Thrombosis & Haemostasis: Research

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Mini Review

The Effect of Platelet-Rich Fibrin on Bone Defects Repair in Experimental Animals: A Mini-Review

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Received: February 20, 2019; **Accepted:** March 23, 2019; **Published:** March 30, 2019

Abstract

Bone is a unique hard form of connective tissue as a result of its heavily calcified extra cellular components. Platelet-Rich Fibrin (PRF), a second generation platelet concentrate, becomes a powerful bioscaffold with an integrated reservoir of growth factors for tissue regeneration. Several studies showed that PRF has positive effect on soft and hard tissue regeneration. Here we present recent literature exploring the osteogenic effects of PRF alone or combined with other materials on bone defects healing in various animal models.

Introduction

Fibrin glue was the first blood-related product used in the surgical field, in the 1980s, and are commonly applied till now topically as hemostatic agent, and to improve wound healing and post-operative motion [1]. In the following years, Transforming Growth Factor β (TGF-β) in the platelets was discovered, and many studies were performed to study its effect on hard and soft tissue healing. In the 1990s, Platelet-Rich Plasma (PRP) began to be used in place of recombinant growth factors, as it is more cost effective than recombinant growth factors and contains higher concentration of platelets than fibrin glue, which resulted in higher benefits [2].

Platelet Rich Fibrin (PRF) was first described by Choukroun et al. (2001), and has been Known as a second generation platelet concentrate. PRF consists of fibrin mesh-work entrapping huge number of platelets, growth factors, and stem cells which acts as a biodegradable scaffold that enhances the development of micro-vascularization [3] and enables epithelial cell migration towards its surface [4].

The fibrin matrix of PRF is obtained as a result of slow polymerization. This matrix can hold many growth factors such as Platelet-Derived Growth Factors-AB (PDGF-AB), Transforming Growth Factor-β1 (TGF-β1), Vascular Endothelial Growth Factor (VEGF), Epidermal Growth Factor (EGF), and Insulin-Like Growth Factor-1 (IGF-1), and release them in the wound site gradually throughout prolonged period [5]. The growth factors present in PRF have been shown to promote fibroblast proliferation and accelerate bone repair. In addition, these factors increase tissue vascularity, the rate of collagen formation, and proliferation of mesenchymal stem cells, endothelial cells and osteoblasts. Several authors have also demonstrated that a fibrin matrix provides an optimal support for mesenchymal stem cells, which contribute to bone defects regeneration and of many other tissues [6].

Advantages of Platelet Rich Fibrin (PRF)

Platelet Rich Fibrin (PRF) preparation is easy and reliable, involving simple centrifugation [7]. It is obtained by autologous blood sample [8], unlike fibrin glue, it does not require the addition of external thrombin, and does not cause any immunological reaction [9]. It consists of natural fibrin framework with growth factors within that may keep their activity for a relatively longer period and stimulate tissue regeneration effectively [10]. It can be used as a sole filling materials in bone defects or in combination with bone grafts, depending on the purpose8. It is an economical and quick option compared with recombinant growth factors when used in conjunction with bone grafts [11]. PRF can be used in different forms as gel or as membrane [12]. Finally, studies used PRF reported it to be more efficient and with less controversies on the final clinical results when compared to PRP [7].

This review focused on the most recent researches that investigated the effect of PRF on bone regeneration on experimental animals, either used alone or in combination with other materials. Table 1 summarizes the recent researches involved PRF application including bone defects size and type of animal models, end point of the study, type of examination and the conclusions of the studies.

Conclusion

Although the limitation of Platelet rich fibrin that it should be used immediately after preparation to prevent contamination, PRF showed promising effect on bone regeneration either alone or combined with other osteogenic materials. Recent studies reported that PRF showed safe and promising results, without contradictory findings, and showed several advantages and possible indications for PRF to be used in the orthopedic field.

