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Review Article

Role of platelet rich plasma gel in tissue regeneration- A review

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ABSTRACT

Objectives: Platelet-rich Plasma (PRP) has been used for over a decade in operative and regenerative (medical and dental) procedures, especially oral and maxillofacial surgery and periodontics to reinforce wound healing and aid in the regeneration of lost hard and soft tissue structures.
A reasonably priced method of healing post-surgery, the plasma (which is rich in growth factors and fibrinogen) is applied in a gel-like form directly on the surgical trauma site to encourage an increased rate of wound healing and bone regeneration. Due to it being an easy extraction (autogenic or allogenic) and a rather economic approach, it has been widely accepted in various cases ranging from dental implant surgery to simple tooth extractions. This article aims to review the literature available on PRP.
Sources from which data was obtained: 1. Case evaluations and literature available in various journals; 2. correspondence with dental surgeons; 3. First-hand observation of the procedure used for extraction of PRP from venous blood for an auto-graft.
Study Selection: Plasma containing high concentrates of growth factors (which includes insulin growth factor, epidermal growth factor, platelet 4 amongst many others) used in case reports as well as literature used in bone grafts and dental implant procedures were analyzed as well as clinicians performing the technique were observed.
Conclusion: Although possessed with multiple benefits such as quicker wound healing, cellular regeneration, and anti-bacterial and anti-inflammatory properties, lack of studies show it is still in its early infancy stages of clinical application. Further studies are needed so that doctors can correctly surmise which conditions need the application of plasma gel.

1. Introduction

"Proteins are the machinery of living tissue that builds the structures and carries out the chemical reactions necessary for life"-Michael Behe.[1]

A wound is caused due to trauma to the epidermal layer and is divided into cellular, humoral and molecular mechanisms. The three stages of healing are the inflammatory, proliferative, and remodeling stage. In a dental scenario, wounds could be a tooth socket from which a tooth was just extracted, dental implants, periodontal surgery amongst others. Several techniques are used to improve the regeneration process for wound healing such as bone grafts and bone substitutes. One of them is the plasma gel.

A crucial part of the hemostasis and wound healing process is the role of platelets in the bloodstream. It possesses multiple cytokines including growth factors which are namely:[2]

1. Three isomers (PDGF$\alpha\alpha$, PDGF$\beta\beta$ and PDGF$\alpha\beta$.
2. Transforming growth factors (TGF-β1 and TGF-β2.
3. Vascular endothelial growth factor (VEGF).
4. Insulin-like growth factor (IGF).
5. Epidermal growth factor (EGF).
6. Active substances- serotonin, antimicrobial proteins, von Willebran factor, osteonectin, catecholamine, etc.

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Platelet gels are biocompatible substances obtained from blood by various procedures to activate growth factors by thrombin/ calcium salts to produce a fibrin gel that is converted from fibrinogen. These gels are directly placed either directly on the wound or they are placed along with grafting materials. Being born of blood, they are biocompatible and physiologically sound that do not damage the tissues and cause necrosis.

1.1. How is Plasma Gel Made

There are various sources of obtaining the platelet cells such as:

1. From the patient's blood (Autologous blood sample)
2. Blood from different individuals but same species (Allogenic blood sample)

Platelet-rich Plasma (PRP) is collected by one of the following procedures:

1. The blood sample collected in tubes that don't contain anticoagulants and in sterile conditions are centrifuged to separate its erythrocytic components without lysing the platelet cells. The activated growth factors will not be secreted if there is any damage to the cells. Three layers are formed- erythrocytic coagulum in the bottom, a fibrin gel in the middle, and the serum on the top. The fibrin gel is placed on top of the membrane rich with platelet-rich fibrin.[3]
2. The platelet cell concentrate is mixed with thrombin and Ca-salt solution using glass beads (after centrifugation) which helps convert the fibrinogen present (by activating the plasma cells) into a fibrin gel or coagulum.[4] It takes up to 20 minutes for the plasma to activate for the formation of thrombin. Ethanol may be added to prevent thrombin decay.
3. Occasionally snake venom can also be used for direct activation of growth factors.[5]

Plasma gel is made in environmentally controlled sterile conditions in Petri dishes with calcium gluconate (10%). Gel formation can be seen forming 50 minutes after mixing and can be stored at -80 degrees Celsius for 15-30 days. After the mixing of platelet cells with thrombin is complete and the fiber gel is formed, it can be frozen and thawed within 20 -25 hours from the sample collection from donors.

Care should be taken that the gel is thawed 30 minutes before application at room temperature and should be used within thirty minutes of thawing.

