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Review Article

Regenerative Treatment by Mesenchymal Stem cells (MSCs): The Alternative Treatment for Knee and Hip Osteoarthritis and Sport Injuries

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Abstract

Traditional methods to treat orthopedic disorders and diseases face difficulties in some cases which have no curative method of treatment. So, it depends on postponing the replacement of the joint in such cases like osteoarthritis and Avascular necrosis. Regenerative treatment aims to regenerate and rebuild the injured tissues instead of replacing them. Regenerative medicine depends on the use of stem cells because of their unique characteristics of duplicating and differentiating to other tissues. From this point, sources of stem cells were investigated and researched and comparison of sources reveilles that adipose derived stem cells were the most convenient and reliable source to regenerate musculoskeletal tissues, especially the cartilages and bones.

Adipose derived stem cells distinguished from other sources of stem cells by its easy and relatively safe way of extraction concurrently it is the richest source according to the available high quantity of fat in adult's body. Some special cases of Meniscal injury that compound with locked knee or complex tear require more than MSCs injection. So, Pre-SVF arthroscopy that joined a new technique of arthroscopy with MSCs from ADSCs in the type of stromal vascular fraction (SVF) will help to prepare the joint to receive MSCs in the best environment by saving the injured structures to maintain the nearest anatomical tissue positioning. So, MSCs can use all their abilities of regeneration for an effective rebuild of the tissues that can lead the joints to their nearest anatomical position like pre-injury.

This simple, minimally risky method of treatment by ADSCs for osteoarthritis and other orthopedic diseases considered the golden method of choice for sport injuries and the elderly patients who have osteoarthritis with chronic existing diseases, such as; hypertension, diabetes mellitus, ARDS, cardiac or any other problems that can be considered contraindications for the traditional methods of treatment like joint replacement. Whereas, the application of MSCs to treat the joints can be applied for all patients who are suitable and good candidates for this kind of therapy those who did not reach the severe advanced stage of osteoarthritis.

Keywords: *Regenerative Medicine; Stem Cells; Adipose Derived Stem Cells; Autologous Mesenchymal Stem Cells; Stromal Vascular Fraction; Meniscus Tear; Osteoarthritis; Pre-SVF Arthroscopy*

Overview

Osteoarthritis (aka degenerative arthritis) usually affects large, weight-bearing joints such as the hips and knees. Osteoarthritis is thus strongly linked to aging-related changes in this cartilage, and also linked to other causes, such as injury, overuse, overweight and genetics.

Physiological view

It is known that cells and tissues in the human body remain in balance between catabolic and anabolic processes. With aging, this balance may deflect to result in decrease of anabolic process. It is also known that stem cells (aka master cells) are responsible of anabolic processes of cells and tissues in the human body.

