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Review Article

Stem Cell Therapy - Current Scenario, Challenges and Future in India: A Review

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Abstract:

This review paper explores the evolving landscape of stem cell therapy in India and globally. Key points included in this review are the historical development of stem cell therapy, diverse sources of stem cells, the current global landscape encompassing research, regenerative medicine, clinical trials, and ethical considerations. India's active involvement in stem cell research, government initiatives, and the cryopreservation of umbilical cord blood stem cells are highlighted.

The paper discusses stem cell therapy's potential in addressing ALS, neuroinflammation, and COVID-19. It concludes by emphasizing the promising future of stem cell therapy, highlighting the need for robust clinical trials and ethical considerations. This concise overview provides insights into the state and potential of stem cell therapy in India and worldwide.

Key Words: Stem cell, Stem cell therapy, Regenerative medicine

Introduction:

Stem cell therapy is a burgeoning field in India, showing promising advancements in medical treatments. It involves using stem cells to repair, replace, or regenerate cells, tissues, or organs affected by various diseases or injuries. In India, stem cell therapy is being utilized to treat a range of conditions, including neurological disorders, cardiovascular diseases, orthopaedic issues, diabetes, and more. The country has a growing number of specialized stem cell centers and research institutions that conduct studies and clinical trials to explore the potential of stem cell treatments. Government regulations and guidelines govern the ethical and safe use of stem cells for therapeutic purposes.[1]

Patients seeking stem cell therapy in India benefit from a comparatively lower cost of treatment compared to many Western countries. Additionally, India has skilled medical professionals and researchers contributing to the advancement of stem cell research and therapy. Ongoing research, collaboration with international experts, and continuous improvements in healthcare infrastructure position India as a potential hub for stem cell research and therapy, offering hope for improved treatment options and outcomes for patients with various medical conditions. [1]

History of Stem cell

In 1956, the first bone marrow transplant took place, heralding the initiation of stem cells' application in modern regenerative medicine. Stem cell therapies have since expanded their indications beyond conventional boundaries and are now utilized to treat various clinical conditions, surpassing their original purposes, particularly in the realm of genetic blood diseases.

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ISSN No. *: (p) 2348-523X, (o) 2454-1982*

DOI: 10.46858/vimshsj.10207

Date of Published : *30th June 2023*

These therapies have exhibited remarkable success in cases where conventional treatments have proven ineffective. This pivotal advancement has shed light on the potential for future treatments through continuous development and improvement of clinical techniques, laying the foundation for the currently available stem cell therapies. There is hopeful anticipation that in the future, stem cells could be employed in the treatment of neurological disorders, including Parkinson's and Alzheimer's disease, as well as other painful conditions.[2]

Identifying different sources of stem cells[3]

1.EMBRYONIC STEM CELLS

Embryonic stem cell possesses a remarkable characteristic as they serve as the origin of all other cell types found in the human body. These cells emerge from the blastocyst, which forms approximately four days after fertilization and signifies the earliest stage of human embryo development. The blastocyst comprises two distinct components: an inner mass of cells and an outer layer of cells that collectively form a hollow sphere. Within the inner cell mass, there exist pluripotent cells capable of differentiating into stem cells and subsequently generating cells with specialized functions.

2.ADULT STEM CELLS

Adult stem cells can be gathered from bone marrow, peripheral blood, and other tissues such as muscles, cardiac tissues, cartilage, and brain tissues. These stem cells can be classified into three distinct categories: hematopoietic stem cells (found in bone marrow and peripheral blood), non-hematopoietic stem cells (found in various tissues), and organ-specific stem cells (found in specific organs and responsible for their daily functioning and repair).

3.MESENCHYMAL STEM CELLS

Mesenchymal stem cells (MSCs) exhibit a remarkable capacity to transform into diverse cell types including cartilage, bone, and other active tissues, making them promising for treating a range of diseases. This distinctive ability enables MSCs to be potentially used for allogeneic transplantation.

4.ADIPOSE TISSUE STEM CELLS

Adipose-derived stem cells (ADSCs) are located in the stromal vascular fraction (SVF) of adipose tissue following enzymatic breakdown. Several studies have demonstrated that ADSCs exhibit similar characteristics to mesenchymal stem cells (MSCs) and express various CD markers typically associated with MSCs. ADSCs exhibit multipotent properties but also exhibit distinct differences from MSCs in several aspects.

5.UMBILICAL CORD STEM CELL

Umbilical cord stem cells can be found in umbilical cord blood, cord perivascular cells, umbilical vein endothelial cells, umbilical lining, chorion, and amnion. Since 1988, hematopoietic stem cells have been successfully extracted from umbilical cord blood with little risk to the donor. Umbilical cord stem cells are easier to get than bone marrow stem cells. Because more than 100 million babies are born each year around the world, the availability of umbilical cord blood as a source of stem cells is considerably enhanced.

