International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 646-650 www.ijprajournal.com ISSN: 2249-7781

Role of stem cell therapy in life threatening diseases – Review

[1]Shoba.S, [2]Aswini.B, [3]Nishvanth.F
[1]*Professor and Head, Adhiparasakthi College of Pharmacy, Melmaruvathur, Tamilnadu, 603319*
[2.3]*Assistant professor, Adhiparasakthi college of Pharmacy, Melmaruvathur, Tamilnadu, 603319*

Submitted: 16-03-2024 Accepted: 30-03-2024

ABSTRACT: Stem cells are found in all multi cellular organisms. They retain the ability to renew themselves through mitotic cell division and can differentiate into a diverse range of specialized cell types. Stem cells are found in the bone marrow and in the peripheral blood. Stem cells constitute only a small fractions (less than 1%) of all cells in the bone marrow and an even smaller percentage of cells in the peripheral blood. Adult stem cells typically generate the cell types of the tissue in which they reside. Stem cells from one tissue may be able to give rise to cell types of a completely different tissue, a phenomenon known as plasticity. The possibility of using adult stem cells for cell based therapies has become a very active area of investigation by researchers.

KEYWORDS: Stem cells, Pluripotent, Bone marrow and High dose chemotherapy.

I. INTRODUCTION

Stem cells are cells found in multi cellular organisms. They retain the ability to renew themselves through mitotic cell division and can differentiate into a diverse range of specialized cell types. Stem cells have two important characteristics that distinguish them from other types of cells. First they are unspecialized cells that renew themselves for long periods through cell division. The second is that under certain physiologic ox experimental conditions they can be induced to become cells with special functions such as the beating cells of the heart muscle or the insulin producing cells of the pancreas. Stem cells are a remarkable type of cell that can divide and develop into any on e of the three main types of cells found in the blood:

Red blood cells: Which carry energy giving oxygen from the lungs to the entire body.

White blood cells: Important immune cells that play an important role in fighting bacteria and viruses that causes infection.

Platelets: Which help blood to clot when bleeding occurs.

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II. PROPERTIES OF STEM CELLS

The classical definition of a stem cell requires that it possess two properties.

1. Self renewal

The ability to go through numerous cycles of cell division while maintaining the undifferentiated state.

2. Potency

The capacity to differentiate into specialized cell types. In the strictest sense, this requires stem cells to be either totipotent or pluripotent – to be able to give rise to any mature cell type although multipotent or unipotent progenitor cells are sometimes referred to as stem cells.

Pluripotent: Embryonic stem cells originate as inner mass cells within a blastocyst. The stem cells can become any tissue in the body excluding a placenta.

Totipotent: Stem cells are produced from the fusion of an egg and sper cell. Cells produced by the first few divisions of the fertilized egg are also totipotent. These cells can differentiate into embryonic and extra embryonic cell types.

Multipotent: Stem cells can produce only cells of a closely related family of cells. Ex: Hematopoietic stem cells differentiate into red blood cells, white blood cells and platelets.

Unipotent:

Cells can produce only one cell type, but have the property of self renewal. This distinguishes them from non-stem cells. All stem cells have three general properties:

1. They are capable of dividing and renewing themselves for long periods.

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2. They are unspecialized.
3. They can give rise to specialized cell types.

III.IDENTIFICATION OF STEM CELLS

The practical definition of stem cell is the functional definition- the ability to regenerate tissue over a lifetime. For example the gold standard test for a bone marrow or hematopoietic stem cell (HSC) is the ability to transplant one cell and save an individual without HSCs. In this case a stem cell must be able to produce new blood cells and immune cells over a long term, demonstrating potency.

Properties of stem cells can be illustrated in-vitro using methods such as clonogenic assays, where single cells are characterized by their ability to differentiate and self-renew. As well, stem cells can be isolated based on a distinctive set of cell surface markers. However in-vitro culture conditions can alter the behaviour of cells, making it unclear whether the cells will behave.

IV. COLLECTION OF STEM CELLS

Most of stem cells in the human body reside in the bone marrow. Today, most autologous transplants utilize peripheral blood stem cells (PBSCs). Bone marrow stem cells are most often used in allogenic transplants, but PBSC are beginning to be used more frequently.

Collecting Stem Cells From Bone Marrow:

a. Collecting or Harvesting

Collecting bone marrow is usually done in a hospital operating room under general anaesthesia. The bone marrow which appears as a thick red liquid, is typically frozen and stored until high dose chemotherapy is completed.

b. Processing and Cryopreservation

After the bone marrow stem cells are collected from the patient they are processed in the laboratory, cryopreserved and stored until needed. Allogenic stem cells typically do not require this step since they are collected just prior to transplant.

c. High dose chemotherapy

After the stem cells are collected, the patient will receive high dose chemotherapy. The higher doses of chemotherapy are designed to destroy cancer cells more effectively than standard chemotherapy. Some patients may receive one or more treatments of high dose chemotherapy possibly in combination with radiation therapy.

d. Infusion

Within a few days after completing the high dose chemotherapy, the stored bone marrow stem cells are transplanted or infused into the patients blood stream

Stem cells are infused patients blood stream. The Infusion process is similar to a blood transfusion. The frozen bags of bone marrow cells are thawed in a water bath and infused into a vein over a period of 2 to 4 hours. The infused stem cells travel through the blood stream and settle in the bone marrow where they begin to produce new white blood cells, red blood cells and platelets.

e. Engraftment and Recovery

During the first few days after transplantation, the reinfused stem cells migrate to the bone marrow and begin the process of producing replacement blood cells, a process is called as engraftment. The stem cells start to produce new blood cells within 12 to 15 days following infusion.

