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Clinical Application of Platelet-Rich Fibrin in Pediatric Dentistry

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Abstract

Platelet-rich fibrin (PRF) is a fibrin matrix in which platelet cytokines, growth factors, and cells are trapped and may be released after a certain time and that can serve as a resorbable membrane. It can be obtained from blood with the help of a simple process. PRF is basically a concentrate of growth factors that promote wound healing and regeneration, which is used in various disciplines of dentistry to repair various lesions and regenerate dental and oral tissues. Although the use of PRF is well-documented, its use in pediatric dentistry remains unexplored, due to its restrictions and on account of the fact that it is a blood-derived product. PRF has been used globally to enhance tissue healing. This article provides an insight into the use of PRF in pediatric dentistry, its benefits, limitations, and recommendations.

Keywords
- apexogenesis
- direct pulp capping
- regenerative endodontics
- scaffolds
- platelet-rich plasma

Introduction

Platelet-rich fibrin (PRF) has been used in dentistry for more than a decade now. Its application in pediatric dentistry can be vital, but it has not been explored. PRF is an autologous product that contains elevated levels of nonactivated, functional intact platelets within a fibrin matrix that releases a relatively constant concentration of growth factors over a few days. Immediately after drawing blood, it is centrifuged, and PRF is produced. It is vitally used in regeneration of hard tissue such as continued root formation, healing after disimpaction, and healing after soft-tissue damage such as gingival surgeries. The production of PRF is easy but the major concern arises in drawing blood from pediatric patients. PRF's application in pediatric dentistry varies from pulp capping and pulpotomy to apexogenesis and healing of extraction socket. Review of literature on the use of PRF in pediatric dentistry is sparse. Studies using bioactive materials containing host's endogenous growth factors represent a paradigm shift from the conservative clinical approach to more predictable regenerative solutions in dentistry.

Platelet-rich Fibrin

PRF is a bioactive surgical additive material prepared from the centrifuging patient's whole blood, a second-generation platelet concentrate described by Choukroun et al.[1] PRF is used to accelerate tissue healing. PRF is a simple and nonexpensive chairside process that results in a resorbable fibrin matrix, supplemented with rich platelets and leukocytes. It

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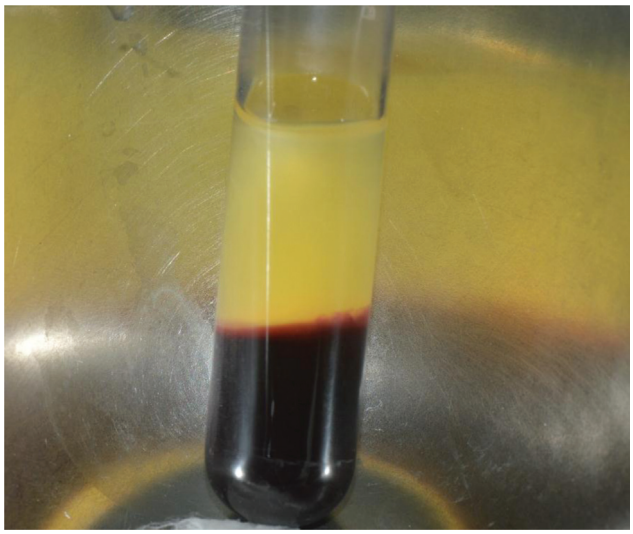

Fig. 1 Platelet-rich fibrin (PRF) in test tube after centrifuging showing platelet-poor plasma, PRF clot, and red blood cells (RBCs).

provides a rich source of growth factors, which includes platelet-derived growth factors, transforming growth factors, vascular endothelial growth factor, and insulin-like growth factor.[2] The growth factors are gradually released during the time of the healing. PRF is used in dentistry due to its unique healing potential.[3,4]

Preparation of PRF

Preparation for PRF production follows a standard protocol, as described by Choukroun et al.[1] A total of 5 mL of whole venous blood is drawn with anticoagulant in 10 mL tubes and immediately centrifuged at 3000 rotations per minute (rpm) for 10 minutes. The blood is contacted with the test tube wall during the centrifuging process, leading to the activation of platelets which, in turn, in turn initiate coagulation cascade. The resultant product will consist of three layers (►**Fig. 1**):

- Platelet-poor plasma.
- PRF clot.
- Red blood cells (RBCs).

Fig. 2 Platelet-rich fibrin (PRF) is squeezed between the sterile gauze pads.

Fibrinogen, which is concentrated on the higher part of the tube, is converted into fibrin by the circulating thrombin, thus the platelet-trapped fibrin clot is formed in the middle, RBCs at the bottom, and acellular plasma at the top. The PRF is then removed from the test tube using surgical tweezers and separated from other layers using sterile scissors. PRF is squeezed between the sterile gauze pads (►**Fig. 2**) to obtain a membranous film, which can be packed into the tooth for specific procedures.

Constituents of PRF

Growth factors released from PRF have been cited in ►**Table 1**.

