Immune- modulator properties When used in conjunction with islets for transplantation. The co-transplants when embedded in a hydro gel matrix adequate glucose sensing and significant insulin release *in vitro* as compared to free islets. Also, the transcript levels of PDX1 exhibited a significant increase in the presence of AT-MSCs [25].

Human undeveloped foundational microorganisms instigated by phosphatidylinositol-3-kinase PI3K p110b inhibitors demonstrated the creation of more developed islet-like cells upon separation. The degree of insulin mRNA was altogether higher in TGX-221PI3K is form-specific inhibitors of class 1b treated cells than in LY294002 nonselective PI3K inhibitor - treated cells. Upon transplantation, these islet-like cells improved glycemic control and improved the endurance result in diabetic mice[14].

Using the LY294002 or TGX-221 as a distributor for the extending -4 and B27 to activate the differentiation of human embryonic stem cells in the beta-cell. Beta-cell were of the correlated with step 5NE islets like a cell, the stage 5NL/5NT islets like cell were smaller and had a reduced cytoplasmic volume [29].

Adult muscle-derived stem cells contain a non-adherent, nestin-enriched multipotent stem cell population[31]. Insulin-communicating and discharging islet-like cell groups shaped upon the separation of these foundational microorganisms express various run of the mill markers of endocrine separation, pancreatic begetter, and develop pancreatic beta-cell separation. MDSC can separate into developing pancreatic beta islet-like cells, upon culture in vitro, yet in addition to vivo after foundational infusion in STX-prompted diabetic mouse models[54].

Multipotent forebears confined from skeletal MDSC are capable to separate in vitro into insulin-communicating and emitting islet-like cell bunches. Russ HA, Parent AV, 2015. These cells bunch express various average markers of endocrine separation, pancreatic forebear, and develop pancreatic beta-cell separation. The islet-like cell groups separated in vitro communicated insulin as affirmed with fluorescent correspondent's eGFP or cherry in bunches shaped from MDSC [30].

PDX1 induces pancreatic differentiation and development by acting as a transcriptional master switch[20]. During pancreas development, PDX1 and PAX4 together activate a series of transcription factors which in turn direct the differentiation of pancreatic endocrine cells toward a β-cell fate. PAX4 markedly enhanced the propensity of PDX1-positive MSCs to differentiate into mature islet-like clusters and functional insulin-producing β-like cells.

PDX1 contains several transcriptional regulatory regions[30]. Such as the N- terminus transcriptional inhibitory elements correlated to the functional structure of the GG and domains of the A3 insulin and are a key point of the gene is needed for the development of the pancreatic endocrine cell[28]. This development of purpose is the additional molecule of the combined GLUT4 and PDX1[28].

Human Multipotent adult progenitor cells enhance islet function

Within the first few days of islet transplantation, the patient is subjected to hypoxia which leads to a considerable loss of islet mass. Human non-endothelial bone marrow-derived multipotent adult progenitor cells MAPCs produced high amounts of angiogenic growth factors, both in vitro and in vivo[28]. A significant improvement in the initial glycemic control, diabetes reversal rate, glucose tolerance, and serum C-peptide concentration was observed after an Islet–human MAPC co-transplantation as compared to islet transplantation alone[28]. Hypoxia in the initial days after islet transplantation leads to considerable loss of islet mass and contributes to disappointing outcomes in the clinical setting [31].

Isolation, expansion, and characterization of AD-MSCs

Preconditioning the MSCs boosts the paracrine potential of these cells, enhancing their therapeutic efficacy[33]. Human adipose tissue-derived MSCs AD-MSCs when pre-conditioned with the iron chelator deferoxamine DFX, showed an increase in the abundance of the hypoxia-inducible factor 1 alpha HIF-1α in a concentration-dependent manner, with no adverse effect on MSC morphology and survival. The expression of potent neuroprotective factors, including nerve growth factor, glial cell-derived neurotrophic factor and neurotrophin-3, and cytokines with anti-inflammatory activity like IL4 and IL5 also exhibited a significant increase [35]. The total antioxidant capacity of the MSC secretome was also increased after DFX preconditioning and the cells showed neuroprotective effects when evaluated in an in vitro model of diabetic neuropathy[33].

