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# Therapeutic Properties of Stem Cells in Muscular Dystrophy

B. Rithik Dharan, Nitheeswar.C, K. Sarika, S. Swaathy, L. Karpagavalli
*Jaya College of Paramedical Science*
*(College of Pharmacy)*
*CTH Road, Thiruninravur, Chennai 602024. Tamilnadu.*

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**ABSTRACT:**
Muscular dystrophy refers to a collection of inherited conditions that cause a progressive wasting away of muscular tissue as well as a weakening of the affected muscles. There are around 30 different forms of muscular dystrophies, however the two most common are as follows: Muscular dystrophy of the Duchenne type, Muscular dystrophy of the Becker type.
A faulty gene located on the 23rd OX chromosome is responsible for the development of muscular dystrophy. This flaw causes the body to be unable to manufacture dystrophin, a muscle protein that is necessary for normal muscle function. The incidence of the condition is significantly lower in females than to males. The muscle is unable to withstand the stress because it does not have enough dystrophin protein. This leads to calcium influx and oxidative stress, both of which cause damage to the muscle cells and tissues.
Patients suffering from muscular dystrophy can have their quality of life improved through the implantation of stem cells. Stem cells are cells that have not undergone differentiation, which means they do not perform a particular role in the body. They are capable of transforming into a wide variety of cell types. In most cases, hematopoietic stem cells are employed for the procedure. These cells are obtained from the patient's bone marrow, then centrifuged, engineered, and transformed by the application of transcription factors. After that, it is implanted into the patient's body once more. When the regeneration of muscle cells and tissues following transplantation is observed. In the following discussion, the specific mechanism of stem cells in individuals with muscular dystrophy is explored in detail.

**Keywords:** Stem cells, Muscular Dystrophy, Hematopoietic Stem cells, Mesenchymal Stem Cells, Duchenne Muscular Dystrophy, Dystrophin

## I. INTRODUCTION:

The term "muscular dystrophy" refers to a collection of inherited conditions that are characterised by a progressive loss of muscle mass and strength. (1) There are over 30 different types of muscular dystrophies, with Duchenne Muscular Dystrophy (DMD), Becker's Muscular Dystrophy (BMD), Facioscapulohumeral Muscular Dystrophy (FSHD), Limb-Girdle Muscular Dystrophy (LGMD), and Myotonic Muscular Dystrophy (MMD) being the ones that affect people the most frequently (MMD). (1) There are three possible inheritance patterns for muscular dystrophies: X-linked recessive, autosomal recessive, and autosomal dominant; nonetheless, boys are more likely to be affected than girls. (2) Males are more likely to be affected than females, and the disease may not manifest itself until the first, second, or fourth decades of life. (2) Of the different types of muscular dystrophies, Duchenne muscular dystrophy is the most frequent and severe form. (3) Mutations in the DMD gene are the root of the problem. There is a protein called dystrophin that assists in the regeneration of muscle fibers, activates the satellite cell pool, anchors and bridges the inflow of ions, and does all of these things simultaneously. It can be found in the deepest part of the sarcolemma as well as the most superficial part of the muscle fibers. Duchenne Muscular Dystrophy is caused by the absence of dystrophin in its whole. Becker's Muscular Dystrophy is caused by dystrophin that functions improperly or just partially. (4) When a person has an injury or trauma, the absence of dystrophin or a partial loss of dystrophin causes the satellite cells in the injured area to remain dormant and prevents them from becoming activated and contributing to the regeneration of muscle fibers. In addition to this, it causes aberrant abnormalities, such as asymmetric division along with defective myogenic differentiation. (4) Dystrophin and other proteins of a similar nature are members of a complex that is called the dystrophin glycoprotein complex (DGC).

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Its activities include the mechanical stabilization of the cytoskeleton as well as signaling tasks that are involved in mediating interactions between the cytoskeleton, the membrane, and the extracellular matrix. (5) A particular form of muscular dystrophy is caused when the Dystrophin Glycoprotein Complex undergoes any kind of protein deficiency or structural change (3). There is currently no cure for muscular dystrophy; however, there are several treatments that can help alleviate the symptoms of the disease, such as glucocorticoids, stem cell therapies, gene-based therapies, and so on. In this study, we discuss the significance of stem cell therapy in the treatment of muscular dystrophy as well as the action mechanism of stem cells in the treatment of muscular dystrophy.

