ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 06, 2021

Platelet-Rich Fibrin Used in Regenerative Endodontics and Dentistry

Pankaj kr. Priyadarshi, Asheesh Sawhny, Richa Singh, Saurabh Sharma, Saurav Paul.

Rama Dental College Hospital & Research Centre, Rama University, Mandhana, Kanpur, Uttar Pradesh- India 209217

ABSTRACT

BACKGROUND

Many new procedures, including pulp implantation, revascularization, and postnatal stem cell therapy, have been made possible by regenerative endodontics. These days, revascularization is successfully applied in clinical settings, giving dentists amazing outcomes. When administered in conjunction with a bone transplant or alone, platelet-rich fibrin (PRF) stimulates bone development and vascularization.This matrix encourages osteoblast migration, cell adhesion, and proliferation, which results in the production of bone. PRF is a packed fibrin complex made up of leukocytes, cytokines, and glycoproteins like thrombospondin. High success rates have been recorded when using PRF in surgical instances such sinus lift surgeries, extraction socket healing, and periapical abscess therapy. PRF is more cost-effective, simpler to make, and practical to employ in routine clinical procedures than platelet-rich plasma. Revascularization made it more difficult to induce a blood clot in the root canal space, a clinical victory. This further led to the use of platelet concentrates as an autologous scaffold for revascularization.PRF has a wide range of uses in regenerative endodontics, including revascularization of young permanent teeth with necrotic pulps and repair of iatrogenic pulpal floor perforations. It serves as a matrix where new tissue can grow.

There was documented evidence of apical closure, root lengthening, regression in the periapical lesion, and gradual thickening of the dentinal walls. The current review seeks to examine the existing applications of PRF in regenerative endodontics dentistry and its application with future recommendations and limitations. More research is required to elucidate the specific mechanism of action of PRF for dental pulp regeneration both in vitro and in vivo.

INTRODUCTION

Regenerative procedures are those that use materials to promote the pulp dentin complex's healing and restoration after the infected or damaged tooth tissue has been restored [1]. Regenerative therapy in dentistry claims that this procedure can restore a missing tooth to its functional state. Many new procedures, including pulp implantation, revascularization, and postnatal stem cell therapy, have been made possible by regenerative endodontics. These days, revascularization is successfully applied in clinical settings, giving dentists astonishing outcomes [2]. Regenerative endodontics plays a crucial role in overcoming posttreatment problems and the increasing likelihood of root canal treatment failure). The goal is to prevent aggressive invasive instrumentation and radiographic exposure [3]. This is performed by the reimposition of β and T lymphocytes that aid in defense against the pathogens leading to pulp damage. The canal is completely sealed, and the vitality of the tooth is sustained, leading to

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 06, 2021

the prevention of tooth fracture and periapical reinfection [4]. Surgery is recognized to require healing, which is accomplished by a cascade of processes including extracellular matrix for tissue repair, chemical signaling, and cellular structuring [5]. When used alone or in conjunction with a bone transplant, platelet-rich fibrin stimulates the growth and vascularization of bone. Osteoblast migration, cell attachment, and proliferation are all facilitated by this matrix, which ultimately results in the production of new bone [6]. Cytokines generated by PRF are important for the development of blood vessels and for boosting the immune system's ability to combat foreign invaders [7]. Research indicates that PRF prepared at low centrifugal strengths has an effective concentration of growth factors and leukocytes comparable to that of PRF prepared at high centrifugal forces [8]. In patients with cleft alveolar ridge defects, a study has demonstrated the improved outcomes of PRF consumption in combination with iliac crest bone transplant; in contrast, results were comparatively unsatisfactory when iliac crest graft alone was employed [9]. Similar to this, an orthodontic surgery case was treated with metronidazole, bovine bone matrix, cancellous bone allograft, and PRF, which resulted in full healing with no complications [10]. Based on study results, the rejuvenation power of each replacement and its acceptance and suitability for the damaged tissue space are enhanced when PRF is paired with biomaterials. Proper assimilation of biomaterial is achieved through the development of cell-to-cell interaction by PRF [11]. The purpose of the current review is to examine PRF's applications in regenerative endodontics and dentistry, as well as its limits and potential future usage.