METHOD OF STEM CELL ORIGINATING FROM UMBILICAL-CORD DIABETIC RAT IN TRANSPLANTATION

NSCs Neural Stem Cell originating from Umbilical Cord-MSCs when transplanted into diabetic rats, showed attenuation in retinal vascular dysfunction. Arden, G.B.ET, et al 2012.The decrease in BDNF Brain-derived neurotrophic factor levels caused by diabetes was also

simultaneously prevented and thus significantly reduced the progression of diabetic retinopathy.

Diabetic retinopathy has been considered a microcirculatory retinal disease and the reason for diabetic retinal causes the metabolic effect of hyperglycemias[34]. The progressive pathogenesis of diabetic retinopathy may be due to the chronic degeneration of retinal nerve tissue, including the reactively glial cell hyperplasia and neuronal cell death. Progressively basic and clinical research is recently under to cure neuroretinal disorder diabetic retinal[35]. MSCs induced to express TGF-β can restore insulin production and also suppress adverse immune responses and these engineered MSCs were more capable than MSCs alone[39].

Thus, a combination Betatrophin is a putative peptide hormone known to increase the rate at which beta-cells undergo cell division.ADMSCs Adipose-derived MSCs upon subjection to Betatrophin over expression [40]. increased human islet viability and β-cell insulin secretion in vitro and in vivo, which may be mediated by the enhanced anti-inflammatory and anti-apoptotic potential of ADMSCs of gene therapy along with cell transplantation might prove to be a useful therapeutic option for the treatment of diabetes Recent progress in regenerative medicine has suggested that Mesenchyme stem cell MSC-based therapy is a novel potential cure for diabetes[39].

Betatrophin, also known as lipase or angiopoietin-like 8 was recently described as a potent stimulator of mouse β-cell proliferation[36]. Its transient over expression in the liver induces β-cell proliferation and improves glucose tolerance in young adult mice miR-375 gene when integrated into the ADSC genome using lent viral vectors to act as a differentiation factor amplified the expression levels of PDX1 in differentiated cells by dozens of times and that of insulin hundreds of times[36].

PDX1 react with upstream with serial of mRNA-375 gene and it is the target of the main of increase in the main role in transcription factor miR-375 targets genes involved in pancreas development such as SOX17, PAX6and its effect genes engaged in proliferation and cell growth, as id3 [36]. The secretion of insulin-regulated by Mirna 375 in responses to glucose challenge this means that exocytosis of insulin from the beta cell can be regulated by miRNA 375 direct via Amyotrophic genes as a thermostat of insulin of flow as well as cause appropriate advancement of islets Langerhans[40].

Adipose tissue is a multipotent MSC typically derived from the adipose tissue and there is derived white adipose tissue recently[44].

Recent developing cell-based therapy requires a new model to bring these new therapies into the clinic because there is the complexity of active and heterogeneous cells of requiring of GMP facilities and scientific expertise at the point of care the need of required for long term follow up and the disease-specific modification of the product 158[45].

Specifically, it was found that enzymatic digestion followed by the cell culture resulted in a population of cells that is culture resulted in a population of cells that we're able to differentiate into the adipogenic chondrogenic myogenic and MSC-derived EVs suppressed Th1 development and inhibited activation of APCs and T cells. They also increased the expression of the immunosuppressive cytokine IL-10 and suppressed Th17 cell development. IL-10 has been considered an immunosuppressive cytokine because of its association with multiple suppressive immune-cell populations. MSC-derived EVs have significant potential as an alternative to cell therapy for autoimmune diseases prevention estrogens cells[45].

Currently successfully in -vitro method producing insulin cells from the stem cell

There are currently successful in vitro protocols for deriving insulin-producing cells from stem cells. These cells are functional in vitro and can secrete insulin in response to glucose challenges in vivo when transplanted to mice[46].

