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Editorial

Efficacy and Safety of Fat-Derived Autologous Expanded Mesenchymal Stem Cell Therapy for the Management of Musculoskeletal Conditions: A 5-Year Experience

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Editorial

This editorial addresses the efficacy of single or repeated fat-derived autologous expanded Mesenchymal Stem Cell (MSC) therapy for orthopaedic conditions, specifically degenerative and injury-related joint and soft tissue disorders.

Over the last five years, we have tried MSC therapy for peripheral large and small joints in several hundreds of clients. Our process starts with rheumatologic consultation at the regenerative clinic to select suitable candidates for MSC therapy. We rule out active cancer and pregnancy. Next, the surgical team performs the fat harvesting process under local anaesthesia. We send the sample to our sterile biologic lab for culture-expansion of the MSCs to many millions based on the area (s) involved and the severity of the condition. The cells remain frozen until the MSCs implantation time.

Frequently, we treated the knee, hip, shoulder and ankle for Osteoarthritis (OA) secondary to the ageing “wear and tear” process or following an injury that led to an accelerated secondary OA [1-4]. We measured success rate based on symptoms control, quality of life improvement, stopping the progression of OA on radiological imaging, positive MRI findings of some repair and elimination of the need for joint replacement. Our finding suggested that 70-80% of cases

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had a good response to a single dose of expanded MSC therapy with long-lasting effects for at least 2-3 years. Around 20% of those patients elected for a second booster dose as the first dose did not control the symptoms completely; those cases indicated a better response to the second dose.

We found that when comparing pre-and post-treatment that MRI was more accurate than X-Ray, picking up subtle abnormalities like bone marrow oedema and subchondral cysts resolutions or meniscus signs of healing. In large joints, we found that the MSC therapy is more effective when combined with Platelet-Rich Plasma (PRP), as the latter has multiple growth factors that work as a scaffolding technique for the MSCs potentiation.

We have also implanted the MSCs in various other joints. Still, we found the success rate was lower, with the smaller joints at around 50-60%. These include elbows, radio-scaphoid, Scaphoid-Trapezius-Trapezoid (STT), 1st Carpometacarpal (CMC) and Metacarpophalangeal (MCP) joints. In lower limb mid-tarsal joints, Metatarsophalangeal (MTP) joints, particularly 1st MTP joint. We concluded from our investigational therapy that a lower PRP volume is more effective when used in smaller joints. Furthermore, when treating small hand joints, both Proximal and Distal Interphalangeal (PIP and DIP) joints. We observed eliminating PRP and letting expanded MSCs alone had a better outcome, indicating the use of concentrated MSCs is more effective; thus, we adapted such protocol as the usual technique for the small joints [5].

The other standpoint of our practice was dealing with injured or degenerative tendons, bursae and ligaments. We frequently treated shoulder rotator cuffs, gluteal tendon and bursa, Achilles tendon, common extensor origin of the elbow, anterior cruciate ligament, medial and lateral collateral ligaments, patellar tendon and pes anserine bursa. We concluded soft tissue pathologies respond better than cartilage defects, particularly rotator cuff tear (s); the response rate is around 80-90%. We described MRI evidence of complete resolution of full-thickness tear of the supraspinatus tendon with retraction in one case and significant improvement of weak and wasted calf muscle for many years after a previous Achilles tendon repair with a transplanted tendon [6-8]. We noted the clinical response rate following a single MSC therapy for a tendon tear is dramatic even in patients who did not have the improved radiological changes within a year of the 1st MSC treatment. Still, we did not do a series of scans due to the costs associated with additional investigations. The clients were satisfied with the good clinical response and improvement of quality of life, especially since up to 90% of those did not require surgical intervention.

We are aware of the challenges we face with cartilage and tendon repair due to the poor supply of those structures, saying that we still must do our best to find a way around that. MSCs could repair damaged tissues through various mechanisms, including direct contact and, more importantly, the cell signaling pathway (paracrine effect). Additionally, the cells can stimulate new blood vessel formation (neovascularization) and other effects of anti-inflammatory and local immune-mediated processes.

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We noted non-responders to the first dose did not achieve a good result in the second dose either when we repeated the same technique; thus, we had to modify the procedure.

Non-responders are in dilemma and restrict the progress with MSC therapy because they create inconsistency in the clinical outcome [9]. We have studied our patients carefully combined with the other literature about non-responders and we concluded a few issues to address as below:

1. The origin of pain: this should identify the source before initiating the process; if the pain continues after the MSC therapy, it could lead to a non-response label. The best example is hip joint osteoarthritis pain versus gluteal bursitis/tendinosis and knee osteoarthritis versus collateral ligament pathology. To solve that issue, we need to recognize the origin of pain. We noticed the same problem had been detected in patients who underwent joint replacement but still get peri-articular soft tissue pain
2. The severity of the OA: the bone-on-bone disease might lead to treatment failure, given no room for cartilage healing. Thus, we recommend prompt early treatment with MSC therapy for a favourable outcome
3. Advance age: traditionally, the MSC therapy works better for younger people because the implanted cells are more actively replicating and differentiating, saying that we have seen sound effects in older people when they are still fit and have a healthy life
4. Overweight: This places more mechanical pressure on the weight-bearing joints. In general, being overweight has been linked to leptin hormone tissue resistance with the metabolic acceleration of the degenerative process; thus, weight reduction would improve the clinical response to MSC therapy
5. Non-tuned cells: We use the same protocol for each case treated, whether it is degenerative pathology, tissue tear, or non-musculoskeletal pathology. The best way to improve response is to modify the technique by getting tuned cells from powerful donor cells like Olympians. That requires ethical approval; thus, we are not using that practice and we believe this approach is good to consider for the future in the well-organized study
6. Genetic factors: there is a genetic variation in response to regenerative medicine, which can be solved in the future by studying patients' blood samples using Mixed Lymphocytic Reaction (MLR) to give us an idea about the individual cases
7. Medical and social background: we feel the MSCs therapy is more effective in fit and healthy individuals with no significant low platelet or white cell counts. Athletics have a better outcome. A healthy diet and good hydration have a positive effect. Prolonged fasting can stimulate stem cell function

Excessive alcohol intake and Non-Steroidal Anti-Inflammatory Medicines (NSAIDs) around the time of stem cell therapy inhibits both MSC therapy and PRP effects.

We believe non-responders should be treated with some challenges by culturing a higher number of MSCs, viability testing throughout the process, achieving a high confluence rate in

culture and adding more scaffold (hydrogel) to the PRP like hyaluronic acid, plasma-derived exosomes (micro-RNA particles), or collagen by trying our best to overcome the poor response to the standard MSC therapy.

The safety of autologous MSCs has been tested in the clinical literature. Those discussions occur during the clinical assessment and we go through pros and cons of the investigational treatment [10- 13]. We have noted the same thus; in the worst-case scenario with no benefit to the patient, there is no harm in trying the therapy.

Our practical conclusion in the 5-year experience is as below:

Even if a stem cell-based therapy does not completely cure a disease, lowering its impact would be an immense economic gain at a global level and could significantly control patients' symptoms and improve their quality of life.

Conflict of Interest

The authors declare no conflict of interest.

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