MATERIALS AND COMPOSITION

Platelet-rich fibrin (PRF), an unnatural biomechanical complex, is made from homologized plasma through the formation of a fibrin clot that results from centrifuging blood derived from humans. This clot later contains a large number of cytokines, growth factors, and platelets that are the product of a polymerization reaction; aside from this, no additional enzyme or anticoagulant is required for its production. The cytokines found in PRF that support osteoblast proliferation, angiogenesis, wound healing, and collagen formation include transforming growth factor-β (TGF-β), platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), insulin growth factor-1 (IGF-1), fibroblast growth factor (FGF), and epidermal growth factor (EGF) [5],

Classification of Plasma-Rich Fibrin

At first, the purpose of platelet concentrates in transfusion therapy was to treat and prevent bleeding caused by a variety of ailments. Fibrin glues were once used to seal wounds and encourage healing using blood-derived products.)Concentrated fibrinogen made up these fibrin glues [6]. The danger of contamination is decreased by autologous origin [7]. As a result, more research in the area led to the discovery that platelet concentrates might substitute fibrin glue; Whitman et al. [8] initially reported this substitution.

As a result, in 2001, platelet-rich fibrin (PRF) was presented as a technique for tissue regeneration in medicine [9].The first-generation platelet concentrate, or platelet-rich plasma (PRP), served as the inspiration for this approach. Despite the disadvantage of blocking the coagulation cascade due to an anticoagulant in the preparation, its effectiveness in a variety of medical sectors was amazing [10–12]. As development progressed, Leukocyte PRF (L-PRF) was created. The greater leukocyte count is the reason for its name. L-PRF has the extra advantage of not containing anticoagulants in its formulation, acting as a three-dimensional fibrin matrix that entraps growth factors [13–15]. Four categories were established for the classification of platelet concentrates based on the leukocyte and fibrin concentration [16].

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 06, 2021

1.Leucocyte-Poor or Pure Platelet-Rich Plasma (P-PRP).

Pure platelet concentrates were first developed for topical use as a supplemental application to the classical platelet units, and their first clinical implementation was reported in maxillofacial surgery [8, 17]. The method of producing platelet concentrates for topical use is called plasmapheresis, which requires a cell separator that separates the blood into different components such as platelets, leukocytes, and erythrocytes, which can then be used and readministered to the patient [18].

2.Leucocyte- and Platelet-Rich Plasma (L-PRP).

The main objective of creating a more practical and alternative approach was to use platelet concentrates in routine medical procedures without requiring a transfusion laboratory. At first, there were a lot of leucocytes in the product that was collected, and they were difficult to remove without a cell separator. But with more thorough testing, pure PRP (leucocyte free) could now be obtained because to the changed collection parameters. This technique's primary drawback is the necessity of purchasing pricey, sophisticated centrifuges and preparatory kits.
Moreover, the finished substance dissolves quickly, just like fibrin glue. As a result, L-PRP becomes rare for everyday use [19].

3. Leucocyte-Poor or Pure Platelet-Rich Fibrin (P-PRF)

To produce pure platelet-rich fibrin, a small quantity of blood is collected into a collection tube. After adding trisodium citrate as a separator gel and anticoagulant, the suspension is centrifuged at a high speed for six minutes.Platelet-poor plasma (PPP) and the separated buffy coat are put into a different tube. Centrifuged with calcium chloride. A stable clot is then gathered and put to use. Since bovine thrombin was not added, the business that created this technology stated that a "natural" platelet formulation is produced. These assertions, however, are dubious because the procedure uses synthetic substances (such as separator gel and anticoagulant) [19].