However, there is especially with pancreatic progenitor's also alarming data on the formation of tumors and teratomas after transplantation to mice [46]. Signals such as cytokines, growth factors, and even oxygen levels are of major importance for the development and differentiation of these cells. Such factors cannot be controlled in vivo, and there will be large inter-individual differences as well as individual fluctuations over time[46]. The best strategy for clinical trials would be to first transplant these cells in a macro-chamber which meet the basic needs for beta-cells regarding oxygen and nutritional needs

Many approaches of stem cell therapy for the type1 diabetes mellitus one of the uses for stem cell replacement of the treatment of diabetes and non- functional islets cell in the native endogenous pancreas; another one is the use of stem cells as an inexhaustible source for islet-cell transplantation[47].

By utilizing case stimulator and multiple sgRNA to targets the endogenous stimulator of pancreatic transcription factor and MSc receptor chemokine[48]. It may be possible to direct the differentiation of Mesenchyme stem cells into surrogate IPCs capability of management of immune-modulator through ex vivo expansion and transplantation.

The accomplishment of this investigation upholds the proposition of stem cell therapy for novel use of transcription record factor of endogenous qualities engaged with their pancreatic improvement such there Pdx1, Neurod1[49]. Therefore to induce discrimination. Advancement in dcase9 transcriptional activity [50].

Mesenchyme stem cell incoming the multipotent it is not only primarily located in the bone marrow tissue it is also self-generated there is the isolated from adipose tissue

Mesenchyme stem cells are capable of participating in islets regeneration based on their accommodation removing the required to deliver multiple images of transcription cDNA for robust gene expression and also say about the capacity to generate insulin-producing cells Thus the new generation and immune-modulator characteristic of allergenic Msc make them natural molecule candidates for stem cell therapy[51, 52].

Mesenchyme stem cell that is the decrease of the glucose level through the paracrine direct Trans differential cell producing insulin cell and to the special thing of the to control diabetes. Cells may use pro-angiogenic and immune-modulator effects [51].

Mesenchymal stem cells there are provide one to more signals for Beta-cell of the regeneration and even re-differentiate into local tissue in diabetes candidate. The use of autologous umbilical cord stem cells in a child with type1 diabetes mellitus resulted in an insignificant difference in regular doses of insulin causes a decline in C-peptide level[53].

MSc is the harvested from a benefactor cell and cryo-preserved preceding administration to a preliminary member moderating the fluctuation of this the necessity of cautiously a trial of clinical preliminary of gathering MSC function and growth characteristics.

Clinical effect on human Stem cell approaches for beta-cell

MSc clinical trial in the phenotype that affects the age and gender affect the MSC function and its property of the growth pancreatic islet and MSC co-transplantation.

The importance of stem cells for the treatment of diabetes mellitus and special thing of the diabetes mellitus is a metabolic complication, diabetes mellitus is dependent of the type 1 diabetes is insulin-dependent and lack of the pancreatic beta-cell[54]. There is a modification in the diabetes of the metabolic state in the changes and also do the reversed using the beta cell of the replacement therapy this concept is support by the success of pancreas islets transplantation[56].

The progression of complications to the eyes, kidneys, and nerves can be largely halted by the prevention of hyperglycemia[57].

Stem cell transplantation during increase no. of the immunosuppressive host cell

MSc Mesenchymal stem cell have the alternative that increases no of the immunosuppressive host cell during transplantation of islets to promote the increase of immunossresive host cell[56,57]. Specifically, the human islet cell that is transplantation humanized model rat model, type1 diabetes Repeated transplantation of human-derived MSc stem cell rearing of pancreatic islet cell NOD mice suffering from STZ induced diabetes[58].

Stromal cells can promote islet regeneration in diabetic animals, the mechanisms of the regenerative process, and the appropriate conditions for using these cells for therapy. The function of BMCs and BM-derived MSCs in healing diabetes in mice[57,58].

The main focus of the review has been the replacement of beta-cell. Stem cell research is the advanced technique for the treatment of diabetes mellitus eventually provides support for diabetes treatment. But it is possible to stem cell biology to be an applicant to manipulate the immune system such as the loss of the tolerance of type1 diabetes is restored[53, 52].