Recommendations

Further studies should be conducted to investigate the possibility of formulating PRF, so that it could be preserved for longer period of time before performing operations.

Citation: Raafat NS and Abdelkader IB. The Effect of Platelet-Rich Fibrin on Bone Defects Repair in Experimental Animals: A Mini-Review. Thromb Haemost Res. 2019; 3(1): 1022.

Table 1: Summary of the most recent researches involved PRF application in bone defects on experimental animals.

	Animals type and number	Bone defect place and size	Materials	End point	Examination method	Study results/conclusion
Zhou et al., 2019 [13]	36 rabbits	Mandibular defects each defect 1.0 x1.0 cm	PRF, autologous micro-morselized bone (autologous), PRF + autologous bone (combined)	2, 8, and 12 weeks	X-ray, electron microscopy, histologic, Cone-beam computed tomography, dual-energy x-ray absorptiometry.	In the PRF and autologous bone the defect area was smaller and filled with osteoporotic trabecular bone. The bone defect in the combined group showed better repair, increased bone mineral content, and denser callus than the other groups. PRF enhanced the effect of the autologous bone.
Cihan Dülgeroglu et al., 2019 [14]	16 Rats	Femoral fracture NA	platelet-rich fibrin	4 weeks	Radiographic and histological scores	The results indicated that platelet rich fibrin is an efficient biomaterial in fracture healing
Jeon et al., 2018 [15]	24 rabbits	Cranium each defect 15 ×15mm	Gelfoam, Gelfoam + nPRP, and PRF membrane	16 weeks	Computed tomography-autopsy, histological analysis.	Bone regeneration in the experimental groups was significantly greater than that in the control group (Gelfoam), suggesting that PRF might be a therapeutic alternative for bone grafts.
Salih et al., 2018 [16]	20 rabbits	Tibia each defect 1 cm	PRFM (membrane) PRFM + AgNPs (silver nanoparticles).	2, 4, 6, and 8 weeks	Radiographic, histopathological examination	PRF reduced healing time and brought a faster bone regeneration. Using a combination of PRFM and silver nanoparticles together gave better acceleration in the bone healing process than using each one of them separately.
Du et al., 2018 [17]	15 rats	Mandible each defect 2 mm x 2 mm	PRF, PRF+aspirin complex	12 weeks	2D/3D μCT, histomorpho-metry.	Both the PRF and PRF/aspirin complex enhanced periodontal bone formation. Aspirin could be sustained-released from PRF/aspirin complex, which caused significand decrease of inflammation and improve of mesenchymal cells function.
Raafat et al., 2018 [18]	48 rats	Tibiae each defect 3mm x 2 mm	PRF, SIM, and SIM+PRF combined	4 and 8 weeks	Histological, immunohisto-chemical, ELISA, digital X-ray	PRF enhanced the effect of SIM on bone regeneration, increased bone metabolic markers expression and enhanced bone mineral density when used in combination.
Horimizu et al., 2017 [19]	20 nude mice	Calvaria 4 mm in diameter	human□cultured alveolar bone□derived periosteal (hCP)+ (PRF)	4 weeks	μCT, histochemical and immunohistological	Platelet□rich fibrin enhanced new bone formation and local angiogenesis in the implantation site when combined with hCP.
Wang et al., 2017 [20]	15 rabbits	Cranium 15 mm in diameter	Mesenchymal Stem Cell (MSC) sheets with 100 mg nano-hydroxyapatite (nano HA) alone or combined with PRF.	8 weeks	Iconography, histological and histomorpho-metric	Combined application of a MSC sheet with nano-HA and granular PRF enhanced bone regeneration and could provide a novel approach for bone tissue regeneration in large bone defects.
Titirinli et al., 2017 [21]	10 rabbits	Mandible diameter of 4.5 mm and depth of 2 mm	PRF, APRF (altered PRF)	8 weeks	Histological	PRF and its variations have positive effects on the new bone tissue and cell number.
Popsuishapka et al., 2017 [22]	18 rabbits	Vertebra (L3, L4) diameter and depth of 3 mm	Platelet-rich fibrin	14 days, 1 and 3 months	Histological study	The introduction of platelet rich fibrin into the perforated defect of the vertebral body of the rabbits promoted bone formation 14 days and 1 month after injury.
Durmuşlar et al., 2016 [23]	40 diabetic rabbits.	Calvaria Bicortical defect, each 15 mm Calvaria Bicortical defect, each 15 mm in diameter	Autogenous bone, PRF, autogenous Autogenous bone, PRF, autogenous bone + PRF combined	4 weeks and 8 weeks	μCT, scanning, histological and histomorpho-metric analysis.	The amount of bone was highest in the combination group. PRF can be used safely and caused enhanced bone healing in diabetic rabbits.
Abdullah., 2016 [24]	45 rats	Calvaria diameter of 3 mm	PRF , PRF+β-TCP combined	1, 2, 3, 4, and 6 post-operative weeks	μCT	The combination significantly improved bone regeneration in the first 2 weeks after surgery. No significant effect was observed after 3, 4, 6 weeks