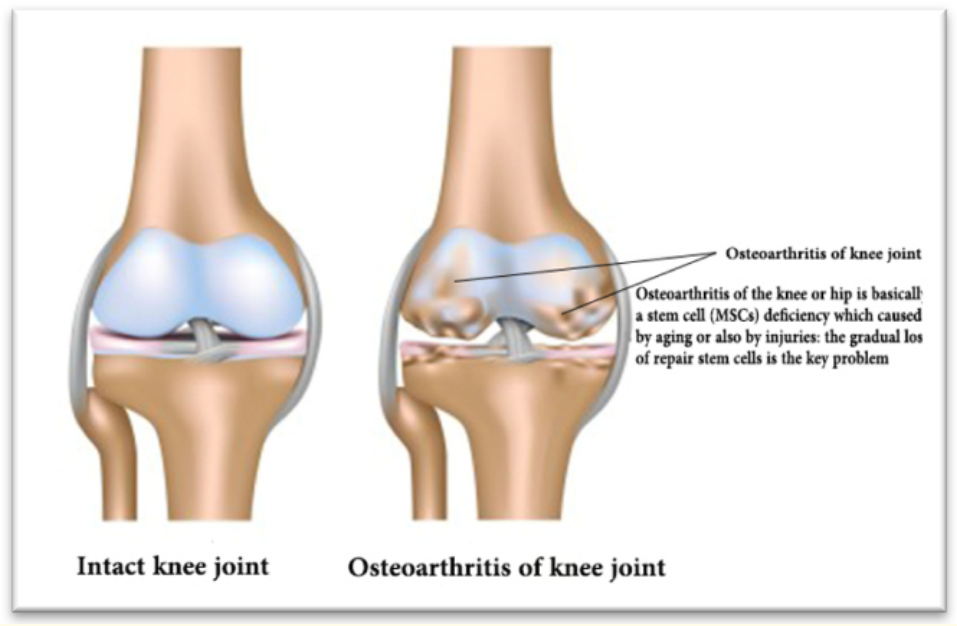

Figure 1: *Osteoarthritis of knee.*

As osteoarthritis of the knee and hip is basically a stem cell (MSCs) deficiency which caused by aging or also by injuries: the gradual loss of repair stem cells is the key problem. Thus, the most obvious, elegant and natural solution to a stem cell deficiency is renew and augment their numbers with fresh, new stem cells derived from the body's SVF. We address what is a stem cell deficiency by injecting and repopulating the joint with new stem cells: cells that naturally regenerate fresh, new tissues to replace the missing stem cells, and helping the body to maintain itself.

Mesenchymal stem cells (MSCs)

MSCs are multipotent stromal cells that can differentiate into a variety of cell types, including: osteoblasts (bone cells), chondrocytes (cartilage cells), and adipocytes (fat cells) and others.

Methods of extracting MSCs:

- Bone marrow: Mainly extracted from posterior superior iliac spine PSIS, this is the method to extract MSCs before discovering the method of extracting from adipose tissue.
- Umbilical cord blood: The blood that remains in the placenta and in the attached umbilical cord after childbirth.
- Adipose tissue: Considered the richest source of MSCs from the previous methods. Adipose tissue is obtained by liposuction procedure of the abdominal wall with local anesthesia, followed by centrifugation process to separate the fat tissues, followed by dismantling process and finally re-centrifugation process to obtain Stromal Vascular Fraction (SVF). This SVF is very rich with MSCs which is injected in the patient's joint.

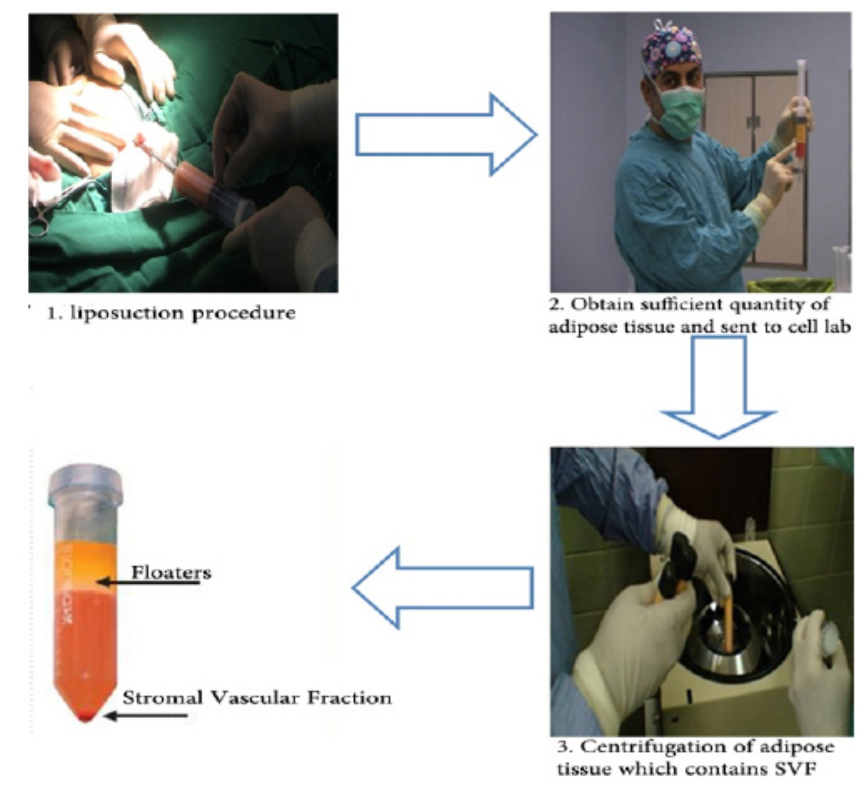

Figure 2: *Obtaining SVF from adipose tissue.*

Extracting MSCs from adipose tissue is the optimal method. Why?