6.PLACENTAL TISSUE STEM CELLS

Placental tissue contains two types of cells, namely stem cells and epithelial cells, which possess the remarkable ability to differentiate into various tissue types such as adipose, muscle, liver, bone, heart, blood vessels, pancreas, lungs, and nervous tissues. Hematopoietic cells arise from the chorion, allantois, and yolk sac, while mesenchymal lineages originate from the chorion and amnion. To simplify, human fetal placental cells can be classified into four distinct groups: amniotic epithelial cells, amniotic mesenchymal stromal cells, chorionic mesenchymal cells, and chorionic mesenchymal stromal cells.

7.BONE MARROW STEM CELLS

Regular biological processes necessitate the presence of stem cells to replenish damaged and aging cells in self-renewing tissues. Hematopoietic stem cells (HSCs), residing in the bone marrow, act as a reservoir for a diverse range of blood cells essential for normal physiological and immunological functions. Both myeloid and lymphoid lineage cells, originating from HSCs, have relatively limited lifespans and depend on a continuous influx of newly differentiated replacement cells to sustain their functionality.

8.AMNIOTIC STEM CELLS.

Historically, embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) have been the two most popular types of pluripotent stem cells.35 Despite numerous research initiatives to advance ESC and iPSC technologies, there are still significant clinical challenges.35 Recently, researchers have isolated pluripotent stem cells from gestatious stem cells. During the second week of gestation, human amniotic stem cells begin to emerge as a result of a small cavity forming within the blastocyst. Within this cavity, primordial cells undergo differentiation and give rise to amnioblasts. Human amniotic epithelial stem cells (hAESCs) are formed when epiblasts undergo differentiation into amnioblasts. On the other hand, human amniotic mesenchymal stem cells (hAMSCs) are derived from the differentiation of hypoblasts.

Current scenario of Stem cell research and therapy in World[4]

Numerous medical applications for stem cell research and therapy have demonstrated promising results.

- *Research in Progress:* Scientists are examining many stem cell types, such as adult, embryonic, and induced pluripotent stem cells (iPSCs), as well as other types of stem cells. They are researching their qualities, prospective applications, and constraints.
- *Disease Modeling:* To develop disease models that aid researchers in understanding a variety of genetic and acquired disorders, stem cells, particularly iPSCs, are used. The development of novel therapies and individualized medical strategies may benefit from this research.
- *Regenerative Medicine:* Stem cell therapy holds promise for regenerative medicine, aiming to repair or replace damaged or diseased tissues and organs. For example, stem cells have been used in clinical trials to treat conditions like spinal cord injury, heart disease, diabetes, and osteoarthritis.
- *Ethical Considerations:* The use of embryonic stem cells remains a topic of ethical debate due to the destruction of embryos during their derivation. However, research efforts have focused on finding alternative sources of stem cells, such as iPSCs, which are derived from adult cells and bypass this ethical concern.
- *Clinical Trials:* Stem cell-based therapies are being tested in numerous clinical trials worldwide. These trials assess the safety and efficacy of stem cell treatments for various diseases and conditions. It is important to note that while some therapies have shown promising results, many are still in the early stages of development and require further research.
- *Regulatory Landscape:* The regulation of stem cell therapies varies across countries. Some nations have established clear guidelines and regulations, ensuring the safety and efficacy of these treatments. It is essential to have appropriate regulations in place to protect patients and advance the field responsibly.

It is surprising that so little progress has been made in the development of therapeutic agents using iPSCs and that iPSC-derived products have only been used on humans for about 7-8 years given that iPSCs have been well known to the world since 2006 and the first iPSC-derived clinical trials were carried out in 2014. The apparent genetic instability of iPSCs could be the cause of the relative dearth of clinical trials concentrating on the delivery of iPSC-based treatments. However, numerous therapeutics research and development companies are working on a wide range of therapies for diverse reasons, and it is anticipated that in the future, the development and clinical acceptance of iPSC-derived therapeutic alternatives will become more commonplace.[3]

A better perspective on the potential future uses of SC technology can be gained by being aware with the background of SC transplantation and the state of SC research today. Recent research has focused on developing strategies to promote SC proliferation within the adult central nervous system and to safeguard the neurons and glial cells generated by endogenous stem cells.

The next phase of SC research will be the conversion of these innovative technological developments from the lab into clinically useful treatments.

