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Titanium-Platelet Rich Fibrin

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ABSTRACT

Platelet Rich Fibrin (PRF) is the second generation platelet concentrate, developed first by Choukroun, et al. in PRF is a three-dimensional fibrin network that promotes accelerated wound healing, immunity and effective neovascularization, and it supports the three crucial steps of wound healing: 'angiogenesis', 'immunity' and 'epithelial proliferation'. In addition, PRF, an autogenous fibrin matrix formed only of concentrated blood, provides successful clinical outcomes for the treatment of soft-tissue defects and comparable keratinized tissue gain and tissue thickness when combined with connective tissue grafts. A newer platelet concentrate i.e. Titanium Activated PRF (T-PRF) is a 3rd generation platelet concentrate that helps in regeneration of tissue. Titanium-Prepared, Platelet-Rich Fibrin (T-PRF) was recently developed by Tunali, et al. that avoids any negative effects caused by dry glass or glass-coated plastic tubes. T-PRF plays an important role in increasing soft tissue thickness. T-PRF is promising, especially in soft and hard tissue augmentation, due to its fibrin structure, which is tighter than that of L-PRF, and it is prepared in Grade IV titanium tubes. It produces faster epithelization, less postoperative bleeding, and better wound healing than spontaneous healing. T-PRF also has osteoinductive properties similar to those of bone and preserves tissue volume. Histologically, with the hematoxylin and eosin staining, the fibrin matrix appeared homogeneous in light pink. T-PRF samples showed a highly organized network with continuous integrity compared to the PRF samples. Various treatment modalities such as Leucocyte Platelet Rich Fibrin (L-PRF), bone grafts and membranes, Wound healing, Periodontal regeneration, Guided bone regeneration, Sinus lifting, Peri-implant soft tissue. Titanium Prepared-Platelet Rich Fibrin (T-PRF) has gained attention due to its biocompatibility, thin fibrin meshwork and its long resorption time. This review article gives a brief idea about effectiveness of T-PRF in various dental treatments.

Key words: *Titanium prepared platelet rich fibrin, Angiogenesis, T-PRF, immunity, Epithelial proliferation, Osteoinduction*

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INTRODUCTION

Plasma, numerous types of cells and platelets make up blood (biologically-active cellular fragments). Thrombocytes are engaged with coagulation and help to stay away from exorbitant blood misfortune in venous wounds. They contain an assortment of cytokines and development factors that direct soft tissue maturation and bone regeneration [1]. These days, periodontal intervention healing is the focus of study. Periodontists are always looking for ways to improve the healing process after surgery through clinical advancements. Periodontists may meet complex tissue remodelling after a variety of procedures, with a variety of outcomes in terms of healing and tissue architecture. Platelet-rich concentrates, such as Platelet Rich Fibrin (PRF) and Platelet Rich Plasma (PRP), are relatively new approaches experimental tissue engineering. Ross et colleagues discovered platelets which contain growth factors which perform functions like accelerated cell mitosis, increased collagen formation, blood vessel expansion, cellular recruitment, and many other processes necessary in tissue healing in 1970's [2]. Platelet concentrates are concentrated solutions of platelet growth factors used as locally administered bioactive surgical additives to speed wound healing.

Biological intervention in regenerative therapies falls into three main categories.

- Gene therapy
- Tissue engineering
- Platelets have been shown to be an excellent site of signalling pathways like Platelet-derived growth factor, TGF, IGF in cell based therapy.

LITERATURE REVIEW

Evolution of Platelet Concentrates (PC)

Kingsley invented the term PRP in 1954 to describe normal platelet concentrate used in coagulation cascade studies [3] Matras was the first to introduce "Fibrin glue"

in 1970, which increased skin wound healing in rat models [4]. Between 1975 and 1978, a number of research publications called "fibrin mixes" proposed a better method for using blood concentrates.

PC was initially proven in 1986 by Knighton, et al. It was dubbed "Platelet Derived Wound Healing Factors" (PDWHF) and was helpful in treatment of percutaneous ulcers [5]. It was 1988 when terms "platelet-rich plasma" and "platelet-rich plasma" were used by Kingsley, et al. and Knighton, et al. in 1990, respectively. "PDWHF" stands for "platelet-derived wound healing formula" [6]. Whitman, et al. addressed the group in 1997. However, when the PRP was prepared; the final outcome seemed to have the cohesiveness of a fibrin gel. As a result, the researchers dubbed "platelet gel" [3].

The advancement of these techniques halted in 1998 until Marx, et al. published a paper that reignited interest in them. However, regardless of their content or architecture, all of these items were labelled as PRP, and this lack of language persisted for many years. Plasma with a increased concentrations of growth factor (PRGF), also known as a precursor for growth factors, is a type of plasma that contains a high concentration of growth factors, was introduced to the market in 1999 as one of the most widely used methods for creating pure platelet rich plasma on a large scale.