1. No need for donor.
2. There is no possibility for the body to refuse the injected cell, because it is extracted from the patient.
3. There is no possibility for infection or virus/bacteria transaction.
4. Cell storage or cultural are not needed. MSCs are extracted from adipose tissue of the patient within few hours and inject it immediately.
5. Patient's body is rich of adipose tissue, and it is easy to obtain without making the patient facing any possible serious risks.
6. Adipose tissue is very rich of MSCs. 1g of adipose tissue contains 500 times more MSCs than 1g of bone marrow.
7. MSCs ratio inside the SVF is approximately 3% of the entire cells, which is 2,500 times more than the MSCs in the bone marrow.

Traditional treatment of knee and hip osteoarthritis

The traditional medical treatments aim to remove damaged cartilage by arthroscopy, provide lubrication with Hyaluronic acid, or use steroid to quiet pain and inflammation. Unfortunately, steroids will lead to a number of side effects with prolonged use. These treatment methods are considered “temporary” treatments; they buy time but do not restore or re-grow the damaged or injured cartilage. Sadly,

most of the patients who use these traditional, temporizing methods of treatment will live to see their condition worsened and may then be offered surgical placement of an artificial joint. Not a pretty picture…except of the terminal cases of osteoarthritis.

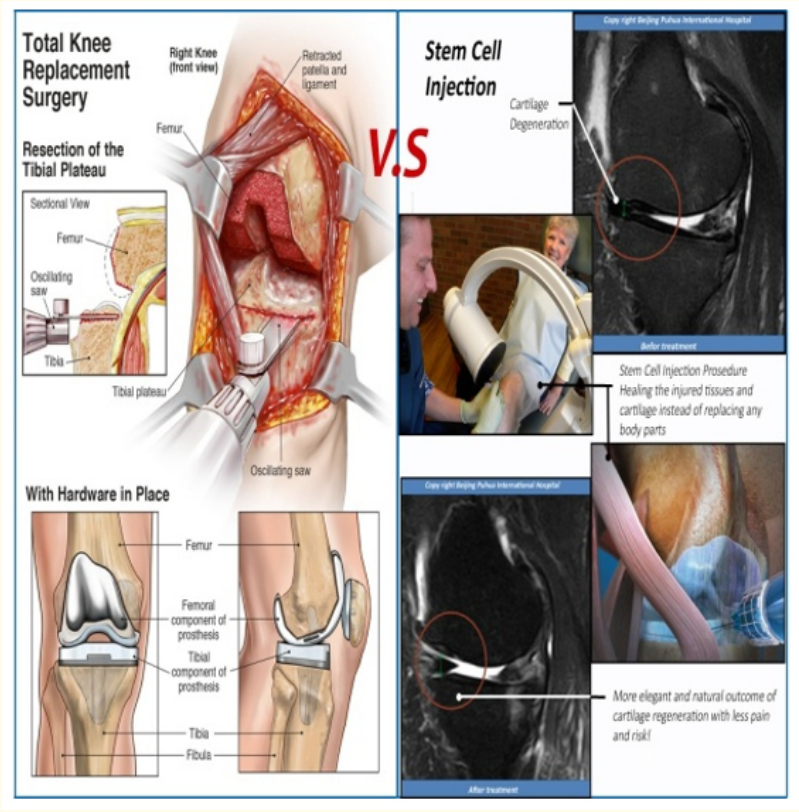

Figure 3: *Traditional treatment OR Regenerative treatment?*

The principle of regenerative medicine of knee and hip

Regenerative medicine is the process of replacing and renewing human stem cell lines to enable tissues and organs to restore and re-establish optimal function. By means of simple MSCs injections for the knee and hip we can prime the body to regenerate, or functionally heal, worn, damaged or injured cartilage and bone cell lines. This SVF (Stromal Vascular Fraction) is obtained by first extracting adipose tissue (fat), and then harvesting it for MSCs which are in the SVF. The refined SVF is injected into the knee or hip joint, and later injections of Platelet Rich Plasma (PRP) activate and stimulate the differentiation of MSCs (within the SVF) into producing new cartilage. The SVF obtained from 100cc adipose tissue contains around 40 million MSCs.

