

Role of Stem Cells in Orthopaedic Surgery

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Received: March 02, 2019; **Published:** May 06, 2019

Volume 3 Issue 1 May 2019

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Mesenchymal stem cells (MSCs) have the ability to develop into any Mesodermal tissue. Therefore, they can be motivated to develop precursor cells to develop in tissues including bone, cartilage, muscle, tendon, and ligaments. The use of stem cells for various orthopedic challenges is outlined below.

Bone Fracture and Bone Defect

After trauma, tumors or infections, Nonunion/delayed union and bone defect are challenging aspects of orthopedic surgery, which may require biological treatment for proper treatment. Bone marrow aspirates, which have stem cells in the ratio 1: 10,000 to 1: 1, 000,000 nucleated cells have been successfully used to enhance the treatment of non-union. Tissue engineering, which involves the use of stem cells with scaffolds like Hydroxyapatite (HA), demineralized bone matrix (DBM) and tri-calcium phosphate (TCP), has been studied and found useful in reducing bone defects. Due to the absence of an external matrix to move on, MSCs alone have not proven beneficial for filling defects due to simple/aneurysm bone ulcers. When used in conjunction with scaffolding, healing rates, however, are increased.

Spinal Injuries

Spine Fusion: In a study, Neen., *et al.* showed that untrained stem cells used with HA scaffolding had the same rates of healing as autologous grafting; to prevent the morbidity of the donor site. **Intervertebral disc degeneration:** Intervertebral disc degeneration is one of the most common causes of back pain in a young population. Despite high prevalence, there is no treatment available that reverses the primary pathology. Animal experiments have enhanced the maintenance of Proteoglycan content and disc height with protocultative stem cell injection.

Spinal cord and peripheral nerve injury: Individuals with spinal cord and peripheral nerve injuries have a significant effect on the quality of life. Animal studies have highlighted some positive effects of the use of MSc through intracathal and local administration, however, the reaction seen in clinical studies is mixed. In a veterinary study, Tamaki., *et al.* showed that muscle derived MSCs aided in successful regeneration of a crushed peripheral nerve. Further clinical studies are essential for establishing the role of MSCs in the management of these patients.

Osteoarthritis - Articular Cartilage

Articular cartilage is a highly specialized tissue, which has a poor internal capacity to repair. The aim of any cartilage process is to restore its integrity so that it can withstand the wear and tear of daily activity.

Citation: Ramji Lal Sahu. "Role of Stem Cells in Orthopaedic Surgery". *Orthopaedic Surgery and Traumatology* 3.1 (2019): 1-3.

Damage to Focal Cartilage: Since the introduction of subcondral drilling in the late 1950s, various processes such as micro fracture and abrasion plasty have been developed to recruit MSCs from adjacent bone marrow to proliferate into chondrocytes.

Osteoarthritis (OA): Due to his role in preventing the catabolism of matrix Metalloproteinase (MMP), MSC has shown beneficial effects in OA. In a recent study, Sato et al showed that with age related to Guinea, pigs treated MSC laden hybridonic injections, which had better cartilage regeneration with high type II collagen and less MMP content.

High Tibial Osteotomy (HTO) and orthoplasty: In a random control test, Dallari., *et al.* showed that grafted bone chips with platelet gels and MSC are considered as grafts, in which HTO contains high amounts of bone storage is. With the proper use of nanotechnology to create optimal implant surfaces, MSCs have a great potential to revolutionize joint replacement surgery by facilitating osteointegration. Three-dimensional scaffolding with MSCs can be used in the future to make autologous osteochondral grafts suitable for 'biologic' arthroplastic.

Avascular Necrosis

Avascular necrosis (AVN) of the femur head is one of the most debilitating disorders among young patients. Bone marrow aspirates have been administered after the core decompression in AVN. Stem cells were isolated and used in a study by Rastogi., *et al.* where 60 hips in early stages of AVN were randomized to be treated either with core decompression and bone marrow injection or with core decompression and injection of isolated stem cells. Two years later the stem cell group showed better functional results and improved radiographic treatment.

Wound healing

Although the orthopedic is not specific in practice, it usually has to deal with poor medical wounds in the treatment of patients with risks such as diabetes or open fracture. As a result of MSC treatment of acute and chronic lesions, accelerated epithelium, formation of granular tissue and accelerated wound closure with angiogenesis.

Tendon-ligament Injuries

It has been shown that MSCs promote early healing of the bone tendon interface by increasing the proportion of Sharpey's fibres. MSCs used with bone morphogenic protein 2 (BMP-2) are associated with improved biomechanical properties of the bone tendon interface, including rigidity and maximum load. A recent study by Adams., *et al.* demonstrated that rats with Achilles tendon tear treated with sutures carrying stem cells have greater resistance to failure and better histological properties. The unselected MSCs were used for ultrasound-guided injections in a series of cases of Pascual-Garrido and others for chronic patellar tendinopathy with good clinical results.

Anterior Cruciate Ligament Lesions: Mesenchymal stem cells and ACL fibroblasts are determined to have regenerative effects on anterior cruciate ligament lesions.

Medial Collateral Ligament Lesions: A study of Saether, *et al.* evaluated the effectiveness of MCSs in the treatment of medial collateral ligament (MCL) injury of rats and stated that primed MSCs resulted in less inflammation and provides high quality of healing in the short time period.

Pediatric Orthopedics

Osteogenesis Imperfecta (OI): is a heterogeneous group of diseases with abnormalities in type I collagen, which lead mainly to increased susceptibility to fractures, slow growth and loss of bone mass. The systemic infusion of allogeneic MSCs by Horwitz., *et al.* in six children with OI showed an improvement in the acceleration of bone mass and bone growth.

Physeal injuries: the formation of bony bridges is an adverse complication after a traumatic, infectious or other lesion in the physis, which leads to angular and/or longitudinal deformities. In a study with pigs, Planka., *et al.* showed that MSCs with scaffolds used in physical defects differentiated into chondrocytes forming hyaline cartilage and prevented the formation of bone bridges. Currently, there are no clinical studies to support this.

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Osteoporosis: Guan., et al. used modified MSCs to express certain surface proteins that allowed them to migrate to the periosteum, leading to increased formation of trabecular bone and bone mass. Concepts such as these are positive steps towards the use of MSC for a generalized disease such as osteoporosis.

Muscular dystrophies: are a group of conditions in which muscle fibers are replaced by fibrotic and adipose tissues, due to genetic mutations in several muscle proteins, which are essential for normal muscle function. There is no cure for these patients and the treatment focuses on comfort care, respiratory assistance and delay of loss of function. Local and systemic transplantation of well-differentiated myoblasts is associated with poor cell survival, limited migration from the site of injection and immunological rejection. In a Phase I clinical trial, Torrent et al showed that muscle derived stem cell-derived with specific surface markers was safely implanted in eight boys without any side effects. Genetically modified MSCs are being developed for possible use of these cells in muscular dystrophy.

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