There were substantial challenges with this technique due to a lack of specialized pipetting stages as well as ergonomics. Choukroun, et al. developing a novel PC configuration known as PRF, France in the twenty-first century, according to robust polymerized of fibrin solution discovered as in case preparedness. It had been labelled as "2nd" platelet concentration production since it was clearly distinguishable by previous PRPs. It was a watershed moment in the advancement of nomenclature [7]. PRP, according to Bielecki, et al. and Cieslik-Bielecka, et al, is inactive, whereas PRG is a biologically stimulated thrombin array rich in platelets and leukocytes, as well as a relatively active chemical. Sacco proposed a novel CGF concept (concentrated growth factors [8].

This categorization recognized four core categories were divided on the product separation using two fundamental criteria: cellular substance (primarily leukocytes) and fibrin structures given by Dohan Ernest [9].

- Platelet Poor Platelet-rich Plasma (LP-PRP) or Platelet-rich plasma or Platelet-rich Plasma (P-PRP)
- Plasma with a high concentration of leukocytes and platelets (L-PRP)
- Pure PRF (P-PRF)-or PRF devoid of leukocytes; and [4] fibrin rich in leukocytes and platelets (L-PRF).

Sohn proposed the sticky bone concept in 2010. (Autologous fibrin glue mixed with bone graft) [10].

In 2012, Mishra, et al. proposed a new classification that was limited to PRP and only used in sports medicine. They discovered four types of PRP, each of which may be separated into two sub-categories depending over whether or not leukocytes are present but not if the PRP is stimulated:

Platelets (>5) baseline (A) or Platelets (5) baseline (B). PRP that has not been activated is referred to as "solution," whereas PRP that has been activated is referred to as "gel." Solution based on L-PRP; L-platelet rich plasma gel; P-platelet rich plasma solution; P-platelet rich plasma gel; Type 1: L-PRP solution; Type 2: L-PRP gel; Type 3: P-PRP solution; Type 4: P-PRP gel DeLong, et al. created a new, classification method known as PAW (Platelets amount, Stimulation phase, existence of WBCs) around the same time. However, it was again limited to platelet-rich plasma families as well as identical to Mishra et al classification's [11] Choukroun introduced APRF, an enhanced PRF, in 2014 [12]. Tunal, et al. introduced Ti-PRF, a novel product (Titanium prepared PRF) [13]. In 2015, a technical note on i-PRF preparation was released by Mouro, et al. [14].

Classification of platelet concentrations

- First generation-Plasma rich in growth factors
  - Platelet Rich Plasma (PRP)
- Second generation-Platelet Rich Fibrin (PRF)
  - Leucocyte Platelet Rich Fibrin (L-PRF)
  - Advanced Platelet Rich Fibrin (A-PRF)
  - Injectable Platelet Rich Fibrin (I-PRF)
  - Pure Platelet Rich Fibrin (P-PRF)
- Third generation-Titanium-Prepared Platelet Rich Fibrin (T-PRF).

Titanium Prepared Platelet Rich Fibrin (T-PRF)

T-PRF is an abbreviation for thrombin rich fibrin prepared with Ti. The method is built on the concept that Ti tubes are much more effective than glass tubes at stimulating clotting factors than Chouckroun's method [6,15-17]. The above substance would be used to eliminate long-term or short-term negative effects of Si issues, as well as parched glass or crystal plastic tubes. Researchers discovered that Ti-induced co-aggregation had been comparable to that of glass vials, and that clots formed in titanium pipes were equivalent. T-PRF has different properties, including better biocompatibility, because platelets are activated using titanium particles rather than silica particles.

Preparation: Blood tests from five rabbits were used for T-PRF procedures after the most appropriate T-PRF clot was experimentally formed (flocculation at 2700 revolutions per minute for 12 min) and scanned EM pictures were produced. Blood was drawn quickly and centrifuged at 2700 rpm for twelve minutes. Following centrifugation, droplets have been eliminated from the pipes with sterile tweezers, isolated from the RBC base, and squeezed between two portions of gauze. Under local anaesthesia, autologous T-PRF membranes were transplanted in sub periosteal flap. After 3, 5, 10, 15, and 1 month, the complete-thickness flaps was lifted with a passivation sub mucosal incision of the lower anterior teeth and 0.1 mm longitudinal incisions from the proximal region of the incisor. Seven millimetre and 7 mm full-thickness tissue samples were removed. A 200

mg/kg intravenous pentobarbital lethal dose due to which the rodents died. After extraction, the sample was placed in a 10% fixative for 24-72 hours (Table 1).

Applications

Various applications of TPRF is as follows

Table 1: Applications of TPRF.