4. Leucocyte- and Platelet-Rich Fibrin (L-PRF)

Choukroun et al. developed a simple technique for producing L-PRF in France [20]. Venous blood is drawn into glass tubes and centrifuged at a low speed [21]. Platelet activation and polymerization of fibrin are instantaneous due to the absence of anticoagulants.)e PRF clot produced has several clinical applications in oral [22], maxillofacial surgery [23, 24], ENT [25], and plastic surgery [26].)is preparation has the advantage of gradual dissolution after application, and the three-dimensional fibrin mesh slowly remodels, corresponding to the physiological blood clot. Moreover, the technique is simple and efficient; higher quantities are obtainable, involving only natural constituents as reactants.)us, L-PRF is most appropriate for everyday practices, and many countries such as France, Israel, and Italy have already employed it [19].

MECHANISM OF ACTION OF PLATELET-RICH FIBRIN

A densely packed fibrin complex made up of leukocytes, cytokines, and glycoproteins such thrombospondin makes up PRF. Leukocytes have a crucial role in both the release of growth factors and the immune response in a compacted PRF scaffold. stimulation of tissue repair and this concentrated solution of platelets rich in growth factors promotes wound healing. By

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 06, 2021

inducing odontoblastic activity, transforming growth factor beta (TGF-β) quickens the process of reactionary dentinogenesis [27]. Infection and inflammatory cascades are inhibited by leukocytes, cytokines, and lymphocytes. Revascularization depends on angiogenesis, which is aided by vascular endothelial growth factor (VEGF) [28].

1. Role of Fibrin in Angiogenesis:

Cytokines including FGF, VEGF, angiopoietin, and PDGF get entrapped into the fibrin matrix's three-dimensional structure, resulting in a slowly progressing release, which is imperative in angiogenesis [29]. Fibrin causes the enhanced expression of αvβ3 integrin which stimulates the binding of endothelial cells to fibrin, fibronectin, and vitronectin [30].

2. Fibrin-Assisted Immune Response:

Adhesion to endothelial cells, fibrinogen, and the transmigration of neutrophils is aided by fibrin. Fibrin acts by heightening the expression of CD11c/CD18 receptors on endothelial cells [31]. The wound colonization by macrophages is modulated by fibrin and fibronectin.

3. Effect of Fibrin on Mesenchymal Stem Cells:

The fibrin matrix provides a scaffold for undifferentiated mesenchymal cells and promotes differentiation, imperative for tissue regeneration [22].

4. Effect of Fibrin on Osseous Tissue:

Similarly, fibrin also acts as a scaffold for bone morphogenic protein, and its sustained release from within the fibrin matrix induces bone formation. Steady release of VEGF, FGF, and PDGF promotes angiogenesis.)e circulating stem cells get entrapped into the fibrin clot resulting in hemostasis, thus enabling tissue restoration [32].

PRF in Dentistry

High success rates in surgical cases, like sinus lift surgeries, have been observed when PRF is used. In addition to wound healing, bone height and width are preserved. When situations When immediate implants are to be inserted, PRF and bone graft are known to have a synergistic effect and have been shown to play a major role in the extraction socket's quick healing. To achieve the clinical attachment loss, intrabony defects are treated with open flap debridement and PRF [33]. A case report states that a triple antibiotic paste was applied until the follow-up and that the canal of an avulsed tooth with a periapical abscess was shaped. In exchange, the canal was irrigated and the antibiotic paste was taken out. Revascularization was performed, and PRF was prepared and inserted in the canal, followed by biodentine and glass ionomer cement placement. After 6 months of follow-up, PRF helped in the apex's closure and repair and thickening of radicular dentin [34].

Platelet-Rich Fibrin in Regenerative Endodontics.

Dental caries and pulpitis, which affect over two-thirds of the world's population, are among the many disorders that call for endodontic intervention [35]. Furthermore, Children's oral trauma causes damage to the pulpal tissue; this is particularly concerning for developing teeth because there are few therapeutic options available when there is open apices [36]. However, the survival rate of the tooth has increased since the introduction of the revascularization

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 06, 2021

treatment approach. It has improved symptom management, and postoperative radiographs verify the completion of the physiological root [37].

