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REVIEW ARTICLE

DISEASES CAN BE TREATED WITH STEM CELL. A REVIEW

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ABSTRACT: Based on their inherent features, stem cells are categorized in three groups of fetal, adult and cord blood stem cells. Fetal stem cells are extracted from the inner cell mass of a 14-16-day old fetus and is capable of producing all cells and tissues of a complete human being. Adult stem cells: are those that are separated from different tissues of an adult human being after birth. Blood-producing stem cells which reside in bone marrow, brain, liver and other tissues are among those which are capable of differentiating some tissues.Cord blood stem cells: cord blood is a kind of blood that remains in cord and placenta after birth; it is then separated and discarded. This blood is fraught with stem cells.Diseases which have been cured using cord blood include stem cells disorders such as aplastic anemia, fanconi anemia, paroxysmal nocturnal hemoglobinurea, chronic and acute lymphocytic leukemia. Diseases related to defective lymphocytic production such as non-Hodgkin's lymphoma, Hodgkin's lymphoma, red globule hereditary anomalies such as beta, major thalassemia, sickle cell anemia and hereditary placket defect are among other blood and skeletal diseases. Other diseases on which the therapeutic effect of stem cells is being investigated include: leukemia, lymphoma and other blood cancers, brain tumors, neuroblastoom, ovarian cancer, hemoglobinopathies, sickle cell diseases, histiocytic disorders, hereditary metabolic disorders, hereditary immune system disorders and MS. Treatment with cord blood stem cells has not yet been considered as a serious therapeutic method. Using stem cell transplants in many diseases cuts down on the need for suppressive immune medication and their side effects. It appears that this method is a turning point in medical science revolution.

INTRODUCTION

Stem cells are the mother of all other cells. They are capable of converting into all body cells. They are also capable of self-reconstruction and conversion into different cells such as blood, muscular, cardiac, neural and cartilaginous cells. Moreover, they are effective in reconstructing injured tissues of various parts of body (1). They can be transplanted into injured tissues whose cells are primarily destroyed and can fix their defects. There are many ways to use stem cells in basic and clinical research. However, technically speaking, it is yet hard to bridge the gap between promising theories of treating diseases and achievement of a proper practical approach (2). It is only made possible through conducting more tests and research. Investigations of human fetal stem cells provide a myriad of information about all that happens throughout human's fetal phase of life (3). A primary finding of such investigations has been the way undifferentiated cells (in fact stem cells) become adult differentiated cells in different body tissues. Occurrence of other new diseases which are not responsive to common treatments or are incurable motivated researchers to employ medical advancements and think of more effective therapies based on stem cells for diseases which are hard to cure (4).

Today extensive research has been conducted on treating neural diseases, damaged cardiac and skeletal tissues, burns, skin diseases, pancreas restoration, insulin production and restoration of other injured tissues. Stem cells of bone marrow, cord blood as well as other stem cells are being investigated in adults (5). Stem cells have been found to be capable of curing a wide range of chronic and acute diseases (1). A wide range of studies are being conducted on using stem cells in treating such diseases as Parkinson's, liver, diabetes, muscular dystrophy, spinal cord injuries and apoplexy.

3. synergic stem cell transplant: in this method, patient's identical twin stem cells that are healthy are used.

STEM CELL TYPES:

Based on their inherent features, stem cells are divided into fetal, adult and cord blood cells.

Fetal stem cells: are extracted from the inner cell mass of a 14-16-day old fetus. They are capable of fully constructing all cells and tissues of an individual.

Adult stem cells: are cells which are separated from an adult's different body tissues after birth.

Blood producing stem cells residing in bone marrow, brain, liver and other tissues are among them. They have the power of differentiation in some tissues (6).

Cord blood stem cells: cord blood is the same blood which remains in cord and placenta and is then discarded. This blood is fraught with stem cells (7).

Cord blood stem cells are the same blood producing stem cells which reside in bone marrow and are divided into the following cells (5):

Red cells: which carry oxygen in the whole body.

White cells: which actively participate in the immune system.

Plackets: which help blood coagulation.

They are also capable of constructing various types of other cells, fixing and protecting them during the time of injury.

Stem cell transplant is done in the following methods (8):

1. Autologous stem cell transplant: in this method the patient's own stem cells are used. That is, patient's stem cells are extracted and are used for killing probable myeloma cells. Then, the stem cells are frozen and stored. After treatments using high doses, the stored cells are washed and returned to the patient.
2. Allogeneic stem cell transplant: sometimes stem cells are extracted from a donator who can be patient's brother, sister or parent, or even a non-relative. Blood tests are used by medics in order to be convinced of the correspondence of the donator's cells and patient's cells.

