ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

Role of platelet mediated release of growth factors on stem cells in the regeneration and repair of the damaged tissue

***Parveen N[1], Ishaq M[1] and Zakia Abid[2]**

1. Salar-e-Millat Sultan Salahuddin Owaisi Research centre, PEH, Deccan College of Medical Sciences.

2. Department of Pathology, Deccan College of Medical Sciences.

Manuscript Info

Manuscript History:

Received: 11 November 2013
Final Accepted: 22 December 2013
Published Online: January 2014

Key words:
Stem cells, Injury,
Orthopedics, PRP

Abstract

PRP and stem cells go hand in hand to repair and regenerate the damaged tissue. Stem cells are the seeds sown in the earth (site of injury) whereas PRP acts as a caretaker providing the necessary environment for the growth of the new tissue.

Introduction

Stem cell research is a new field that is advancing at an incredible pace with new discoveries being reported from all over the world. Scientists have looked for various approaches to use stem cells to replace cells and tissues that are damaged or diseased.

They are naturally occurring cells in the body that help to create new cells in existing healthy tissues. They provide enormous potential for appropriate tissue repair and renewal of damaged cells with cellular processes of self-renewing and transdifferentiating themselves into other specialized cells including heart, liver, bone, cartilage, nerve and other cells under appropriate conditions.

Adult stem cells are found within many tissues of the body where they function in tissue homeostasis and repair. They are derived from the patient's own fat tissue and bone marrow which eliminates the issues of rejection of tissue transplantation and unintended infectious agents that would be a potential risk for using tissue derived from another person.

Mesenchymal stem cell (MSC) plays a major role in the field of cell-based tissue engineering and regenerative medicine (Friedenstein AJ et al., 1974, Deans RJ et al., 2000 and Minguell JJ et al., 2000). MSCs are mesoderm-derived cells that reside in the stroma of solid organs and function as precursors of nonhematopoietic connective tissues. They are characterized by a high proliferative activity, self renewal capacity and low immunogenicity. These plastic adherent cells appear as spindle-like cells *in vitro* culture. When given or in the presence of appropriate stimuli, MSC are able to undergo multi-lineage differentiation especially towards mesodermal lineage such as bone, ligament, muscle, tendon, and joint surface and have the ability to home at sites of injured tissues where they can promote repair which made them feasible for targeted regenerative medicine (Figure 1).

Platelet-Rich Plasma (PRP)

The body's first response to tissue injury is to deliver platelet cells. Packed with growth factors platelets initiate repair and attract the critical assistance of stem cells by activating them to generate new, healthy tissue (Minguell JJ et al., 2000, Borrione P et al., 2010). Platelet-rich plasma (PRP) is an emerging biological tool in regenerative medicine. It has the significant advantage over other potential therapies in that it is autologous.

PRP therapy's natural healing process by providing required growth factors intensifies the body's efforts by delivering a higher concentration of platelets. The concentrated platelet rich plasma is injected into and around the

point of injury, jump-starting and significantly strengthening the body's natural healing signal. It has many potential uses in tissue regeneration by inducing proliferation and differentiation of stem cells in *vitro*, when added to cell-seeded constructs at the time of implantation, and also can be introduced alone to locally induce endogenous regeneration.

Other *in vitro* studies have confirmed that PRP enhances the proliferation of a variety of human cell types. There was increase in cell growth and synthesis of vascular endothelial growth factor in tendon cells when they were cultured along with the PRP. It induces the bone marrow stem cells especially MSC proliferation.

Pre-clinical studies showed that intra-articular PRP injection influences cartilage regeneration in all severities of knees in osteoarthritis (Yu W et al., 2011). In antigen-induced arthritis (AIA) model of knee joint, it was demonstrated that PRP attenuates the arthritic changes as assessed histologically and based on typical protein synthesis of typical inflammatory mediators in the synovial membrane and cartilage (Kwon DR et al., 2012).