Revascularization has historically made it more difficult to induce a blood clot in the root canal space [38, 39]. This has since been shown to be a clinical success.is ultimately directed toward platelet concentrates as an autologous scaffold for potential revascularization [40]. There are several uses for platelet-rich fibrin (PRF) in regenerative endodontics. When combined with MTA, it was utilized by Bains et al. as the agent for mending iatrogenic perforation of the pulpal floor of the mandibular first molar [41]. Since PRF provides a scaffold rich in growth factors, it is appropriate for revascularizing immature permanent teeth with necrotic pulps. This process enhances cellular proliferation and differentiation. For tissue ingrowth, it serves as a matrix [42].

Furthermore, the gradual release of growth factors as the fibrin matrix resorbs ensures a steady healing process [43]. Evidence of progressive thickening of dentinal walls, root lengthening, regression in the periapical lesion, and apical closure was reported by Shivashankar et al., following the use of PRF on a tooth with pulpal necrosis and open apex [44].

Similarly, autologous platelet-rich fibrin membrane used as an internal matrix and MTA used as an apical barrier allowed for effective healing and apexification, reported in [45] by B. Rugadi and Rudagi K. Furthermore, PRF induced a time-dependent increase in osteoprotegerin expression, elevation of alkaline phosphatase activity, and dental pulp cell proliferation [46]. Positive outcomes for pulpotomy with PRF in young permanent teeth have been documented [47]. Furthermore, a preferable therapeutic option for quick healing is to combine PRF with β-TCP, a biomaterial, rather than relying just on biomaterials for bone augmentation after treating periapical lesions [48]. Its radiographic and clinical bone regrowth is more consistent [49].

CONCLUSION

A major setback for clinical research on PRF is the difficulty and at times improbability of obtaining histologic evidence for its success. However, clinical and radiographic evaluations indicate a favourable tissue response to this material. When considering its versatility, ease of preparation and excellent biocompatibility, PRF may be regarded as a very valuable adjunct to endodontic procedures. Even though PRF is a member of a relatively novel class of platelet concentrates, its considerable cicatricial capacity can be explained by the fibrin molecule's biologic activity alone. The PRF membrane has a particularly advantageous physiological architecture to aid in the healing process because of the slow polymerization mode.

Further investigation into this biomaterial's platelet and inflammatory properties is now required, nevertheless. We won't be able to fully comprehend the clinical outcomes and thus expand the therapeutic application domains of this protocol unless we have a thorough comprehension of each of its constituent parts and their respective roles.

REFERENCES

[1] P. E. Murray, F. Garcia-Godoy, and K. M. Hargreaves, “Regenerative endodontics: a review of current status and a call for action,” Journal of Endodontics, vol. 33, no. 4, pp. 377–390, 2007.

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 06, 2021

[2] D. Johns, V. Shivashankar, S. Krishnamma, and M. Johns, "Use of photoactivated disinfection and platelet-rich fibrin in regenerative endodontics," Journal of Conservative Dentistry, vol. 17, no. 5, p. 487, 2014.

[3] N. Shah, A. Logani, U. Bhaskar, and V. Aggarwal, "Efficacy of revascularization to induce apexification/apexogensis in infected, nonvital, immature teeth: a pilot clinical study," Journal of Endodontics, vol. 34, no. 8, pp. 919–925, 2008.

[4] C. M. Sedgley and H. H. Messer, "Are endodontically treated teeth more brittle?" Journal of Endodontics, vol. 18, no. 7, pp. 332–335, 1992.

[5] S. V. Khiste and R. Naik Tari, "Platelet-rich fibrin as a biofuel for tissue regeneration," International Scholarly Research Notices, vol. 2013, Article ID 627367, 6 pages, 2013.

[6] H. Matras, "Die wirkungen vershiedener fibrinpraparate auf kontinuitat-strennungen der rattenhaut," Osterr Z Stomatol, vol. 67, no. 9, pp. 338–359, 1970.

[7] J. Gibble and P. Ness, "Fibrin glue: the perfect operative sealant?" Transfusion, vol. 30, no. 8, pp. 741–747, 1990.

[8] D. H. Whitman, R. L. Berry, and D. M. Green, "Platelet gel: an autologous alternative to fibrin glue with applications in oral and maxillofacial surgery," Journal of Oral and Maxillofacial Surgery, vol. 55, no. 11, pp. 1294–1299, 1997.