1.2. Factors that affect the characteristics of plasma gel

Various factors are responsible for the quality and quantity of the gel:

1. Method of preparation of the gel (most important)[6]
2. Donor variability[7]
3. Amount of growth factor concentrate[8]
4. Amount of thrombin concentrate[9]
5. The potency of other activators[9]

1.3. Treatment procedure of gel application:[10]

The procedure can be carried out in hospitals and blood banks as long as they have the equipment. The concentrate of platelet concentrate should meet qualifying criteria for the procedure such as platelet count, donor variability amongst other variables. The most important factor is the preparation of plasma cells from a blood sample as it can impact:

1. Platelet count[11]
2. The concentration of growth factors activated[12]
3. Quantity and quality of proteins in the plasma[12]
4. Content of leucocytes, cytokines, and other molecules[13]

A verbal set of instructions is given to the patient, outlining the purpose and procedure of the plasma gel. After the patient is seated comfortably, the site of the application is made free of any granulation tissue and debris using curettes, irrigation with saline, and a saliva-free environment is established using ejectors or barriers. Around 20 ml or less venous blood is drawn from the patient and centrifuged for 60 seconds. After plasma gel is formed (refer to the procedure given in the above section). The gel is liberally applied directly to the graft site and a contact layer (non-absorbent) such as a GTR membrane or moisture permeable and an absorbent layer of cellulose strip is sutured covering it to keep the gel in place. The gel can be re-applied once or twice depending on the wound healing and the judgment of the clinician.

1.4. Properties of plasma gel

1. Antibacterial- some studies reveal that the gels secrete antibacterial activity against bacteria such as E Coli, K pneumonia, and pseudomonas. The extent and durability of the activity are to be investigated further.[14]
2. Cell growth in vitro- platelets when given growth medium help in the generation of chondrocytes, keratinocytes, and fibroblasts- all in vitro. Ex vivo, human stem cells are generated from adipose tissue, dental pulp, bone marrow. Studies show that if the platelet cells are not toxic, they help in tissue regeneration and healing in vivo.[15]
3. Anti-inflammatory – platelet gels help in decreasing pain and inflammation after the surgical procedure by decreasing the effects of interleukin factors, nuclear factors, and CXCR4 genes.[16]

4. The concentration of growth factors- multiple growth factors are activated for soft tissue regeneration such as PDGF$\alpha\alpha$, PDGF$\beta\beta$, and PDGF$\alpha\beta$, TGF-β1 and TGF-β2 amongst others.[17]

1.5. Advantages of using plasma gel in clinical setting

The following are some of the advantages of plasma gel which is why it is a success with clinicians:

1. Cold plasma is used as a treatment for severe burns as helps in cell regeneration and repair.[18]
2. Used in cases of ulcers, acute wounds, chronic wounds, and surgical inflammation.
3. Used in ocular and nerve lesions.
4. Used as filler material in case of plastic surgery and reconstructive surgery.
5. Used in the treatment of extractions, dental implants, and periodontal surgery.
6. Has anti-bacterial and anti-inflammatory properties.
7. Biocompatible and does not cause tissue necrosis.

1.6. Disadvantages of plasma gel

Although plasma gel is slowly getting incorporated into the world of clinical practice, there are a few disadvantages associated with it:

1. Although the chances of allergy are bare minimum due to plasma gel being made from the patient's blood, it may cause irritation, bleeding, or pain at the site of needle insertion.
2. It is usually not covered under medical/dental insurance.
3. Can carry a risk of virus transmission in case the blood sample is allogenic in nature.[19]
4. In case bovine thrombin is used for platelet activation,[20] it can cause transmission of diseases that are zoonotic.
5. The use of growth factors gives the chance of an increased risk of cancer (oncogenic side effects).[21]
6. Iatrogenic causes for contamination or failure of adequate grafting.

1.7. Clinical case observed and recorded

Chief complaint-A female patient, 65 years of age, wanted restoration of lost mandibular anterior teeth.

Tests Advised-Patient has advised an OPG, CBP, RBS, CT, BT tests, after studying the results; the patient was advised for implant surgery.

Treatment given-Four implants were to be placed in the regions 33,31,42,43.

The cortical plates lacked adequate thickness and height for non-aided implant placement and hence bone graft reinforced with PRP was utilized to enhance the prognosis of the surgery. 20 ml of venous blood was drawn and centrifuged for 1.5 minutes and a thick plate rich plasma condense was obtained. This was directly applied on the site of insertion of implants and secured with a cellulose membrane sutured on the buccal and occlusal portion.

Result- The implant osseointegrated within 3 months with a considerable increase in thickness of the mandibular cortical plate. When compared with a procedure that was done without the aid of PRP and bone graft, the results and period of osseointegration were subpar and the prognosis was average in the latter.

2. Conclusion

Platelet-rich plasma has been proven to be an efficient method for enhancing cellular regeneration, increasing the integrity of the healing tissues with its anti-bacterial and anti-inflammatory properties and ease of availability.

Application of this might result in increased prognosis after the surgical procedures, periodontal health and shorten the period of healing resulting in patient compliance and clinical turnover.

Although lack of equipment such as the centrifuge and surgical equipment in a general dental set up, patients fear of the procedure due to lack of awareness of such procedures in regular practice and inefficiency of the clinicians to practice these techniques might be why such procedures are still in their infancy stages of clinical application. Further studies are needed so that doctors can correctly surmise how and which conditions need the application of plasma gel.

3. Source of Funding

None.

4. Conflict of Interest

The authors declare that there is no conflict of interest.

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