

Regenerative Medicine to Enhance Orthopedic Surgical Outcomes



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COLUMN ARTICLE

Regenerative adjunctive treatment is the next logical step in the progression of surgical intervention. The new paradigm shift in stem cell research has been reflected in the field of orthopaedic indications with limited therapeutic approach which could be benefited using cellular therapy. The relative lack of blood supply as compared with other tissues make these structures incapable of quick healing like other body organs. Consequently, chronicity tends to become a hallmark of musculoskeletal injuries. Clinical use of stem cells have been used in cases of non-unions, avascular necrosis (AVN), spinal fusions, bone defects, tendon healing and cartilage repair etc.

Bone is an excellent tissue and the natural tendency of bone when fractured is to unite by forming bone. Non-union results from a gap at the fracture site resulting from bone loss. Non/delayed unions occur in approximately 5-20% of fractures and despite their regular occurrence, management remains challenging. They are defined as non-bridged areas after 6 months of periosteal and endosteal healing and results in severe functional impairment. The most common method to treat non-union has been bone grafting to provide osteo-inductive, osteo-conductive substrates and to supply osteo-progenitor cells. Bone grafting is considered as the gold standard procedure for non-unions. However, the autogenous bone grafting technique tends to produce donor site morbidity and use of allograft has the tendency to produce immunological reaction. Several studies have shown a promising effect of autologous bone marrow mononuclear

cells combined with allogenic bone graft for the repair of pseudo-arthritis of long bones. Bone marrow mononuclear cells (BMMNCs) comprise of progenitor and stem cells with pro-angiogenic and pro-osteogenic properties. The combination of autologous BMMNCs and allogenic or synthetic bone graft could constitute an easy, safe, inexpensive and efficacious attempt to treat long-bone pseudoarthrosis and non-union by reproducing the beneficial properties of autogenous bone grafting by reducing its limitations. Thus, stem cells are helpful in promoting union in cases of non-union fractures either used alone or in combination. Also percutaneous injection of mesenchymal stem cells (MSCs) has shown to promote union of non-unions bone fractures.

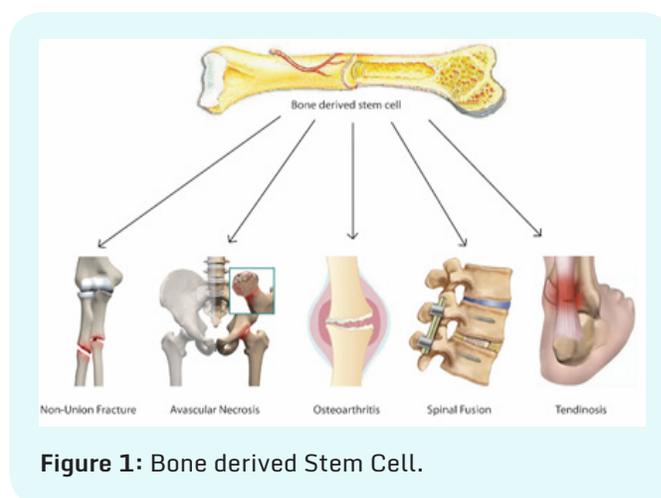


Figure 1: Bone derived Stem Cell.

Avascular necrosis of the femoral head is usually seen in patients following trauma, steroid intake, alcohol consumption etc. Loss of vascularity leads to the death of os-

teocytes present in the sub-chondral region and causes collapse of the femoral head that alters the femoral head shape and produces pain, flaccid, and movement restriction. Treatment options available till date primarily focus on core decompression, reducing the intra osseous pressure by drilling channels into the head through the neck if presented in early stage of the disease. MSCs have been applied for the re-growth of the dead area of the femoral head. Several studies have shown promising results using bone marrow concentrate injection, a common method of application to promote angiogenesis. Recent studies reported debridement, autogenous bone grafting and bone-marrow mononuclear cells implantation as an effective procedure in patients with small lesion, early-stage AVN of the femoral head. The concept of introducing osteo-progenitor cells into the area of dead bone seems logical. Limitation for the use of stem cells in this condition is the stage of presentation. Overall, with proper patient inclusion/exclusion criteria selection, the stem cells do appear to be a promising prospect for management of AVN of femoral head.

Cartilage defects as a result of its vascularity and once damaged the ability to repair on its own is very poor. Cartilage is considered to have minimal capacity to repair and approximately 15% of the world's population suffers from joint diseases. Current treatment management include drug therapy, arthroscopy, and joint replacement as well as autologous chondrocyte implantation (ACI). However, ACI requires the chondrocyte extraction from the patient that causes trauma to healthy articular cartilage. There is clinical evidences to demonstrate the repair of articular cartilage defects in the patello-femoral joint with expanded autologous bone marrow derived MSCs. Currently, research is being explored to demonstrate the potential use of MSCs with or without the combination of biodegradable scaffolds.

The treatment of osteoarthritis includes a wide spectrum of approaches. Currently with the exception of surgery, all other treatments are palliative that could relieve pain and increase function. However, on the basis of medical evidence, these treatments do not change the course of the disease. Surgical interventions, including joint replacement and osteotomy, reverse the progress of osteoarthritis and provide long term improved function and pain relief

for specific joints. Bone marrow derived progenitor cells including MSCs, Cytokines, growth factors and chemokines are well reported to demonstrate their roles in the control of the articular cartilage changes.

Tendons are one of the less vascular structures of the body and once injured, does not tend to heal quickly. This tendency of non-healing produces a condition called tendinosis. Platelet rich plasma (PRP) has been used for enhancing tendon healing that is rich in cytokines and growth factors which aims to heal of natural ligaments and tendons with a more biologic plausible tissue and to prevent the above complications. Generally, following a surgical procedure there is a void left behind in the bone. Such a scenario is seen in cases of benign bone tumours such as simple bone cysts for which curettage has been done and in cases where there is a bone defect. Although, autogenous bone graft may be used to fill up these voids, use of stem cells in conjugation with bone grafts has been done by investigators. Studies reported the use of stem cells for filling the voids in simple bone cysts with good results.

In the coming years, the incidence rate of musculo-skeletal disorder will raise exponentially causing healthcare and socioeconomic burden. Current treatment strategy is limited to the pain management followed by end-stage joint replacement and loss of functional movement. Cell-based therapies serve as an alternate biological option in the field of orthopaedics, as they could regenerate and restore the skeletal tissue function by exploiting the intrinsic stem cell-like capacity of progenitor cells to differentiate into bone and cartilage.

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