**Stem Cells:**

There is a substantial likelihood that stem cells will one day be put to use for therapeutic reasons in the context of tissue regeneration and repair. This prospect is largely based on the fact that stem cells are able to contribute to the development of every type of tissue in the human body. In order for cells to be referred to as "stem cells," they need to display not just one but two essential characteristics. This is a need. To get things rolling, stem cells have to be able to replicate themselves endlessly and produce progeny that are genetically indistinguishable from the parent cell from which they originated. This property is also shared by cancer cells, which divide in an uncontrolled manner, in contrast to the highly regulated manner in which stem cells replicate themselves. Cancer cells proliferate in an unregulated manner. Because of this, it is vital to be aware of additional criteria for stem cells: they must be capable of giving birth to a specialized cell type that eventually becomes a component of the healthy animal. In other words, stem cells must be able to pass on their genetic information. (6) The umbrella term known as "stem cell" refers to a vast array of distinct types of cells. These cells can come from embryonic or adult sources. Adult stem cells, which are more appropriately referred to as "somatic" stem cells meaning "from the body," can be found in the foetus, the placenta, the blood from the umbilical cord, and babies. Other sources of adult stem cells include umbilical cord blood. The terms "embryonic" and "adult" are frequently used to differentiate stem cells based on the developmental stage of the animal from which they originate. However, these terms are becoming insufficient as new research has discovered how to turn fully differentiated adult cells back into embryonic stem cells. (7) As a consequence of this study's findings, stem cells are going to be divided into two categories: pluripotent stem cells and multipotent stem cells. These categories will be determined by the biological characteristics that set pluripotent and multipotent stem cells apart from one another. We investigate their beginnings, characteristics, ways in which they are distinct from one another, and therapeutic applications.

**PLURIPOTENT STEM CELLS:**

The phrase "embryonic stem cells" comes from the fact that the vast majority of pluripotent stem cells used in research today come from embryos, which is also where the name "embryonic stem cells" originates. Only 10–15 percent of the cells in the "inner cell mass" of pre-implantation embryos that have only been grown for a few days. These embryos have only been in culture for a few days. These pluripotent cells can be isolated and then cultured above a layer of "feeder" cells, which provide unidentified stimuli for multiple rounds of growth while yet allowing the isolated cells to preserve their pluripotent status.

Recently, two independent groups of scientists used molecular manipulation to put adult cells back into the pluripotent state, which yielded "induced pluripotent stem cells." These so-called "induced pluripotent stem cells" (iPS) exhibit some of the same properties as embryonic stem cells, including proliferation, shape, and gene expression, among other similarities. Also, these "induced pluripotent stem cells" have the ability to develop into a variety of other cell types. (8-12) Both teams of researchers used retroviruses to insert genes for transcription factors into adult cells. These genes were transported into the cells by retroviruses. These genes are transcribed and translated into proteins that influence the expression of other genes. The end goal of this process is to reprogramme the adult nucleus so that it is in the same state as an embryo. Both of them were accountable for the development of the embryonic transcription factors known as Sox2 and Oct4 and their introduction. Although the other group was responsible for the discovery of Lin28 and Nanog, the first group was also responsible for Klf(9) and c-Myc (7). (10) As many of the early animal studies resulted in the creation of odd solid tumours known as teratomas, pluripotent stem cells have not yet been used therapeutically in people. This is due to the fact that many of the early animal trials. Because of this unintended consequence,

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researchers were unable to employ pluripotent stem cells in human patients. Teratomas are a form of tumour that are made up of several different cell types that start in the early germ layers of the embryo. After that, successful animal research made use of pluripotent cells that had been modified to have a more mature phenotype, which reduces the cells' ability to multiply. This allowed the researchers to study the effects of ageing on animal behaviour. Cells that were derived from pluripotent cells were the ones that proved to be most successful when applied to the treatment of animals. It has been demonstrated that the generation of insulin-producing cells that are sensitive to levels of glucose can be a successful treatment for diabetic animals, for example. In addition, the generation of new myelinated neurons or retinal epithelial cells has been shown to be effective in curing animals suffering from acute damage to the spinal cord or visual impairment, respectively. These treatments have been tested on both humans and animals. Regarding the possibility of continuing with human trial testing, commercial companies and the FDA are currently in the process of conducting negotiations with one another. Further study has been carried out on animals in order to explore the efficacy of prospective treatments for a wide range of illnesses, such as heart failure, muscular dystrophy, and Parkinson's disease. (13,14,15,16)

It is the hope of those working in the field of medicine that stem cell therapy will one day be able to improve cardiac function. This improvement will be accomplished by incorporating newly produced cardiac myocytes that are beating into the myocardium, which will allow the myocardium to produce more force. Patches of cardiac myocytes produced from human embryonic stem cells have the ability to develop healthy human myocardium (14), and some of these patches have even showed evidence of electrical integration when they are transplanted into animals. (15),(16) Damaged mice hearts revealed a modest increase in their capacity to conduct cardiac function after being injected with cardiac myocytes produced from human embryonic stem cells. This was observed after the injection. (18) It is likely that only a fraction of the improvement in function is directly attributed to the incorporation of new heart cells that are beating, despite the fact that the specific processes that are behind the improvement in function are not totally known. Because of effects known as paracrine, which are advantageous to other cardiac cells that are already present, this is more likely to occur.