Cases can be treated with Stem Cell injections:

- Osteoarthritis: Knee, Hip, Ankle and other joints.
- Articular Cartilage Injury, Sport Injury.
- Meniscal Injury.

- Ligaments Injury.
- Nonunion fractures.
- Avascular Necrosis – AVN (?)

Regenerative treatment: An optimal and natural solution. Why?

The most obvious, elegant and natural solution to a shortage of repair stem cells is to replace them, to augment their numbers with new stem cells. In treating osteoarthritis of the knee or hip with repair stem cells, patients receive a safe, relatively painless procedure that has the potential to mitigate (perhaps indefinitely) against the need for potentially risky, and relatively painful hammer and chisel surgery.

Figure 4: *Knee and Hip injection process.*

Patients who follow this relatively simple treatment program generally begin to feel symptomatic relief within ~2 weeks, followed by long-term of cartilage regeneration. We can see the new cartilage growth by MRI comparison only 3 months after the procedure. This technique can thus be seen as optimal treatment for knee and hip arthritis. This procedure is extremely safe and does not entail any surgical risks or even involve general anesthesia. Thus, patients have moderate OA with advanced age, diabetes, hypertension and other medical issues are good candidates for this gentle and elegant treatment.

Regenerative treatment: The Pre-SVF arthroscopy

In some cases (such as severe osteoarthritis, or some sport injuries) the articular cartilage increase its area in order to decrease pressure on the cartilage by building Osteophytes, which limit the mechanical movement of the joint. In addition, the loose bodies which fell from destroyed cartilage will be locked inside the joint and harm the articular cartilage while movement. As well as in some sport injuries

which result with severe tear of the meniscus or partial tear of ligaments. In these special cases patients are advised to receive Pre-SVF Arthroscopy procedure, which considered being the optimal solution for these cases. By this procedure, we eliminate osteophytes and loose-bodies inside the joint which impede the joint's mechanical movement. This procedure prolongs the joint's lifetime and aim to restore almost the full function of the knee/hip joint.

It is known that pain and range of motion are the only indications for joint replacement surgeries. And as long as the above mentioned regenerative treatment success in treating pain and improve the range of motion, thus there is no need for the traditional joint replacement surgery! (Except some very special cases which are around 5%).

Replacement Surgery	Stem Cell Injection
Surgical Incision	No surgery
General anesthesia	Local anesthesia
Inevitable loss of bone: tibia, femur and knee cap	Injection only; no bone or tissue loss
Placement of a mechanical prosthesis	Anatomy kept pristine
Extended recovery, more pain	Speedy return to normal function
Physical limitation of mechanical prosthesis	No prosthesis, no such limitations
Greater risks; surgery, post-operative and failure of metal.	Extremely low risks; safe procedure and opportunity for surgery anytime.

Table 1: *Comparison table replacement Vs. injection.*

The objective of arthroscopy before stem cell injection (Pre-SVF Arthroscopy):

- Immediate improvement of the symptoms related to the joint's range of motion after arthroscopy, which caused by (Impingement + Osteophytes).
- Removing the loose bodies which constantly harm the articular cartilage.
- Prepare the meniscus for regeneration process by simplifying the injury which prevents a future osteoarthritis of the articular cartilage.
- Clean the joint from the rotten tissues which may impact part of the stem cell effectiveness.
- Provide better environment for the stem cells to regenerate the cartilage and the injuries tissues [1-10].

Conclusion

The advanced regenerative treatment with the use of stem cells for orthopedic disorders is considered as revolution in the world of healthcare, which always aims to provide the most advanced technologies for the patients with the least risks, also provide better clinical results to improve the patient's quality of life. Patients who were partially (if not totally) rely on others for practicing their activities of daily living whether at home or work, now they become a productive member in the society and can practice their activities of daily living individually, without following the traditional major surgery which brings a high risks to patients.

The Pre-SVF Arthroscopy has been proven its success and effectiveness in the fast recovery time clinically after the procedure within few days, which can be seen in the improvements of the joint's range of motion, pain relief, and returning to the previous daily life habits without rely on pain killers or other medications. It is also worth to mention that stem cells can continue the regenerative process for the

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