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RESEARCH ARTICLE

PLATELET-RICH FIBRIN: A REVIEW.

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Abstract

Periodontitis is a chronic bacterial infection resulting in the destruction of the periodontal ligament, alveolar bone & supporting structures. Regeneration of the lost tissues has faced difficulties primarily due to the lack of support during the healing period. A surgical additive which can will help the healing process to a more predictable regenerative process is always on the wish list of any periodontist. Platelet-rich fibrin (PRF) is a second generation platelet concentrate that has been considered to be an important, easy to obtain, predictable surgical additive for periodontal regeneration. This autologous scaffold provides the much needed bio-chemical mediators which has the potential for enhancing reconstruction of the periodontium.

Introduction:-

The primary goal of periodontal treatment is the maintenance of the natural dentition in a healthy state with proper functioning. Regeneration has been defined as the reproduction or reconstitution of a lost or injured part to restore the architecture and functioning of the periodontium[1]. Growth factors are substance (proteins) capable of stimulating cellular growth, proliferation, healing, and cellular differentiation. Most of the growth factors are stored naturally in platelets and are secreted upon platelet activation giving the platelets a crucial role in wound healing and regeneration of injured tissues besides their haemostatic functions.[2] it was classified as a second generation platelet derivative, unlike PRP; PRF is a strictly autologous fibrin matrix containing a large quantity of platelets and leukocytes[1].

Classification of PRF Products:-

According to leukocyte content Dohan et al; classified PRF into pure PRF (P-PRP) or leucocyte poor PRF and leucocyte-rich PRF (L-PRF) [3].

Leukocyte-Poor Or Pure Platelet-Rich Fibrin (P-PRF) Concentrates :-

In this category, there is only one method available. The Fibrinet PRFM kit by Cascade Medical (New Jersey, USA). The company claims that the system produces a 'natural' platelet concentrate owing to the absence of bovine thrombin. However, doubts has been raised because the blood is mixed with anticoagulant and separation gel, leading to what could be considered unnatural conditions. This protocol is similar to other typical L-PRP protocols. The main difference is that only very low amounts of leucocytes are collected owing to the specific separator gel

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used in the method. However, the platelet collection efficiency is high and the preservation of the platelets during the procedure seems to be acceptable, but studies demonstrating the efficiency of Fibrinet PRFM are not yet available [3].

Leukocyte-rich PRF (L-PRF) Also named Choukroun's PRF, Advanced PRF (A-PRF), and commonly named PRF Membrane :-

Developed by Dohan & Choukroun[4]. The PRF Box (Process Ltd., Nice, France) is commercially available to prepare the PRF membrane. The PRF clot is placed on the grid in the PRF box and covered with compressor lid which squeezes out the fluid from the clot. The membranes formed using this method had constant thickness of 1mm which remains hydrated for several hours. The serum exudates are also collected under the grid for further use. The serum exudates expressed from the clot is rich in proteins such as vitronectin and vitronectin. These exudates may be used to hydrate graft materials, rinse the surgical site, and store autologous graft [5].

However, another alternative to obtain a PRF membrane developed by Raja et al,[6] is by pressing the clot between two gauzes thereby squeezing out the fluids in the fibrin clot. Toffler et al. showed that the PRF clot can also be slowly compressed in a cylinder in the PRF box with an opposing piston to obtain PRF plugs measuring 1 cm in diameter. Which can be used in socket preservation procedures.

Significance of PRF:-

Role of Fibrin Matrix:-

The three dimensional structure of the matrix resembles that of physiologic fibrin[7]. The enmeshed cytokines influence the extracellular matrix which allows migration, division and phenotypic change of endothelial cells, thus leading to angiogenesis.

Role of Platelets and Growth Factors:-

Periodontal regeneration is a multi-factorial and requires an orchestrated sequence of biological events including cell adhesion, migration, multiplication and differentiation[8]. The scientific rationale behind the use of platelet concentrates lies in the fact that the platelet α granules are a reservoir of many growth factors (GFs) that play a crucial role in hard and soft tissue repair mechanism[9,10]. Platelet growth factors exhibit chemotactic and mitogenic properties that promote and modulate cellular functions involved in tissue healing, cell proliferation and regeneration[10]

The growth factors released by α granule encompass a group of cytokine polypeptides with relatively low molecular weight ranging from 6-45kDa. PRF growth factors include Platelet derived growth factors (PDGFs), Transforming growth factor –β (TGF-β), Vascular endothelial growth factor (VEGF), Epidermal growth factor (EGF) and Insulin-like growth factor -1(IGF-1) [11].

PDGF:-

PDGF plays role in regulation, migration, proliferation and survival of mesenchymal cell lineages. It has mitogenic effects on stem cells and osteoblasts, stimulates pre-mitotic partially differentiated osteoprogenitor cells, stimulates cell replication of endothelial cells and promotes angiogenesis [12]. It modulates the effects of other growth factors and promotes perivascular healing of the wound.