For many patients, SC therapy offers hope; however, this optimism should be restrained by the knowledge that the scientific and medical communities have not yet fully understood the complexities of SC biology and have not yet produced sufficient data to support the logical, evidence-based use of SCs for therapeutic purposes. Few researches have used randomized clinical trial designs to develop into comprehensive, crucial investigations. For SC therapies to receive the requisite clearances for their future use as common treatments, the outcomes of such trials will be crucial.[3]

Dental Stem cells:

The results of recent research revealed the DSC's global tendencies. The United States made the most contributions to the research and held the top spot in the field globally. The majority of articles in the topic were published in the Journal of Endodontics. Clinical studies involving DSCs in the field of regenerative medicine are likely to gain more attention, and the newest research hotspots include "regenerative endodontic treatment," "hydrogel," "immunomodulation," "stem cells from apical papilla," "hypoxia," and "stem cells from human exfoliated deciduous teeth."[4]

Stem cells for treating ALS: Current Developments

ALS, a neurodegenerative condition characterized by severe motor neuron degeneration, include muscle atrophy, weakness, fasciculation, and stiffness. Given SCs' extraordinary plasticity and capacity to develop into a variety of neuronal lineages, SC therapy is a possible alternative treatment for ALS. SCs are a valuable source of cellular replacement as a result. Stem cells can move to disease-related loci after local or systemic transplantation to have therapeutic effects. Modern cell therapies can use a variety of stem cells to change the pathophysiology of disease, including delaying or preventing disease progression, likely by supplementing surrounding cells with protective substances.[5]

Neuroprotective role of SCs in Neuroinflammation

Stem cell therapy has the potential to fill an alarmingly bleak gap in current subacute and chronic therapies for patients with neuroinflammatory disorders by assisting the injured brain in recovering from an ischemic or hemorrhagic event by reducing endogenous neuroinflammation and promoting reinnervation. Numerous cell types have been studied in lab research throughout the years, including fetal cells, NT2N cells, CTX0E3, embryonic stem cells, neural stem/progenitor cells, umbilical cord blood, amnion, adipose, and induced pluripotent stem cells.[5]

Current scenario of stem cell research and stem cell therapy in India

The study of stem cells has the potential to revolutionize cell biology and open up new avenues for the treatment of numerous diseases that are currently incurable. The potential lies in these cells' capacity to differentiate into a variety of different cell types throughout the body. There are numerous initiatives underway in India to promote this region holistically. The creation of a dedicated institute for stem cell science and regenerative medicine with its translational units, a system for multi-centric clinical studies using autologous adult stem cells, national and international training courses for teaching students and young scientists about both embryonic and adult stem cells, and the formulation of guidelines to conduct clinical trials using adult stem cells are some of the more recent initiatives.[6]

In India, stem cell research and therapy have advanced significantly and shown tremendous promise in a variety of medical disciplines. India has been actively involved in both adult and embryonic stem cell research with an emphasis on understanding their biology, investigating their therapeutic applications, and developing regulatory frameworks to ensure ethical procedures. In India, the government's science agencies are actively promoting stem cell research with a particular focus on specific diseases and research areas. Through discussions in various forums, priority areas for research have been identified, both in basic and applied research involving embryonic and adult stem cells.

Several programs have been supported, encompassing a wide range of activities such as establishing human embryonic stem cell lines, using limbal stem cells for corneal surface disorders, and exploring the potential of various stem cell types like hematopoietic, mesenchymal, and liver stem cells.[6]

Reliance Life Science, for instance, in Mumbai has examined 10 stem cell lines, two of which are neuronal cell lines. Neurons that produce dopamine and neurons for stroke sufferers. The National Center for Cell Science has received a cell line for deposit in Pune. The focus of their study is on ESC; hemopoietic stem cells; treatment for skin and tissue cancer, sickle cell disease, and leukemia. India's government has implemented stem cell research policies and stem programs developing both basic and translational research are in the works. Public-private collaborations are one type of collaboration between governmental and commercial entities which is crucial in the study of stem cells. The main source of preserved stem cells in India is umbilical cord blood, which is the only blood type that is banked. The cryopreservation of stem cells produced from cord blood is a business that several private companies are engaged in. In these private banks, stem cells are stored for use by a specific person, such as an autologous transplant. On the other hand, open cord blood banks act as a collection of HLA-matched donor samples that are accessible to anyone in need.[7]

There is significant potential for the application of stem cell-based therapies as cutting-edge medicines to repair and regenerate injured or damaged tissues. Around the world, a variety of adult stem cell types, as well as embryonic and iPSC stem cells, are presently used to treat a wide range of illnesses. Because they are easy to separate from a number of sources, such as bone marrow, peripheral blood, and cord blood, HSCs are a superior stem cell type for transplantation for the treatment of several blood diseases. Currently, more than 50,000 bone marrow transplants are performed annually throughout the world, and they are the accepted standard of care for many hematological diseases. In its policy program, Stemline declares its commitment to the use of "Bench to Bedside" therapy. Stemline collaborates with about 20 corporate hospitals in India to carry out proof-of-concept research on experimental stem cell therapies. Patients receiving these treatments include those with Parkinson's disease, spinal cord injury, critical limb ischemia, avascular necrosis, motor neuron disease, end-stage liver disease, psoriasis, vitiligo, and myocardial infarction. These treatments make use of mesenchymal stem cells that are derived from bone marrow. [8]