References

1. Thoms RJ, Marwin SE. The role of fibrin sealants in orthopaedic surgery. J Am Acad Orthop Surg. 2009; 17: 727-736.

2. Kökdere NN, Baykul T, Findik Y. The use of Platelet-Rich Fibrin (PRF) and PRF-mixed particulated autogenous bone graft in the treatment of bone defects: An experimental and histomorphometrical study. Dent Res J (Isfahan). 2015; 12: 418-424.

3. Najeeb S, Khurshid Z, Agwan MAS, Ansari SA, Zafar MS, Matinlinna JP.

Regenerative Potential of Platelet Rich Fibrin (PRF) for Curing Intrabony Periodontal Defects: A Systematic Review of Clinical Studies. Tissue Eng Regen Med. 2017; 14: 735-742.

4. Cortese A, Pantaleo G, Borri A, Caggiano M, Amato M. Platelet-Rich Fibrin (PRF) in implant dentistry in combination with new bone regenerative technique in elderly patients. Int J Surg Case Rep. 2016; 28: 52-56.

5. Su CY, Kuo YP, Tseng YH, Su C-H, Burnouf T. *In vitro* release of growth factors from Platelet-Rich Fibrin (PRF): a proposal to optimize the clinical applications of PRF. Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology. 2009; 108: 56-61.

6. Gassling V, Douglas T, Warnke PH, Açil Y, Wiltfang J, Becker ST. Platelet-rich fibrin membranes as scaffolds for periosteal tissue engineering. Clin Oral Implants Res. 2010; 21: 543-549.

7. Simonpieri A, Del Corso M, Vervelle A, Jimbo R, Inchingolo F, Sammartino G, et al. Current knowledge and perspectives for the use of Platelet-Rich Plasma (PRP) and Platelet-Rich Fibrin (PRF) in oral and maxillofacial surgery part 2: Bone graft, implant and reconstructive surgery. Curr Pharm Biotechnol. 2012; 13: 1231-1256.

8. Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, Dohan SL, et al. Platelet-Rich Fibrin (PRF): A second-generation platelet concentrate. Part IV: Clinical effects on tissue healing. Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology. 2006; 101: e56-e60.

9. Kang YH, Jeon SH, Park JY, Chung JH, Choung YH, Choung HW, et al. Platelet-rich fibrin is a Bioscaffold and reservoir of growth factors for tissue regeneration. Tissue Eng Part A. 2011; 17: 349-359.

10. Wu CL, Lee SS, Tsai CH, Lu KH, Zhao JH, Chang YC. Platelet-rich fibrin increases cell attachment, proliferation and collagen-related protein expression of human osteoblasts. Aust Dent J. 2012; 57: 207-212.