[9] J. Choukroun, F. Adda, C. Schoeffler, and A. Vervelle, "Opportunities in implant dentistry: PRF," Implantodontie, vol. 42, p. e62, 2001.

[10] G. Anfossi, M. Trovati, E. Mularoni, P. Massucco, G. Calcamuggi, and G. Emanuelli, "Influence of propranolol on platelet aggregation and thromboxane B2 production from platelet-rich plasma and whole blood," Prostaglandins, Leukotrienes and Essential Fatty Acids, vol. 36, no. 1, pp. 1–7, 1989.

[11] R. Fijnheer, R. Pietersz, D. Korte et al., "Platelet activation during preparation of platelet concentrates: a comparison of the platelet-rich plasma and the buffy coat methods," Transfusion, vol. 30, no. 7, pp. 634–638, 1990.

[12] R. E. Marx, "Platelet-rich plasma: evidence to support its use," Journal of Oral and Maxillofacial Surgery, vol. 62, no. 4, pp. 489–496, 2004.

[13] M. Toffler, "Guided bone regeneration (GBR) using cortical bone pins in combination with leukocyte- and platelet-rich fibrin (L-PRF)," Compendium of Continuing Education in Dentistry (Jamesburg, N. J.: 1995), vol. 35, no. 3, pp. 192–198, 2014.

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 06, 2021

[14] V. Lekovic, I. Milinkovic, Z. Aleksic et al., "Platelet-rich fibrin and bovine porous bone mineral vs. platelet-rich fibrin in the treatment of intrabony periodontal defects," Journal of Periodontal Research, vol. 47, no. 4, pp. 409–417, 2012.

[15] V. Y. Shivashankar, D. A. Johns, S. Vidyanath, and G. Sam, "Combination of platelet rich fibrin, hydroxyapatite and PRF membrane in the management of large inflammatory periapical lesion," Journal of Conservative Dentistry: JCD, vol. 16, no. 3, pp. 261–4, 2013.

[16] M. Del Corso, Z. Mazor, J. L. Rutkowski, and D. M. D. Ehrenfest, ")e use of leukocyte- and platelet-rich fibrin during immediate postextractive implantation and loading for the esthetic replacement of a fractured maxillary central incisor," Journal of Oral Implantology, vol. 38, no. 2, pp. 181–187, 2012.

[17] R. E. Marx, E. R. Carlson, R. M. Eichstaedt, S. R. Schimmele, J. E. Strauss, and K. R. Georgeff, "Platelet-rich plasma," Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology, vol. 85, no. 6, pp. 638–646, 1998.

[18] G. Weibrich, W. K. G. Kleis, G. Hafner, W. E. Hitzler, and W. Wagner, "Comparison of platelet, leukocyte, and growth factor levels in point-of-care platelet-enriched plasma, prepared using a modified curasan kit, with preparations received from a local blood bank," Clinical Oral Implants Research, vol. 14, no. 3, pp. 357–362, 2003.

[19] D. M. Dohan Ehrenfest, L. Rasmusson, and T. Albrektsson, "Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (LPRF)," Trends in Biotechnology, vol. 27, no. 3, pp. 158–167, 2009.

[20] B. Naik, P. Karunakar, M. Jayadev, and V. R. Marshal, "Role of platelet rich fibrin in wound healing: a critical review," Journal of conservative dentistry: JCD, vol. 16, no. 4, pp. 284–293, 2013.

[21] D. M. Dohan, M. Del Corso, and J. B. Charrier, "Cytotoxicity analyses of choukroun's platelet-rich fibrin (PRF) on a wide range of human cells: the answer to a commercial controversy," Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology, vol. 5, no. 103, pp. 587–593, 2007. 6 International Journal of Dentistry

[22] J. Choukroun, A. Diss, A. Simonpieri et al., "Platelet-rich fibrin (PRF): a second-generation platelet concentrate. part IV: clinical effects on tissue healing," Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology, vol. 101, no. 3, pp. e56–e60, 2006.