Diseases treated with cord blood stem cells (9, 10):

Stem cell disorders: aplastic anemia, fanconi anemia and paroxysmal nocturnal hemoglobinurea, and chronic and acute lymphocytic leukemia

Defects in the production of lymphocytes: Hodgkin's and non-Hodgkin's lymphoma.

Hereditary red globule anomalies: beta, major thalassemia, sickle cell anemia.

Placket hereditary defect: usually 10-20 cc of fresh and not coagulated blood is taken out of an individual's vein. Placket concentration is then raised 8 times as much. Activation of stem cells is made possible through stimulation of growth factor production. This is done by plackets. Placket growth factors are PDGF-VEGF and TGF-B. Therefore, stem cells are capable of producing muscular, skeletal, skin and hair tissues (5, 11).

Hereditary diseases: Lesch-Nyhan syndrome, cartilage hypoplasia (5)

Congenital immune system disorders: Castleman's syndrome, Leukocyte adhesion deficiency, DiGeorge syndrome (12).

The use of stem cells can cure infants born with congenital defects. Prior research indicated that muscular and skeletal tissues of neck and shoulders had a special type of stem cell which was capable of making up for congenital defects. Recent investigations have revealed that while the stem cells of muscles, neck and shoulder are the same as those of other parts of body, they can modify the structure of adjacent bones (6).

Plasma cell: (multiple myeloma): is a malignant breeding in plasma cells which occurs as a result of an individual clone. Its manifestation is in the form of skeletal pain or fracture, kidney failure, potential of infection, anemia, hypercalcemia. Some patients afflicted with multiple myeloma are treated with stem cell transplant which makes the reception of high dose of chemical medicines, chemotherapy, radiotherapy or both possible (10). High dose of such therapies causes damage to the blood cells nearby the myeloma cells of bone marrow. Subsequently, the patient receives healthy stem cells through a flexible tube inserted into a big vein in neck or chest. New blood cells are produced by these newly transplanted stem cells (1).

Other diseases: Alzheimer's, diabetes, Parkinson's, spinal cord injuries, heart and brain apoplexy, liver diseases, muscular dystrophy (13).

1. Spinal cord injuries: with the help of human fetal cells, scientists managed to help patients with spinal cord injuries to retain the feeling and control of their lower body limb. This therapy has been approved by the U.S. food and medicine supervising organization. Stem cells have the capability of breeding and differentiating other specialized cells such as bone, fat and other tissue specific cells (14). According to research findings, cells extracted from the area between vertebras have the differentiation power of neural cells. It has been recently found out that mortality of lumbar disc cells can be stopped in a laboratory and their functioning can be maintained (7).
2. Diabetes: researchers suggest that beta islet cells are one type of cells which are automatically differentiated in fetal objects. Currently, researchers think that neural growth factor might be one key sign of differentiating beta cells and can be viewed as a method of directly differentiating cells in a lab (15).

Recent research on fetal objects revealed that fetal stem cells automatically converted into fetal objects contain high percentages of cells that produce insulin. Based on the connection of antibodies to insulin protein, it is estimated that 1-3% of fetal object cells are beta insulin producing cells. Moreover, researchers have realized that cells existing in fetal objects of glut-

2 gene and the specialized glucosamine of islets of Langerhans are important for the functioning of beta cells and insulin production (11).

3. Cardiac disease: are among the most fatal diseases in the world.

Recently stem cells have helped cardiovascular patients. In their recent research scientists realized that the injection of these cells into damaged cardiac tissues can return heart natural pumping and improve blood circulation process (16).Researchers investigated many patients suffering from cardiac diseases. Through direct injection of stem cells into heart tissue and muscle they managed to remove the pain caused by heart failure, and return the capability of blood pumping to heart. Furthermore, researchers attempt to use stem cells to cure such cardiac disorders as ischemia (17). To do this, stem cells were extracted from patient's bone marrow. Then they were injected into damaged cardiac tissue and managed to activate the damaged area to be healed. After injection, stem cells produce topical hormones to repair the damaged issue. It takes about six months when the damaged tissue is healed. In fact, cardiac blood pumping is significantly improved within 9 months after the injection in these patients (13).

After injection into heart, stem cells cause a growth of new blood arteries and muscular tissues. Very soon, this method will be considered as one of the most effective therapeutic methods in the world in treating incurable heart diseases. Treating cardiac tissue defect with the help of stem cells postpones the need for heart transplant in patients. It also lengthens their age (18).

4. Parkinson's disease: stem cells have also helped patients suffering from Parkinson's disease. Parkinson's is a neural atrophy disease which causes motor and verbal problems as well as muscle stiffness. Considered as a neurologic disease, Parkinson's occurs at the age above 60. For the first time, scientists have managed to use stem cells to improve the health state of patients suffering from this disease (19). In this method, nose stem cells are used. Stem cells were cultivated in order to produce neural tissue. A little while before full growth, these cells were planted into the damaged organs. After this operation and within 4 to 6 months patients being treated with this method began to heal. Their motor functioning was also observed to be dramatically improved (20). Researchers hope to be able to use this method widely in treating patients suffering from Parkinson's disease (7, 19).