Stem cell therapy for COVID-19:

The USFDA has approved clinical trials using MSC-based therapy to treat COVID-19, and more than sixty studies have been registered at clinicaltrial.gov. These MSCs were used to treat severely ill patients who need ventilators or who experienced acute respiratory distress syndrome (ARDS).[9]

Stem Cell Therapy - Challenges and Future

Stem cell therapy has become one of the emerging and promising scientific research topics. Stem cell therapy now a ray of hope in the field of medicine because it holds strong promise for the treatment of a wide range of diseases and injuries such as Parkinson's disease, Multiple sclerosis, Amyotrophic lateral sclerosis, Spinal cord injury etc. As the time progresses, with advancement in technology, the future of stem cell therapy looks brighter and assured. Stem cell therapy is becoming a standard practice in healthcare. In recent years, successful translation of stem cell therapies to patients making to believe that such regenerative strategies may one day become a treatment for deadly uncurable diseases. Cell-based therapy, a cornerstone of regenerative medicine, is widely regarded as one of the most auspicious fields in modern science and medicine. This cutting-edge technology presents boundless opportunities for revolutionary and potentially remedial interventions in the face of grave human illnesses. [10]

Regenerative medicine is swiftly emerging as a groundbreaking frontier in healthcare, with a primary objective of restoring and potentially substituting impaired cells, tissues, or organs to reinstate normal physiological function. Stem cell therapy has the potential to revolutionize the concept of personalized medicine. By utilizing a patient's own cells, known as autologous stem cells, treatments can be tailored to the individual's specific needs. This approach not only enhances the efficacy of the therapy but also reduces the risk of rejection or adverse reactions. In the coming years, stem cell-based tissue engineering could pave the way for the creation of lab-grown organs and tissues. By combining stem cells with bioengineered scaffolds, scientists aim to produce functional replacements for damaged or diseased organs. This breakthrough could significantly alleviate the burden of organ shortages and transplant complications. Recent research highlighting the successful implementation of stem cell therapies in patients has instilled a sense of hope that such regenerative approaches hold the potential to emerge as a feasible treatment option for a wide range of challenging diseases. In fact, there has been a notable surge in clinical trials dedicated to exploring the capabilities of stem cell-based therapies, resulting in significant advancements. Noteworthy breakthroughs have been observed in various conditions, demonstrating remarkable outcomes. For example, a case study involving Epidermolysis Bullosa revealed positive indications of skin regeneration following treatment with cultured keratinocytes derived from epidermal stem cells. Similarly, individuals with macular degeneration experienced substantial improvements in visual acuity after undergoing transplantation of patient-specific induced pluripotent stem cells programmed to differentiate into retinal pigment epithelial cells. [11]

Clinical inquiries involving stem cell therapies in the field of regenerative medicine are encompassing a diverse range of ailments utilizing various stem cell categories. Thus far, there have been limited accounts of safety concerns emerging from autologous or allogeneic transplants. Numerous administered cells demonstrate a transitory presence lasting a few days, exerting trophic effects on immune or inflammatory reactions. Ensuring the safety and efficacy of stem cell therapies is important. Rigorous preclinical and clinical trials are necessary to assess the potential risks and benefits associated with the use of stem cells in various treatment modalities. Ethical considerations regarding the utilization of embryonic stem cells continue to spark discussion. The retrieval of embryonic stem cells entails the demise of human embryos, evoking ethical apprehensions among certain individuals. Immunological compatibility presents a notable hurdle in stem cell therapy. Allogeneic stem cell grafts, involving the utilization of cells from a donor, can provoke immune rejection reactions in the recipient. It explores the limitations of these therapies and ongoing challenges in the field, while also addressing the ethical into safe and efficacious therapies. [12]

Conclusion:

With the advancements in medical technology in India and scope of collaborative research, India has good opportunity in stem cell therapy research and development. India showing shift in the disease pattern from communicable to non-communicable diseases, and increasing life span of Indians, there is more scope on use of Stem cell therapy to cure many non-communicable diseases. We conclude that stem cell therapy research centres should be established and government should provide necessary resources and device a policy for more collaborative stem cell therapy research in India for public-private partnership.

Conflict of interest: None

Source of Funding: None

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