**MULTIPOTENT STEM CELLS:**

In the future, it is feasible that multipotent stem cells will find use in many therapeutic contexts. These cells have the potential to differentiate into any of the progenitor cells that comprise a particular germ layer. Alternatively, they can be instructed to differentiate into just one or two types of specialised cells that comprise a particular tissue. Both of these possibilities are possible. The embryo has the multipotent stem cells that have the greatest ability to differentiate into various cell types at the stage of development known as gastrulation. This is the stage at which the embryo is known (day 14-15 in humans, day 6.5-7 in mice). Because these cells are responsible for the birth of all of the cells that make up their particular germ layer, they maintain the capability to differentiate in a manner that is both flexible and adaptable. These cells are no longer capable of differentiating into cells that belong to any of the three germ layers; hence, it is impossible to classify them as pluripotent stem cells. On the spectrum of cell plasticity, unipotent cells are at the very beginning of the process. These cells have the potential to differentiate into a single type of specialised cell, such as muscle stem cells or skin stem cells, for example. In most cases, you may look for these stem cells within the tissues of their respective organs. Even though their capacity for differentiation is limited, the few progenitor cells that they contain serve a key role in the preservation of tissue integrity by replenishing cells that have been destroyed or that have aged. This ensures that the tissue can continue to function normally. There are a large number of other subtypes of multipotent stem cells, and each of these subtypes is capable of a different amount of differentiation than the others. For example, multipotent cells that are produced from the mesoderm of the gastrula go through a differentiation stage that limits them to just becoming muscle and connective tissue. This happens because this step reduces their ability to become other types of cells. However, further differentiation causes an increase in the cells' level of specialisation towards only connective tissue, and so on and so forth, until the cells are able to give rise to only cartilage or only bone.

Because of the therapeutic applications that began using stem cells in the 1960s, multipotent stem cells, such as those that can be

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found in bone marrow, have become the most well-known type of stem cell.

(17) (their potential will be examined in greater detail in a later section) (their potential will be discussed in greater detail in a later section). According to the findings of a recent study, the placenta and the blood from the umbilical cord both have the potential to become new sources of multipotent stem cells that have improved flexibility. (18) In addition, stem cells that have the potential to develop into cardiac myocytes have been discovered in the heart, an organ that was thought to be devoid of stem cells until quite recently. These stem cells were found in areas of the heart that were previously thought to be devoid of stem cells. (19) Along these same lines, neuro-progenitor cells have been uncovered within the human brain. (20) \s. These cells are essential in the process of developing bone as well as cartilage. It is anticipated that in the not too distant future, multipotent stem cells will be of service in the treatment of a wide variety of additional clinical conditions and illnesses. This is due to the fact that these cells have the potential to differentiate into any type of cell in the body. In order to treat a variety of heart diseases, clinical trials are currently being conducted using stem cells that have been isolated from bone marrow. (21) The upcoming review of this series will devote greater attention to this subject matter and provide more in-depth coverage of it.

The potential for stem cells to reverse the effects of cell death is an exciting development. These cells have the potential to develop into muscle stem cells, which subsequently aids in the process of tissue regeneration. In the treatment of muscular dystrophy, mononuclear stem cells generated from bone marrow, also known as hematopoietic stem cells, are the type of stem cells that are currently being used for transplantation. Because it is not only risk-free but also practical, efficient, and has little negative effects. (22) Another study found that patients with Duchenne muscular dystrophy have a population of cells in their blood and muscles that are CD133+ and have myogenic potential. Isolated from DMD patients, these CD133+ cells were then genetically modified and transduced with lentiviral vectors. When the cells are transplanted into mdx mice, they improve the dystrophic phenotype and result in dystrophic expression, as well as a recovery of muscle function. The cells are delivered by intramuscular and intraarterial delivery. (23)