Until engraftment is complete a transplant recipient is susceptible to infection, anaemia and bleeding caused by low blood cell counts. Therefore special precautions are necessary during recovery. For the first 2-4 weeks after the transplant patients are very susceptible to developing infections. This is because the effects of the high dose chemotherapy and loss of blood cells weaken the body's immune system. Antibiotics are often prescribed to help prevent infection.

V. TRANSPLANTATION OF STEM CELLS

Stem cells transplantation is complex process that involves several steps. The process is similar for both autologous and allogenic stem cell transplants. However in the case of autologous transplants, the patient will undergo the stem cell collection procedure prior to receiving high dose chemotherapy and their cells will be frozen and stored until needed.

The Center for International Blood and Marrow Transplant Research (CIBMTR) estimates that approximately 4700 stem cell transplants of various types were performed in patients with myeloma in North America in 2003.

The first step in the process of stem cell transplantation is the collection of stem cells from a patient or a donor. When a patient's own stem cells are used they are frozen and stored until needed. The patient then receives high dose chemotherapy. The stem cells travel to the bone

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marrow and begin to produce new blood cells replacing the normal cells lost during high dose chemotherapy. High dose chemotherapy and stem cell transplantation are typically performed following several cycles of conventional chemotherapy. Induction therapy is performed first in order to reduce the tumour burden.

VI. TYPES OF STEM CELL TRANSPLANTS

There are many types of stem cell transplants. Stem cell transplants are defined by the source of the stem cells.

a. Bone marrow transplants

These are those that are obtained from bone marrow. However they are rarely performed today in myeloma because of the ability to collect stem cells from the peripheral blood. Bone marrow transplants are sometimes used if insufficient numbers of stem cells can be obtained from the peripheral blood.

b. Peripheral blood stem cell transplants

These are obtained from peripheral blood. PBSC transplants are now performed much more often than bone marrow transplants because they are easier to collect, they provide a more reliable number of stem cells, the procedure puts less strain on the donor's system and the patient recovers more quickly.

c. Cord blood transplants

It refers to transplants where the stem cells are obtained from umbilical cord blood. Historically they have not been used frequently due to limited numbers of stem cells that can be collected from each umbilical cord.

Stem cells transplants are further categorized based on the donor who provides the stem cells.

i. Autologous stem cell transplants (autografts)

It refers to stem cells that are collected from an individual and given back to that same individual. Most stem cell transplants in myeloma are autologous transplants.

ii. Allogeneic stem cell transplants (allografts)

It refers to stem cells that are taken from one person and given to another. Currently these types of transplant are performed much less frequently in myeloma in the US and are usually performed in the context of clinical trials.

iii. Syngeneic stem cell transplants

It refers to stem cells that are taken from an identical twin of the recipient.

These types of transplants are quite rare.

Lastly, there are also several types of transplants under investigation in clinical trials.

1. Tandem autologous transplant

It is also known as a double autologous transplant, requires the patient undergo two autologous stem cell transplants within 6 months.

2. Mini (non myeloablative) allogeneic transplant

It involves the use of moderately high dose chemotherapy in combination with an allogeneic stem cell transplant.

VII. STEM CELL TRANSPLANTS

Medicinal researchers believe that stem cell treatments have the potential to change the face of human disease and alleviate suffering. In the future medical researchers anticipate being able to use technologies derived from adult and embryonic stem cell research to treat cancer, Type 1 diabetes, spinal cord injuries and muscle damage amongst a number of other diseases and impairments.

BRAIN DAMAGE

Stroke and traumatic brain injury lead to cell death characterized by a loss of neurons and oligodendrocytes within the brain. Healthy adult brains contain neural stem cells that divide and act to maintain stem cells numbers or become progenitor cells. Recently, a research conducted in rats subjected to stroke suggested that administration of drugs to increase the stem cell division rate and direct the survival and differentiation of newly formed cells could be successful. It was found that within a weeks recovery of brain structure is accompanied by recovery of lost limb function suggesting the potential for development of a new class of stroke therapy or brain injury therapy in humans.

CANCER

Research injecting neural (adult) stem cells into the brains of dogs can be very successful in treating cancerous tumors. With traditional techniques brain cancer is almost impossible to treat because it spreads so rapidly. Researchers at the Hardward Medical School caused intracranial tumours in rodents. Then, they injected human neural stem cells. Within days the cells had

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migrated into the cancerous area and produced cytosine deaminase, an enzyme at converts a non-toxic pro-drug into a chemotherapeutic agent. As a result the injected substance Was able to reduce tumor mass by 80 percent.