[23] J. Choukroun, A. Diss, A. Simonpieri et al., "Platelet-rich fibrin (PRF): a second-generation platelet concentrate. part V: histologic evaluations of PRF effects on bone allograft maturation in sinus lift," Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology, vol. 101, no. 3, pp. 299–303, 2006.

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 06, 2021

[24] A. Diss, D. M. Dohan, J. Mouhyi, and P. Mahler, “Osteotome sinus floor elevation using choukroun’s platelet-rich fibrin as grafting material: a 1-year prospective pilot study with microthreaded implants,” Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology, vol. 105, no. 5, pp. 572–579, 2008.

[25] J. I. Choukroun, F. Braccini, A. Diss, G. Giordano, P. Doglioli, and D. M. Dohan, “Influence of platelet rich fibrin (PRF) on proliferation of human preadipocytes and tympanic keratinocytes: a new opportunity in facial lipostructure (Coleman's technique) and tympanoplasty?” Revue de laryngologie-otologie-rhinologie, vol. 128, no. 1-2, pp. 27–32, 2007.

[26] F. Braccini and D. Dohan, “)e relevance of choukroun’s platelet rich fibrin (PRF) during facial aesthetic lipostructure (coleman’s technique): preliminary results,” Revue de Laryngologie Otologie Rhinologie, vol. 128, no. 4, pp. 255–260, 2007.

[27] A. J. Smith, P. E. Murray, A. J. Sloan, J. B. Matthews, and S. Zhao, “Trans-dentinal stimulation of tertiary dentinogenesis,”Advances in Dental Research, vol. 15, no. 1, pp. 51–54, 2001.

[28] M. Toffler, D. Holtzclaw, M. del Corso, and N. Toscano, “Introducing choukroun’s platelet rich fibrin (PRF) to the reconstructive surgery milieu,” Journal of Implant and Advanced Clinical Dentistry, vol. 1, no. 6, pp. 21–30, 2009.

[29] H. F. Dvorak, V. S. Harvey, P. Estrella, L. F. Brown, J. McDonagh, and A. M. Dvorak, “Fibrin containing gels induce angiogenesis. Implications for tumor stroma generation and wound healing,” Laboratory Investigation; a Journal of Technical Methods and Pathology, vol. 57, no. 6, pp. 673– 686, 1987.

[30] X. Feng, R. A. F. Clark, D. Galanakis, and M. G. Tonnesen, “Fibrin and collagen differentially regulate human dermal microvascular endothelial cell integrins: stabilization of αv/β3 mRNA by fibrin1,” Journal of Investigative Dermatology, vol. 113, no. 6, pp. 913–919, 1999.

[31] J. D. Loike, B. Sodeik, L. Cao et al., “CD11c/CD18 on neutrophils recognizes a domain at the N terminus of the A alpha chain of fibrinogen,” Proceedings of the National Academy of Sciences, vol. 88, no. 3, pp. 1044–1048, 1991.

[32] M. Kawamura and M. R. Urist, “Human fibrin is a physiologic delivery system for bone morphogenetic protein,” Clinical Orthopaedics and Related Research, no. 235, pp. 302–310, 1988.

[33] R. J. Miron, G. Zucchelli, M. A. Pikos et al., “Use of plateletrich fibrin in regenerative dentistry: a systematic review,” Clinical Oral Investigations, vol. 21, no. 6, pp. 1913–1927, 2017.

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 06, 2021

[34] H. Bakhtiar, S. Esmaeili, S. Fakhr Tabatabayi, M. R. Ellini, M. H. Nekoofar, and P. M. H. Dummer, "Second-generation platelet concentrate (platelet-rich fibrin) as a scaffold in regenerative endodontics: a case series," Journal of Endodontics, vol. 43, no. 3, pp. 401–408, 2017.

[35] T. Larsen and N. E. Fiehn, "Dental biofilm infections—an update," Apmis, vol. 125, no. 4, pp. 376–384, 2017.

[36] H. L. Ray Jr., J. Marcelino, R. Braga, R. Horwat, M. Lisien, and S. Khaliq, "Long-term follow up of revascularization using platelet-rich fibrin," Dental Traumatology, vol. 32, no. 1, pp. 80–84, 2016.