Successes of the transplantation in islet

There is a potential role of the stem cell that is a particularly attractive increase of type2 diabetes is dependable.Type-2 diabetes mellitus in the B-cell of the replacement and diabetes type1 and type-2 deficiency of pancreatic beta-cell and the diabetic state will be reversed by the beta cell replacement therapy. The first successful transplantation of islets cells in the liver in 1989 there is introduced the proof of principle for the cell transplantation in diabetic candidates[60]. There is a potential role of the stem cell that is particularly attractive to increase of the type-2 diabetes is dependable.Type-2 diabetes mellitus in the B-cell of the replacement and diabetes type1 and type-2 deficiency of pancreatic beta-cell and the diabetic state will be reversed by the beta cell replacement therapy.

Beta cells in Langerhans of islets cell that is responsible for the generated of insulin and then there is the pathology of diabetes losses to be attributed to the loss can be beta-cell no of function Many factors to be found to be a proliferation of Beta-cell. Beta-cell capability to be sustained through slow replication [33].

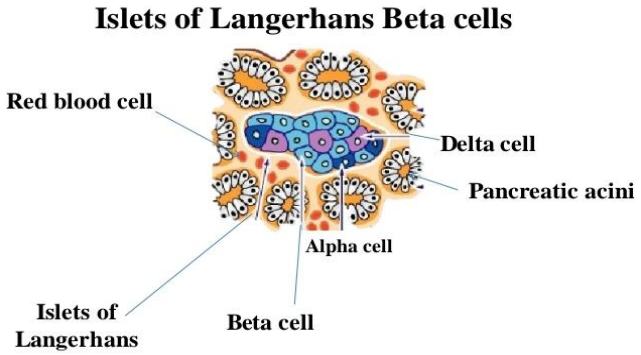


Figure no. 6

Cell therapy is the most important thing of type1 diabetes mellitus therapy and the pancreatic Beta-cell of transplantation. Islets cell of transplantation that is the most important role in the cure of type1 diabetes mellitus that is the most thing of islets beta cell of transplantation through injection in an umbilical vein[62].

The most important role of type1 diabetes in beta cell role in the design by the genetically to cure artificial beta cells of transplantation recently to therapy in the beta cells of surrogates that are recently available in the transplantation of beta-cell[43].

Stem cell therapies are being investigated, namely the potential role of induced pluripotent stem cells iPSCs, which can be harvested from almost any somatic cell type [43, 44].

Possibility of the stem cell -

The stem cell that is the capability of the possess the production of undifferentiated the daughter cell that is pancreatic beta-cell the special thing of the stem cell type. The stem cell of the special thing that passes the different signal generates. Usually, the embryonic stem cell differentiates the pluripotent stem cell that is blastocyst mass cell. After four to five days after to fertilize the stem

cell [43,44].The potential role of the promise of hypoimmunogenic Msc of the deep study of the demonstrated ability to stem cell differentiate into producing insulin cell as well as amiloride destroyed by the immunoglobin.

The pancreatic beta-cell of a new generation of beta Cell

Recently added to the capacity to differentiate into the IPCS Msc also promoted the endogenous pancreatic beta-cell by migration to the injured pancreatic beta islet cell. The most important role of MSC in the repair process by secreting a variety of growth factors and cytokines' that have both paracrine and autocrine actives[46,48]. MSC migrated to the islet of the streptozotocin-induced in the diabetes mice also they are promoted by the repair by the primarily by creating a microenvironment that is also give allowed the endogenous cells to proliferate and reuptake the normal function[66].

CONCLUSION

The main aim of transplantation is to control blood sugar levels and also restoring the Beta-cell function. There is tightly to control the blood glucose level it is obtaining the intensive insulin therapy but there is has been shown great benefits in control the micro and macro vascular complication diabetes but there is increased risk of the hyperglycemias.The innovative method of the treatment of type1 diabetes is based on the transplantation of stem cell hematopoietic stem cells. These are taken from the patient self bone marrow.

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