Study	Aim	Methodology	Result
Uzun BC, et al. Clinical trial: 2018	To assess the productiveness of T-PRF in gingival recession.	Patients with Class I/II Gingival recession with abrasion defects had their clinical periodontal indices, epithelial tissue, gingival width, and recession depth measured prior to actually surgical procedure, as well as at 1-6 and twelve-month for review.	Gingival thickness and KTW were both increased by 93.29 with T-PRF; T-PRRF is both safe and effective.
Arabaci T, et al. A randomized split-mouth clinical study. 2018	To evaluate how GCF biological markers and periodontal outcomes were changed by T-PRF combined with open flap debridement (OFD).	People with periodontal diseases were managed by autologous Ti-PRF+OFD or Open flap debridement alone was compared on clinical measures.	OFD+Ti-PRF sites had majorly larger mean PD decreases, RAL gains, and GML changes than OFD sites. (P=0.033,P=0.029, P=0.026)
Mitra DK, et al. An *in vitro-in vivo* study. 2019	To compare the effects of titanium produced platelet rich fibrin on infrabony deformities (Titanium derived PRF).	Each group (Test group=T-PRF) and Control group=PRF, given ten sites at random. Clinical, radiographic, and histological parameters were evaluated.	Between baseline and nine months, both the groups showed a substantial reduced PPD and an increase in CAL in intragroup comparisons.
Valladao CA, et al. A backward-looking clinical study. 2020	To characterize the bone gain associated with GBR operations for vertical and horizontal bone augmentation that combine membranes, bone transplants, and PRF.	Study comprised individuals who required vertical or horizontal bone regeneration before receiving dental implants. CBCT measured bone gain at baseline and after 7.5 (1.0) months.	The maxilla gained more than mandible in horizontal deformities, and anterior portion gained more than posterior. There was no variation in vertical faults.
Ustaoglu G, et al. RCT. 2020	Contrast efficacy for T-Platelet Rich Fibrin, connective tissue transplant at peri-implant STT, CTG, KMW	This implant then inserted into thin tissue regions and thickened using a T-PRF around the same period. As in sample group, a barrier was used, whereas in the comparison group, a CTG was used. A periapical radiographs were used to evaluate the crestal bone alterations.	This control subjects showed a significant rise in peri-implant STT and KMW as compared to the sample group. No evidence of crestal bone loss was found.
Ustaoglu G, et al. RCT: 2020	To see how T-PRF compared into Open Flap Debridement (OFD) and GTR in Intra Bony Defects (IBDs) (GTR).	The Depth of Probing (PD), Clinical Attachment Level (CAL), and Inflammatory Bowel Disease (IBD) were all observed. The radiographic depth of IBD was also measured.	T-PRF was as successful as GTR for therapeutics outcomes of IBDs with endo-perio lesion.
Ortega-Mejia H, et al. A systematic review. 2020	The main purpose of this research was to evaluate how effective platelet concentrates for sinus augmentation were on their own.	A systematic review was conducted using PRISMA guidelines. Reviewer Editor program was used to do pooled assessment.	There were no supplemental positive benefits of PRF in sinus advancement in terms of bone height or proportion of soft tissue area, according to meta-analyses.

DISCUSSION

In 2001, Choukroun, et al. first developed Platelet Rich Fibrin (PRF) which is a 2nd generation platelet concentrate. Titanium activated Platelet Rich Fibrin (TPRF) is 3rd generation platelet concentrate. In recent studies, it is found useful in regeneration of tissues, faster epithelisation, better wound healing, periodontal regeneration and sinus lifting. It has been found that it has better bio-compatibility, thin fibrin meshwork, and long resorption time when compared to other generations of platelet concentration. T-PRF clot was experimentally formed on flocculation at 2700 revolutions per minute for 12 min. Uzun BC, et al. in the year 2018, did a clinical trial on Gingival recession and it resulted that T-PRF increased Gingival thickness and keratinization. Valladao CA, et al. in 2020 compared variation in vertical faults in maxilla and mandible, but no significant change observed. In 2018, Arabaci T, et al. proved that titanium rich platelet fibrin leads to RAL gains, GML changes. The above studies show the effectiveness of titanium platelet rich fibrin in various dental treatments nowadays.

CONCLUSION

L-PRF has been increasingly relevant in recent years, and it has been employed in a number of clinical trials. Our research will aid in the advancement L-platelet rich fibrin bio-compatibility and safety T-PRF is defined like an autogenously fibrin product rich in platelets and leukocytes a robust The fibrinogen web in this first *in vitro* study, although more *in vitro* and *in vivo* research is needed to determine its precise importance. T-PRF is found effective in wound healing, periodontal regeneration, guided bone regeneration, sinus lifting, and soft tissue regeneration around implants. We expect that T-PRF will become more frequently used especially then in the later expensive value of titanium tube preparing in contrast to glass tubes may be restricted its adoption. However, the T-Platelet Rich Fibrin is certainly an intriguing experimental products, as well as additional clinical trials are needed, T-Platelet Rich Fibrin metrics, like resorption duration as well as clinical success, were required.

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