[37] T. Jeeruphan, J. Jantarat, K. Yanpiset, L. Suwannapan, P. Khewsawai, and K. M. Hargreaves, "Mahidol study 1: comparison of radiographic and survival outcomes of immature teeth treated with either regenerative endodontic or apexification methods: a retrospective study," Journal of Endodontics, vol. 38, no. 10, pp. 1330–1336, 2012.

[38] R. Y. Ding, G. S. P. Cheung, J. Chen, X. Z. Yin, Q. Q. Wang, and C. F. Zhang, "Pulp revascularization of immature teeth with apical periodontitis: a clinical study," Journal of Endodontics, vol. 35, no. 5, pp. 745–749, 2009.

[39] Z. C. Cehreli, B. Isbitiren, S. Sara, and G. Erbas, "Regenerative endodontic treatment (revascularization) of immature necrotic molars medicated with calcium hydroxide: a case series," Journal of Endodontics, vol. 37, no. 9, pp. 1327–1330, 2011.

[40] A. Nosrat, A. Seifi, and S. Asgary, "Regenerative endodontic treatment (revascularization) for necrotic immature permanent molars: a review and report of two cases with a new biomaterial," Journal of Endodontics, vol. 37, no. 4, pp. 562–567, 2011.

[41] R. Bains, V. K. Bains, K. Loomba, K. Verma, and A. Nasir, "Management of pulpal floor perforation and grade II Furcation involvement using mineral trioxide aggregate and platelet rich fibrin: a clinical report," Contemporary Clinical Dentistry, vol. 3, no. Suppl 2, pp. S223–S227, 2012.

[42] D. Keswani and R. K. Pandey, "Revascularization of an immature tooth with a necrotic pulp using platelet-rich fibrin: a case report," International Endodontic Journal, vol. 46, no. 11, pp. 1096–1104, 2013.

[43] A. Simonpieri, M. Del Corso, G. Sammartino, and D. M. Dohan Ehrenfest, the relevance of choukroun's platelet-rich fibrin and metronidazole during complex maxillary rehabilitations using bone allograft. part I: a new grafting protocol," Implant Dentistry, vol. 18, no. 2, pp. 102–111, 2009.

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 06, 2021

[44] V. Y. Shivashankar, D. A. Johns, S. Vidyanath, and M. R. Kumar, "Platelet rich fibrin in the revitalization of tooth with necrotic pulp and open apex," Journal of Conservative Dentistry: JCD, vol. 15, no. 4, pp. 395–8, 2012.

[45] K. Rudagi and B. Rudagi, "One-step apexification in immature tooth using grey mineral trioxide aggregate as an apical barrier and autologus platelet rich fibrin membrane as an internal matrix," Journal of Conservative Dentistry, vol. 15, no. 2, p. 196, 2012.

[46] F. M. Huang, S. F. Yang, J. H. Zhao, and Y. C. Chang, "Platelet-rich fibrin increases proliferation and differentiation of human dental pulp cells," Journal of Endodontics, vol. 36, no. 10, pp. 1628–1632, 2010.

[47] H. Hiremath, S. Saikalyan, S. S. Kulkarni, and V. Hiremath, "Second-generation platelet concentrate (PRF) as a pulpotomy medicament in a permanent molar with pulpitis: a case report," International Endodontic Journal, vol. 45, no. 1, pp. 105–112, 2012.

[48] B. J. Kim, T. K. Kwon, H. S. Baek et al., "A comparative study of the effectiveness of sinus bone grafting with recombinant human bone morphogenetic protein 2-coated tricalcium phosphate and platelet-rich fibrin-mixed tricalcium phosphate in rabbits," Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology, vol. 113, no. 5, pp. 583–592, 2012. International Journal of Dentistry 7

[49] K. Jayalakshmi, S. Agarwal, M. P. Singh, B. T. Vishwanath, A. Krishna, and R. Agarwal, "Platelet-rich fibrin with β-tricalcium phosphate—a noval approach for bone augmentation in chronic periapical lesion: a case report," Case Reports in Dentistry, vol. 2012, Article ID 902858, 6 pages, 2012.