Table 1 Growth factor cells present in PRF and their function[5,6]

Cells	Functions
Interleukin 1	Key moderator of inflammation control and stimulates T-helper lymphocytes
Interleukin 6	Activates B lymphocytes, stimulates secretion of antibodies
Interleukin 4	Aids in multiplication and differentiation of activated B lymphocytes. Aids healing by controlling inflammation
Tumor necrosis factor-α	Activates monocytes, stimulates remodeling capacities of fibroblasts
Cytokine vascular endothelial growth factor	Promotes angiogenesis
Platelet-derived growth factors	Maintains migration, multiplication and endurance of mesenchymal cell lineages
Insulin-like growth factor	Cell proliferation arbitrator in apoptosis, employs chemotactic results against human osteoblasts
Transforming growth factor β1	Triggers multiplication of fibroblasts and periodontal ligament cells, amplifies collagen manufacture
Vascular endothelial growth factor	Supports the cohesion of the endothelial cell lining of the blood vessel and stimulates neoangiogenesis throughout the wound healing
Fibroblast growth factor	Controls ectodermal origin cells and demonstrates chemotactic and mitogenic efforts on periodontal ligament fibroblast cells

Abbreviation: PRF, platelet-rich fibrin.

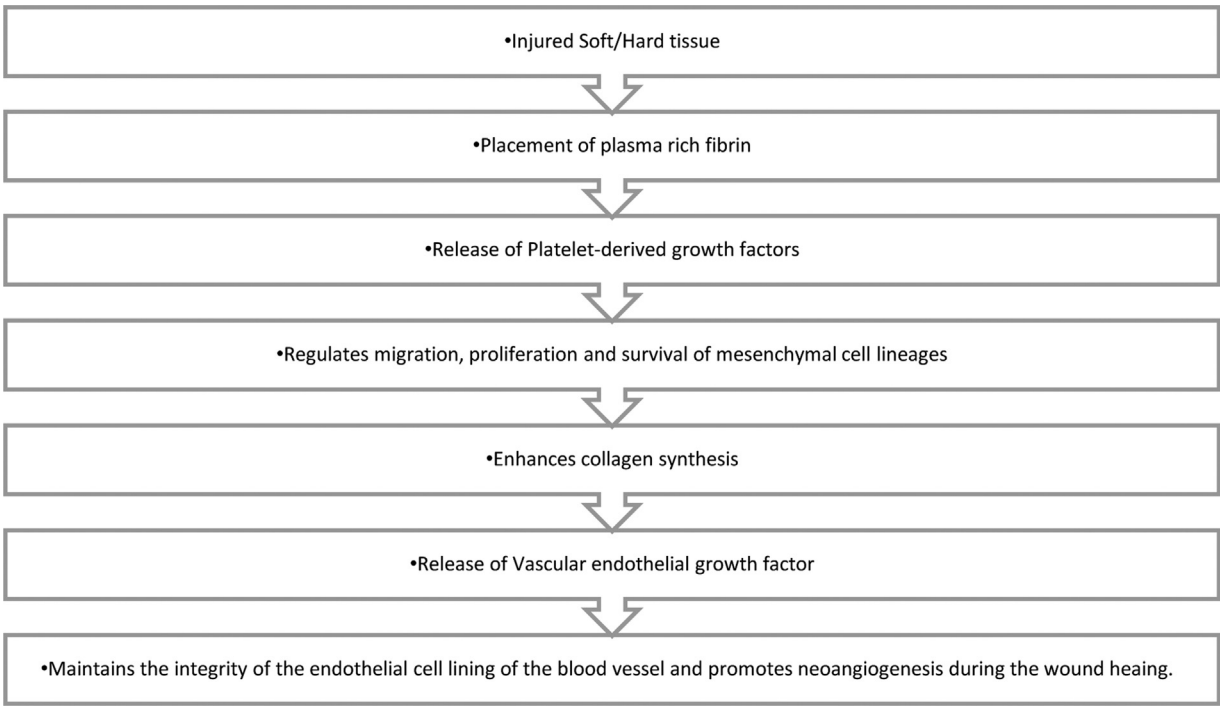

Fig. 3 Mechanism of action of platelet-rich fibrin (PRF) in wound healing.

Mechanism of Action

PRF aids in wound healing mainly through the action of growth factors,[5–10] which are present in abundance in it. A flowchart describing the series of action is given in ►**Fig. 3**.

Uses of PRF in Pediatric Dentistry

As Medicament in Pulpotomy

Patidar et al[11] conducted a clinical study evaluating PRF and mineral trioxide aggregate (MTA) as a pulpotomy medicament in primary molars. Clinical evaluation was done at 1-, 3- and 6-monthsintervals to check symptoms of pain, tenderness to percussion, soft-tissue swelling, pathologic mobility, and sinus formation. Radiological evaluation was performed at an interval of 6 months and considered successful if there was no furcal or periapical radiolucency, no canal calcification, and no internal and external resorption. The findings from this study revealed that PRF can be used successfully as an appropriate alternative material in pulpotomy of primary teeth. Manhas et al[12] in a clinical study evaluated and compared PRF as pulp dressing material in primary molar pulpotomy. The current study evaluates MTA, PRF + MTA, and PRF + Ca $(OH)_2$ as a pulpotomy medicament in primary molars at 1-, 3-, and 6-months followed by clinical and radiographic assessment. It was concluded that there is a favorable future for PRF in the specialty of deciduous tooth vital pulp therapy.