**Physiology of Muscle Repair:**

Satellite cells are another name for muscle stem cells. These cells can be found in the satellite cell pool, which is located just below the basal lamina of adult skeletal muscle fibres. (24) They are in a dormant stage, but they become active very quickly in response to any kind of tissue injury or traumatic event in order to repair the damaged tissue. (25) Satellite cells play a significant role in the process of myogenesis. Many genetic markers and muscle regulatory factors, including as Pax7, MyoD, MyoF, and Myogenin, are used to identify and classify muscle stem cells. These genetic markers and factors are also used to describe the muscle stem cells. Muscle Regulatory factors are another name for Pax-3 and Pax-7, which are both types of the Paired Hemobox factor. After an injury or trauma to the muscle tissue, the process of creating new muscle cells, also known as myogenesis, is helped along by muscle regulatory factors. This process is known as regeneration. (26) The regulation of myogenesis, often known as the process by which dormant cells become active, is not completely understood. The activation and maintenance of quiescent stem cells are both significantly impacted by the Notch signalling pathway. (27) The expression of Pax 7 happens during the stimulation of quiescent stem cells, and this expression then transcribes to Myf5 and MyoD. These transcripts participate in a dynamic way in the myogenic commitment process. (28) Following the activation of muscle stem cells, the myogenic regulatory proteins Myf5 and MyoD were responsible for regulating the commitment of daughter myoblasts, which in turn produces the muscle lineage. (29) The daughter myoblasts begin to differentiate into myotubes and myofibers after they induce the expression of myogenesis and MRF 4. This process causes the daughter myoblasts to proliferate. (30)

**Stem Cell Therapies in Muscular Dystrophy:**

Mesenchymal stem cells and hematopoietic stem cells have been shown to be more effective in treating muscular dystrophy than other types of stem cells due to their high growth potential, paracrine effects, immunomodulatory properties, and very few reported cases of adverse reactions. Other types of stem cells are also used to treat muscular dystrophy. (31) Mesenchymal stem cells are capable of undergoing self-renewal and differentiating into muscle lineages. They can also differentiate into several other types of cells, including endothelial cells, hepatocytes, and beta

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cells in the pancreas. (32) Hematopoietic stem cells, which are derived from bone marrow, are the cells that are now being employed to cure muscular dystrophy. Mesenchymal stem cells have the ability to develop into myoblasts and have a wide range of potential fates. (33) Mesenchymal stem cells have an extra effect on tissue regeneration and differentiation in the form of an anti-inflammatory and paracrine signalling function. (34) Mesenchymal stem cells have properties that prevent apoptosis and create chemicals that are part of the extracellular matrix. After receiving therapy, patients have a lower risk of getting malignancies, and there is no risk of developing a disease called Graft versus Host rejection. This is one of the side effects that has been described (GvHD). (35) The mesenchymal cells possess myogenic capacity, which means they contribute to the regeneration of muscle tissue and have the ability to colonise the niche in which stem cells are found. These cells also express CD 133+ cells. (36) Mesenchymal stem cells are responsible for the secretion of a variety of growth factors, including the vascular endothelial growth factor (VEGF), the transforming growth factor- (TGF-), the transforming growth factor-ß (TGF-ß), the epithelial growth factor (EGF), the basic fibroblast growth factor (BFGF), and the hepatocyte growth factor (HGF). These growth factors are responsible for cell proliferation and angiogenesis. (35) Mesenchymal cells have greater anti-inflammatory and immunomodulatory characteristics than other cell types. (36) Pro angiogenic potential, which means that they are active in the development of blood vessels and in the process of angiogenesis. Moreover, via direct differentiation, they produce or support the niche cells that are necessary for vascular regeneration. (36) I need to add extra points in this section, therefore let me just skip this section and concentrate on adding more points.

In an open study, Sharma et al. and colleagues (37) selected 150 patients and performed an open study to determine the safety and efficacy of autologous bone marrow mononuclear transplantation either by intrathecally or intramuscularly with patients suffering from Becker's Muscular Dystrophy (BMD), Duchenne Muscular Dystrophy (DMD), and Lower Grid Muscular Dystrophy. The patients were given the transplantation either intrathecally or intramus (LGMD). (38) When a year had passed since their transplant, 87% of the patients out of the total of 150 had exhibited functional improvement.

I. 53% of cases shown an increase in trunk muscle strength.
II. 48% of the patients shown an increase in upper limb strength.
III. 59% of patients showed an increase in lower limb strength
IV. 10% of patients showed an improvement in gait.

## II. CONCLUSION:

Stem cells could offer hope in the treatment of Muscular Dystrophy. In its initial stages it has been difficult to identify whether the injected cells have been differentiated into myoblasts. Now in the latest research significant progress has been made. The injected stem cells could able to survive in the environmental and has the capacity and ability to regenerate on its own. Patients with Muscular Dystrophy after getting treated with Stem Cells shown to be improved in mobility, delaying symptoms and delays the cell death. Although there is no cure for Muscular Dystrophy several gene based treatments are promising and effective in the clinical trials.

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