SPINAL CORD INJURY

A team of Korean researchers reported that they had transported multiopotent adult stem cell for umbilical cord blood to the patient suffering from spinal cord injury. The patient can not able to stand up for the last 19 years. After the transplant of stem cells from umbilical cord now walk on her own without difficulty. For the unprecedented clinical test, the scientists isolated adult stem cells from umbilical cord blood and then injected them into the damaged part of spinal cord . Then the researchers have followed up with a case study write up on their work. It is located in the journal cytotherapy.

University of California researches injected human embryonic stem cell into paralysed mice, which result in the mice regaining the ablity to move or walk four months later. The researchers discovered upon desecting the mice that the stem cells regenerate not only the neuron but also the mylin sheath which initates neural impulses and speed them facilitating communication with brain.

HEART DAMAGE

Adult stem cell therapy for heart disease is commercially available on at least five continents. The most well known company Theravitae a private company located in bangkonk provide this type of stem cell therapy. More rthan 250 heart patient have travelled through Thailand to receive Theravitae's adult stem cell therapy called Vascell to treat their heart disease. Theravitae reports that 75% of their heart patients have an improved quality of life after receiving their aduld stem cell treatment. The plethoras of more recent USA FDA approved clinical trials are showing much the same results as Theravitae's 75% success rate.

Using the same bone marrow derived stem cells, Dr. Amit patel at the university of Pittsburgh; McGowan Institute of Regenerative medicine has shown a dramatic in ejection fraction for patients with conjestive cardiac failure. A Brazilian stem cell bank has performed sample manipulation in more than 30 cell therapy procedures in cardiac patients.

HAEMATOPOIESIS

In December 2004, a team of researchers led by Dr.Luc Douay at the university of paris developed a method to produce large number of red blood cells. Erythropoietin, a growth factor is added ,coaxing the stem cells to complete terminal differentiation into red blood cells.

Further research technique will have potential benefits to gene therapy, blood transfusion and topical medicine.

BALDNESS

Hair follicles also contain stem cells and some researchers predict research on these follicle stem cell may lead to successes in treating bladness through "hair multiplication" also know as "hair clones". This treatment is expected to work through taking stem cells from exsisting follicles, multiplying them in cultures and implanting the new follicles into the scalp. Later treatments may be able to simply signal follicle stem cells to give off chemical signals to nearby follicle cells which have shrunk during the aging process, which in turn respond to these signals by regenerating and once again making healthy hair .

MISSING TEETH

Researchers are confident that stem cell therapy can be used to grow live teeth in human patients.

In Theory , stem cells are taken from the patient could be coaxed in the lab into tooth bud, which when implanted in the gums, will give raise to new tooth, which could be expected to take two months to grow.

It will fuse with the jaw bone and release chemicals that encourage nerves and blood vessels to connect with it. The process is similar to what happens when human grow their original adult teeth.

DEAFNESS

There has been success in regrowing cochlea hair cells with the use of stem cells.

BLINDNESS AND VISION IMPAIRMENT

Researchers have successfully transplanted retinal stem cells into damaged eyes to restore vision. Using embryonic stem cells, scientists are able to grow a thin sheet of totipotent stem cells in the laboratory. When these sheets are transplanted over the damaged retina, the stem cells stimulate renewed repair, eventually restoring vision.

Doctors in UK transplanted corneal stem cells from an Organ donor to the cornea of the women who has blinded in one eye when an acid was thrown in her eye in night club. The cornea, which is the transparent window of the eye, is particularly suitable for transplant. The majority of corneal transplant carried out today are due to

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degenerative disease called Keratoconus which causes vision impairment and has no known cure after corneal transplant.

ALS (Lou Gehrig's disease)

Stem cells to cure rats of an ALS like disease. The rats were injected with a virus to kill the spinal cord motor nerves related to leg movement. These migrated to the sites of injury where they were able to regenerate the dead nerve cells restoring the rats which were once again able to walk.

VIII. MERITS AND DEMERITS

Merits of stem cell therapy:

1. Ethically Sensitive

Stem cells that are derived exclusively from human umbilical cords of full term births under informed consent donations and are therefore not subject to ethical issues.

2. Safety

Stem cells that are certified infectious disease free in accordance with the American Association of Blood Bank Safety Standards. Cells are tested for HIV1, HIV2,Hepatitis B, Hepatitis C and CMV.

3. Standardization

Stem cells that are manufactured using Good Laboratory Practice by a team of specialized researchers. All vials are stored under highly monitored vapour phase liquid nitrogen conditions which ensure extended uncompromised viability. All vials are transported on dry ice using time sensitive medical transports.

Demerits of Stem cell therapy:

- Most of the significant potential side effects of stem cell transplantation are a result of the high dose chemotherapy. Some of the more common temporary side effects include nausea, vomiting, diarrhoea, mouth sores, skin rashes and hair loss.
- Patients are very closely monitored during high dose chemotherapy, with daily weight measurements as well as frequent measurements of blood pressure, heart rate and temperature.

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