Several studies have revealed the wound healing capacity of the PRP. It may be an alternative to surgery for patients with chronic elbow tendinosis, it improved the clinical outcome of the patients undergoing Achilles tendon repair surgery, and it improved wound healing in total knee replacements and rotator cuff tears treated surgically (Lippross S et al., 2011). PRP may help in initiating, enhancing, or accelerating the soft tissue healing (Spakova T et al., 2012). The proliferative activity of the mesenchymal stem cells increased significantly after incubation of the cells with plasma/thrombin/ calcium and platelet factors. Thrombin and calcium plays an important role in inducing the PRP to release the growth factors (PDGF, TGF, VEGF, IGF and EGF) when added to it (Petrungaro PS et al., 2001). Growth factors are involved in proliferation, differentiation of the cells and morphogenesis of the tissues and organs during embryogenesis and postnatal growth (Figure 2). Concentrated platelet factors preparation comprises not only the effect of one growth factor, but affects every special growth factor in the presence of other growth factors, resulting in a cascade of signals, leading to induction or enhancement of proliferation, differentiation and migration of the cells.

Platelet derived growth factor (PGDF) and Epidermal growth factor (EGF) are known to be mitogens for mesenchymal cells and endothelial cells which act as a differentiation factor for various cell lines. EGF alone or in combination with other cytokines is a mediator for wound healing processes (Bennett NT et al., 1993). The transforming growth factor-beta (TGF-ß) acts as chemoattractant and mitogen for fibroblasts, marrow stem cells and preosteoblast and it increases type I collagen production (Anitua E et al., 2004). Vascular endothelial growth factor (VEGF) stimulates angiogenesis resulting in the formation of new blood vessels (Staudenmaier, R et al., 2009). Insulin like growth factor (IGF) stimulates osteoblastic cell proliferation and differentiation (Ann Hoeben et al, 2004). It is well understood that the platelet rich plasma (PRP) and stem cells are rich in healing and growth factors. PRP may help in employing a few stem cells to the affected area; stem cell injection therapy is much more advanced. Stem cells are considered as the fountain of Youth where PRP nourishes and guide them to achieve their goal i.e., to repair and regenerate the damaged tissue. Thus platelet works as the supervisor and the stem cells as constructive workers. Therefore stem cells derived from autologous source combined with platelet rich plasma (PRP) injected within and around the site of injury (Figure 3) will be a budding, more powerful strategy for growth and repair of the damaged tissues in patients where the condition is not well managed by conventional medication.