TGF –β:-

Of the three isoforms TGF-β1 is the most significant. It is an inflammatory regulator and the most powerful fibrosis agent amongst all cytokines[12]. TGF-β1 and TGF-β2 activate fibroblasts, which undergo cell division and produce collagen[13]. They control cellular differentiation and proliferation of cementoblasts and activate osteoprogenitor cells and further differentiates them to produce bone matrix; activate endothelial cells to produce new capillaries.

VEGF:-

It is the most powerful and omnipresent known vascular growth factor. The main role is includes initiation of angiogenesis.

IGF -1:-
Although present mainly in plasma it exerts chemotactic effects towards human osteoblasts, regulates cell migration, proliferation, differentiation and matrix synthesis. Acts as cell multiplication mediators in apoptosis by inducing survival signals protecting cells.

Role of Leukocytes:-
Fibrin mesh provides natural immunity under the influence of fibrinogen degradation products (FDP) that stimulate the migration of neutrophils, modulates phagocytosis and enzymatic degradation of the neutrophils. Also chemotactic agents trapped in fibrin control wound colonization by macrophages[14]. Leukocytes trapped in PRF have antiinfectious effect and act as an immune regulation node. PRF contains all key immune cytokines like IL 1β, IL 6, IL 4 and TNF [14]. They have the ability to control the inflammatory response at the wound site.

PRF preparation:-
The advantages of PRF over PRP are its simplified preparation and lack of biochemical handling of the blood. The required quantity of blood is drawn in 10 ml test tubes without an anticoagulant and centrifuged immediately. Blood is centrifuged using a table top centrifuge (REMY Laboratories) for 12 minutes at 2,700 rpm [15]. The resultant product consists of the following three layers : ï Top most layer consisting of acellular PPP ï PRF clot in the middle ï RBCs at the bottom Because of the absence of an anticoagulant, blood begins to coagulate as soon as it comes in contact with the glass surface. Therefore, for successful preparation of PRF, speedy blood collection and immediate centrifugation before the clotting cascade is initiated, is absolutely essential. PRF can be obtained in the form of a membrane by squeezing out the fluids in the fibrin clot [15].

Table 1:- Cytokines present in PRF and their functions

	Cytokines present in PRF	Functions
1	Transforming growth factor-β(TGF-β)	(i) Released from α-granules of platelets (ii) Stimulates proliferation of osteoblasts (iii) Synthesis of collagen type I and fibronectin (iv) Enhanced woven bone formation (v) Enhanced chemotaxis of osteoblast cells (vi) Stimulates angiogenesis
2	Platelet-derived growth factor (PDGF)	(i) Migration and proliferation of mesenchymal lineage cells (ii) Angiogeniceffect on endothelial cells
3	Vascular endothelial growth factor (VEGF)	(i) Initiates angiogenesis
	Insulin growth factor-1 (IGF-1)	(i) Stimulates osteoblast proliferation[16] (ii) Chemotactic effects towards human osteoblasts (iii) Increased expression of osteocalcin (iv) Enhances wound healing
	Fibroblast growth factor (FGF)	(i) Stimulates osteoblast proliferation[16] (ii) Chemotactic effects towards human osteoblasts (iii) Increased expression of osteocalcin (iv) Enhances wound healing
	Epidermal growth factor (EGF)	(i) Stimulation of cell proliferation and extracellular matrix turnover [17] (ii) Chemotactic effect on periodontal fibroblast cells

Applications:-
The vast benefits of PRF have led to its applications in different fields of medicine and dentistry:
1. Ear, nose, throat and plastic surgery [48]
2. Oral and maxillofacial surgery, [21]
3. Pre-implant and implant surgery [49].

Conclusion:-

Platelet concentrates as a whole have shown to have great scope in the field of reconstructive and regenerative medicine and dentistry. And PRF being the more recent of the Platelet Derivatives is safer and simpler than the previous PRP concentrates hence they are easily used clinically. The healing and regenerative properties of the PRF are attributed to its basic fibrin composition. This autologous fibrin matrix has the ability to release cytokines over a period of 7-11 days along with the slower release of growth factors, which helps in reducing the healing time. The three-dimensional architecture of the fibrin matrix also helps in better wound healing by an efficient direct stem cell migration. Also the elastic nature of the fibrin matrix allows the clinician to manipulate the material according to the use. It also helps in reducing the shrinkage and necrosis of flap, maintenance of the flap in a stable position and wound coverage owing to the mechanical adhesive property of the fibrin matrix. PRF was found to accelerate endothelial, epithelial and endodermal regeneration along with neo-angiogenesis and enhanced collagen synthesis. In dentistry, they have been used most in conjuncture with membranes and grafts in cases relating to sinus augmentation, implants placement and endo-perio lesions (including intra-bony defects, gingival recession) and alveolar bone loss to increase the rate of healing and repair owing to the release of various growth factors such as PDGF and TGF.Therefore, animal and clinical studies investigating the ability for PRF to improve wound healing and new bone formation for future clinical benefit remain necessary.

Conflict Of Interest:-

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