11. Girish RS, Bhat P, Nagesh KS, Bharthi M, Kharbhari L, Gangaprasad B. Bone regeneration in extraction sockets with autologous platelet rich fibrin gel. J Maxillofac Oral Surg. 2013; 12: 11-16.

12. Jankovic S, Aleksic Z, Klokkevold P, Lekovic V, Dimitrijevic B, Kenney EB. Use of platelet-rich fibrin membrane following treatment of gingival recession: a randomized clinical trial. Int J Periodontics Restorative Dent. 2012; 32: e41-e50.

13. Zhou T, Yang HW, Tian ZW, Wang Y, Tang XS, Hu JZ. Effect of Choukroun Platelet-Rich Fibrin Combined With Autologous Micro-Morselized Bone on the Repair of Mandibular Defects in Rabbits. J Oral Maxillofac Surg. 2018; 76: 221-228.

14. Dülgeroglu TC, MeTineren H, Metineren H. Evaluation of the Effect of Platelet-Rich Fibrin on Long Bone Healing: An Experimental Rat Model. Orthopedics. 2017; 40: e479-e484.

15. Jeon YR, Kim MJ, Kim YO, Roh TS, Lee WJ, Kang EH, et al. Scaffold Free Bone Regeneration Using Platelet-Rich Fibrin in Calvarial Defect Model. J Craniofac Surg. 2017; 29: 1.

16. Salih SI, Al-Falahi NH, Saliem AH, Abedsalih AN. Effectiveness of platelet-rich fibrin matrix treated with silver nanoparticles in fracture healing in rabbit model. Vet World. 2018; 11: 944-952.

17. Du J, Mei S, Guo L, Su Y, Wang H, Liu Y, et al. Platelet-rich fibrin/aspirin complex promotes alveolar bone regeneration in periodontal defect in rats. J Periodontal Res. 2018; 53: 47-56.

18. Raafat SN, Amin RM, Elmazar MM, Khattab MM, El-Khatib AS. The sole and combined effect of simvastatin and platelet rich fibrin as a filling material in induced bone defect in tibia of albino rats. Bone. 2018; 117: 60-69.

19. Horimizu M, Kubota T, Kawase T, Nagata M, Kobayashi M, Okuda K, et al. Synergistic effects of the combined use of human-cultured periosteal sheets and platelet-rich fibrin on bone regeneration: An animal study. Clin Exp Dent Res. 2017; 3: 134-141.

20. Wang X, Li G, Guo J, Yang L, Liu Y, Yu W. Hybrid composites of mesenchymal stem cell sheets, hydroxyapatite, and platelet-rich fibrin granules for bone regeneration in a rabbit calvarial critical-size defect model. Exp Ther Med. 2017; 13: 1891-1899.

21. Titirinli K, Tekin U, Atıl F, Onder ME. Evaluation of Advanced Platelet Rich Fibrin (A-PRF) on Bone Healing. Is It Better than Old Version? A Histological Animal Study. J Biomater Tissue Eng. 2017; 7: 478-483.

22. Popsuishapka K, Ashukina N, Radchenko V. Determination of the role of fibrin-enriched platelets in the process of regenerating the defect of the vertebral body (experimental study). Orthop Traumatol Prosthetics. 2017; 32-38.

23. Durmuşlar MC, Ballı U, Öngöz Dede F, Bozkurt Doğan Ş, Mısır AF, Barış E, et al. Evaluation of the effects of platelet-rich fibrin on bone regeneration in diabetic rabbits. J Cranio-Maxillofacial Surg. 2016; 44: 126-133.

24. Abdullah WA. Evaluation of bone regenerative capacity in rats claverial bone defect using platelet rich fibrin with and without beta tri calcium phosphate bone graft material. Saudi Dent J. 2016; 28: 109-117.

Thromb Haemost Res - Volume 3 Issue 1 - 2019
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