In Apexogenesis of Young Permanent Teeth

Mittal et al[13] evaluated the regenerative ability of PRF and artificial scaffolds in dying incomplete root development of permanent teeth, and observed that PRF and collagen are superior scaffolds to chitosan and placentrex for apexogenesis. Hongbing et al[14] conducted a retrospective controlled study and concluded that using PRF as scaffold for revascularization achieved similar results compared with the technique of inducing periapical bleeding with regard to the healing of the periapical lesion, continued root formation and resolution of clinical signs and symptoms.[15,16] A systematic review conducted by Miron et al[17] evaluated 7 in vitro, 11 in vivo, and 31 clinical studies. As much as 100% of the in vivo studies and 85.7% of the in vitro studies affirmed a statistically significant superiority for combining PRF with regenerative treatments. As much as 87% clinical studies suggested the use of PRF for the regeneration of tissues and wound healing for various treatment procedures in dentistry.[18,19]

As a Pulp Capping Material

According to Bakshi et al,[20] PRF showed promising results when used as a direct pulp capping medicament, compared with MTA. Dou et al[21] conducted a study to investigate the effect of $Ca(OH)_2$, MTA, iRoot BP, PRF and concentrated growth factors (CGF) on the proliferation, viability, apoptosis, and mineralization of human dental pulp cells and concluded that PRF and CGF are potential pulp-capping materials for vital pulp therapy. However, further studies on the potency of PRF and CGF as vital pulp-capping material and in vivo studies are necessary.[22–25]

For Surgical or Extraction Wound Closure

PRF is a well-known to have wound healing and regenerative properties, which can used to enhance the healing of surgical wound after cyst or any other defect that causes a large amount of bone loss. In such cases, PRF can be mixed with bone graft and can be packed to the surgical site, in order to enhance healing in children (►**Fig. 4**).[26–29]

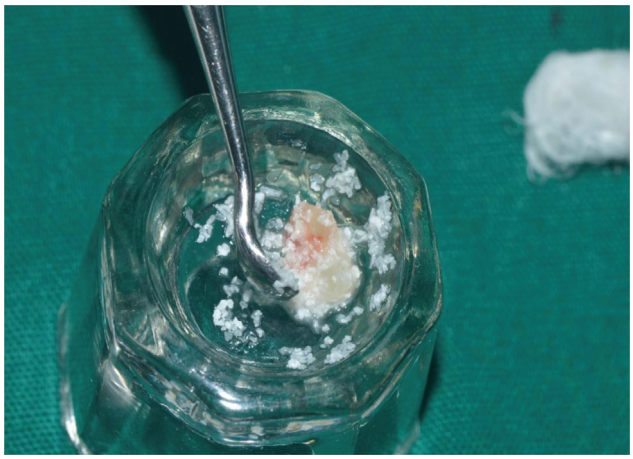

Fig. 4 Platelet-rich fibrin mixed with bone graft ready for loading in surgical site.

Limitation of PRF in Pediatric Dentistry

- PRF cannot be used to fill large defects in case of cysts. Since autologous blood sample is used to obtain PRF, the quantities produced are low.[30,31]
- Allogenic graft tissue is impractical, since PRF membranes are highly specific to the donor.[32,33]
- Preserving PRF is not feasible, as it will result in shrinkage due to dehydration and modification of the structural integrity as well as reduced growth factor content in PRF.[34]

Advantages of PRF

- No biological handling of blood.
- Simplified and cost-effective process.
- Anticoagulants not required.
- Favorable healing due to slow polymerization.
- More efficient cell migration and proliferation.
- PRF has supportive effect on immune system.

Disadvantages of PRF

- Amount available is low, because of autologous blood.
- Quick handling of blood is needed, immediately after collection.
- Drawing blood from pediatric patients is the major difficulty encountered in this procedure, since children are generally apprehensive to needles.

Conclusion

This article edifies the application of PRF in pediatric dentistry. PRF has been in use for over a decade in regenerative endodontics with an abundance of literature explaining its effectiveness; however, very less or few studies have been conducted on its use in primary dentition and young permanent teeth. Although PRF is found to be a promising material, there is vital need for clinical studies on the primary dentition to support its use, clinical efficacy, and long-term stability in pediatric patients.

Authors' Contributions
All the authors contributed equally to the study. S.G. made substantial contributions to conception and design and was involved in drafting the manuscript and revising it critically for important intellectual content. S.S. made substantial contributions to conception and design, acquisition of data, and analysis and interpretation of data, besides providing the final approval of the version to be published. S.B.M. made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data, besides providing the final approval of the version to be published. G.B. made substantial contributions to conception and design and revised it critically for important intellectual content. V.V. made substantial contributions to conception and design and revised it critically for important intellectual content.

Conflict of Interest
None declared.

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