5. Alzheimer's disease: it is a prevalent disease during which the patient loses his/her memory power. Current therapeutic methods can only slow down the progress of this disease (21). In this disease, similar to Parkinson's, fetal stem cells can be one therapeutic solution. For the first time, researchers converted fetal stem cells to a specific type of neurons which are damaged as a result of Alzheimer's disease and managed to repair these neurons (22). These cells are called 'stem forebrain cholinergic neurons' and are used in hippocampus for the recovery of stored memories in brain(5). The ability of restoring memories in the initial stages of Alzheimer's progress is terribly damaged due to the destruction of these cells (21). Researchers managed to produce cholinergic neurons from fetal stem cells. Then, the produced cells were transplanted to rats' hippocampus. New axons and acetylcholine neural transmitters were observed to be produced in these rats (6, 9).

Researchers managed to show that human stem cells have tremendous effects on restoring memory in animals afflicted with Alzheimer. This disease is more prevalent in developing countries. It is positively correlated with the rise of age. Statistics show that 5.3 million American citizens are now afflicted with this disease. Researchers have attempted to improve cognitive defects observed in animal models of Alzheimer (22). They have found out that stem cells are capable of improving the negative effects of the protein beta amyloid plaques as well as neurofibrillary tangles. These plaques act as an insulation and then disconnect neurons. Therefore, Alzheimer can be somehow defined as the loss of some synopses and finally a reduction of their overall number in brain (9). According to researchers' investigations rats that received stem cells had a 75% rise in the number of synopses which seems to be the main reason for their healing. In the next phase, the team investigated how to use these research findings in treating human beings. Now they hope that stem cells follow the same route as in animals and improve the health state of human beings (23).

6. Muscular dystrophy: a main barrier in developing cell-based therapies for such muscular-neural disorders as muscular dystrophy is access to adequate productive muscles to create an effective therapeutic reaction. However, scientists solved this problem and paved the way for curing muscular dystrophy with the help of stem cells. This therapeutic method will soon be employed in medical centers (7).

7. Knee abrasion: a very common therapeutic method using stem cells is treatment, repair and reconstruction of knee

abrasion. This therapy has a high probability of success. It requires the use of other concomitant therapeutic methods (7).

There are many diseases currently being treated with the help of stem cell transplants. However, in the following diseases, treatment using stem cells has been fruitful at least in research phase or clinical tests: leukemia, lymphoma and other blood cancers, brain tumors, neuroblastoom, ovarian cancer, Small Cell Lung Cancer, testicular cancer, renal cell carcinoma, bone marrow suppression, hemoglobinopathies and sickle cell disease, histiocytic disorders, hereditary metabolic disorders, hereditary immune system disorders and MS (23, 24). In these diseases stem cell therapy has not yet been employed as a serious and definitive therapeutic method (5, 12).

Conclusion:

There are many types of stem cells in accordance with the types of body tissues as well as an individual's life stages (4). At least two of them are 'embryonic' which is accessible only at the initial stages of embryo formation and 'tissue-specific' stem cells or 'adult' stem cells which are separable from various tissues since fetal age to death (25). Our body makes use of different types of tissue-specific stem cells in order to serve different purposes. Tissue-specific stem cells have a limited capability of conversion into a specific type of cells which are required in that particular tissue (11, 26). As an instance, blood-producing stem cells in bone marrow can produce various types of blood cells. Neural stem cells in brain are capable of converting into neural cells primarily (27). Each stem cell has a particular pre-defined function and cannot be used to reconstruct all body tissues (5). Therefore, it seems that a specific stem cell is not capable of curing a wide range of diseases such as diabetes and Parkinson's (1).

However, in future, we might be able to use embryonic stem cells in a wide range of diseases. But we are aware that the mere injection of stem cells void of any differentiation is unable to be effective. Even in the case of embryonic stem cells, in order to observe better therapeutic effects, it is better to differentiate stem cells in a direction that is more fitted to the damage caused to the injured tissue (28, 29). Yet the number of diseases which can be treated with the help of stem cells is very limited. Often the therapeutic effect of stem cells in clinical studies is being investigated (30). One disease which is widely cured using bone marrow blood-producing stem cells or cord blood is blood-related diseases as well as cancers. Some skin, skeletal, cartilage and cornea diseases are currently treated using the stem cells of their own tissues (4). Diseases which were mentioned in this article are only some of the many diseases the treatment of which is possible using stem cells and has been approved by scientific communities (9).

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