Figure 1: Differentiation of the Mesenchymal stem cells

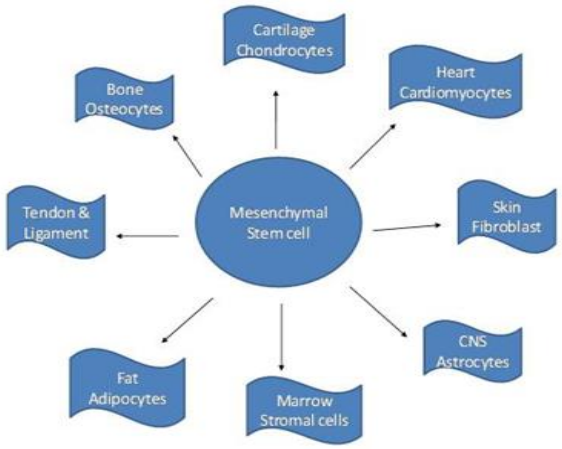


Figure 2: Release of various growth factors by the platelets

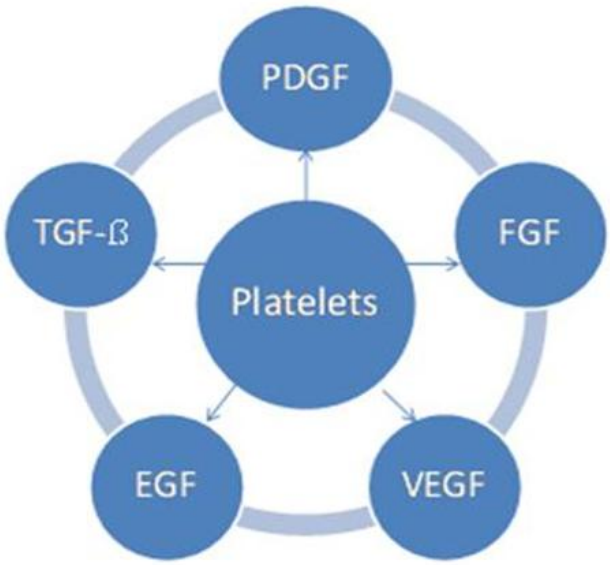
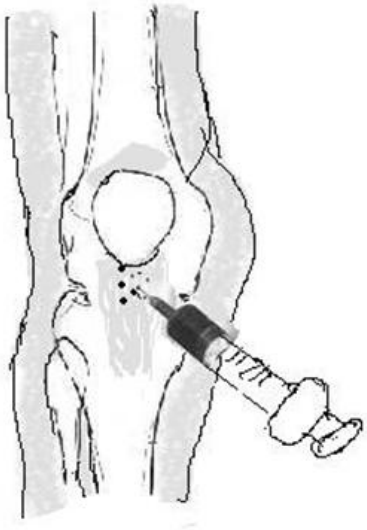


Figure 3: Injection the stem cells and PRP at the injury site



References

- Anitua E, Andia I, Ardanza B, Nurden P, Nurden AT Autologous platelets as a source of proteins for healing and tissue regeneration. Thromb Haemost 2004; 91:4-15.
- Ann Hoeben, Bart Landuyt, Martin S. Highley, et al. De Bruijn. Vascular Endothelial Growth Factor and Angiogenesis. Pharmacol Rev 56:549–580, 2004.
- Bennett NT, Schultz GS. Growth factors and wound healing: biochemical properties of growth factors and their receptors. Am J Surg 1993; 165:728-737.
- Borrione P, Gianfrancesco AD, Pereira MT, Pigozzi F: Platelet-rich plasma in muscle healing. Am J Phys Med Rehabil 2010, 89:854–861.
- Deans RJ, Moseley AB. Mesenchymal stem cells: biology and potential clinical use. *Exp Hematol* 2000; **28**: 875–884.
- Friedenstein AJ, Deriglazova UF, Kulagina NN, et al. Precursors for fibroblasts in different populations of hematopoietic cells as detected by the in vitro colony assay method. *Exp Hematol* 1974; **2**: 83–92.
- Kwon DR, Park GY, Lee SU: The effects of intra-articular platelet-rich plasma injection according to the severity of collagenase-induced knee osteoarthritis in a rabbit model. Ann Rehabil Med 2012, 36:458–465.
- Lippross S, Moeller B, Haas H,et al : Intraarticular injection of platelet-rich plasma reduces inflammation in a pig model of rheumatoid arthritis of the knee joint. Arthritis Rheum 2011, 63:3344–3353.
- Minguell JJ, Conget P, Erices A. Biology and clinical utilization of mesenchymal progenitor cells. *Braz J Med Biol Res* 2000; **33**:881–887.
- Petrungaro PS. Using platelet-rich plasma to accelerate soft tissue maturation in esthetic periodontal surgery. Compend Contin Educ Dent 2001; 22:729-732.
- Spakova T, Rosocha J, Lacko M, Harvanova D, Gharaibeh A: Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. Am J Phys Med Rehabil 2012, 91:411–417.
- Staudenmaier, R**,** Froelich, M. Birner, J. Kindermann et al. Optimization of Platelet Isolation and Extraction of Autogenous TGF-ß in Cartilage Tissue Engineering. Artificial Cells, Blood Substitutes and Biotechnology**.** December 2009, Vol. 37, No. 6 , Pages 265-272.
- Yu W, Wang J, Yin J: Platelet-rich plasma: a promising product for treatment of peripheral nerve regeneration after nerve injury. Int J Neurosci 2011, 121:176–180.