The role of platelet-rich fibrin (PRF) in periodontology

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ABSTRACT
Periodontal disease is characterized by the loss of attached connective tissue and other periodontal tissues. Growth factors secreted from platelets promote tissue formation and wound healing. Platelet-rich fibrin (PRF) is composed of fibrin, platelets leukocytes, and other cells that have a great role in different wounds healing processes. The aim of the current review was to highlight the role and mechanism of PRF usage in periodontal regeneration for periodontally affected teeth. A systematic search was made using an online database Medline to locate relevant peer-reviewed articles and textbooks published between 1990 and 2017 in English. Specific search keywords were used to obtain all possible articles concerned with the subject. We found 25 articles meeting our criteria and 20 of them which were specifically related to the subject were selected for final analysis. Few studies have focused on the role of PRF in periodontology, especially for periodontal regeneration and most of them were trials. PRF is considered a simple and inexpensive way for successful periodontal regeneration.

Keywords: Periodontal regeneration, platelet concentrate, platelet-rich fibrin.

Introduction
Periodontal disease is considered as a multifactorial disease that destroys the attached tissue and supporting bones which may lead to tooth loss. Periodontal disease is caused mainly by bacterial plaque. The aim of periodontal therapy is to remove the destructed inflamed tissues and regain healthy periodontal tissue [1]. Periodontal regeneration requires a multi-dependent orchestrated sequence of biological events, including cell adhesion, migration, proliferation, and differentiation. There are many ways and steps for periodontal tissue regeneration like root surface biomodifications, guided tissue regeneration, tissue grafts, and bone grafts [2]. But it is obvious that the previous regenerative therapies could only restore the original tissue volume [2] and had limited ability for restoring all healthy periodontal tissues. For treatment of intrabony defects and periodontal tissue regeneration, various biomaterials are used, in addition to autogenous and allogeneic bone grafts. Periodontal regeneration requires regaining all periodontal tissues (epithelial tissue, fibroblasts, periodontal ligament fibers, and osteoblasts) [3]. It has been found that during wound healing, platelets and cytokines aggregate within the fibrin clot and several growth factors are released into tissues from the platelets [4]. The presence of growth factors and cytokines in platelets has a great role in wound healing [5]. Platelets secrete fibrin, vitronectin, and fibronectin, which act as a matrix for the connective tissue. All of these indicate that the usage of platelets concentrates can play a potent role in periodontal tissue regeneration [6]. Platelet concentrates can be divided into two generations; the first is platelet-rich plasma (PRP) while the second is platelet-rich fibrin (PRF) [7].

Platelet-Rich Plasma
PRP is a type of platelet concentrate that can act as a source of growth factors which are important for wound healing and periodontal tissue regeneration. From the previous studies, it has been found that PRP accelerates the rate and degree of bone formation, so it could be used for treating intrabony defects and loss of periodontal bony tissues [8]. PRP can release various growth factors that have found to pose crucial chemotactic
and mitogenic effects promoting and modulating tissue healing, regeneration, and cell proliferation [9].

**Platelet-Rich Fibrin**

PRF consists mainly of fibrin matrix with a large number of platelets and leukocytes [10]. PRF was first prepared by Dr. Choukroun from the own patient blood specimen which was centrifuged without adding any anticoagulants or bovine thrombin or any other jellifying agents. PRF is usually dense, consisting of fibrin tissue, leukocytes, and platelets, which is characterized by releasing growth factors and cytokines at a slow rate during a period of 7 days [10]. On the contrary, PRP releases growth factors in large quantities over a short period of time [11].

**PRF Role in the Prevention of Infection**

For successful periodontal regeneration, the wound site should be kept out of infection. Leukocytes are considered the firewall for the wound against infection. Also, fibrin mesh characterized by its ability to modulate phagocytosis and enzymatic degradation of the neutrophils. Chemotactic agents which are trapped in the fibrin mesh can impair wound colonization by macrophages [12].

**Applications of PRF in Periodontology**

PRF is a biocompatible tissue which is totally autogenous material with a high ability for stimulation of tissue regeneration and wound healing. So, it is used in different modalities of periodontology such as treatment of furcations, periodontal intrabony defects, and sinus lifting [13]. It can also be used in the tissue engineering field like being a scaffold for human periosteal cells in vitro [14].

**Treatment Modalities used by PRF**

**Dry socket**

Dry socket is a multifactorial condition that may occur secondary to teeth extraction. It is characterized by an inflamed socket with severe pain. It usually occurs in wisdom teeth socket more than the other teeth. There are various treatment modalities for dry socket; one of them is PRF. Many studies have shown that PRF usage in dry socket has an analgesic effect and hence decreases the pain [15].

**Periodontal furcation**

Furcation defects are considered a hard area for treatment due to low accessibility and anatomy irregularity. So, this area is usually treated surgically to allow proper root planning, periodontal regeneration, and osseous recontouring [16]. This way for furcation treatment has shown great results, especially with early grade II furcation involvement. Periodontal regeneration can be enhanced using many regenerative procedures such as using many growth factors, guided tissue regeneration, bone graft, and PRF. PRF has many growth factors and cytokines that have to show great results in periodontal regeneration [16].

**Intrabony defects**

The periodontal pocket is one of the most common dental intrabony defects. It is a multifactorial condition characterized by a loss of periodontal attachment. PRF contains a lot of growth factors that when applied in the dental pocket can induce tissue regeneration and gingival attachment after 3–6 months [17].

**Sinus lifting**

During implant placement in the maxilla, the surgeon may face atrophic maxillary bone with decreased bony height needed for implant placement. In these cases, sinus lifting should be done with bone graft to increase the bony height [18]. Many studies have shown that PRF can be used as a graft material in sinus lifting. The results have concluded that PRF can induce bone formation in the sinus floor if applied in sinus lifting procedures [18].

**Characteristics of PRF**

**Advantages of PRF**

PRF is characterized by the prolonged release of growth factors for over 300 minutes after its preparation, it also releases leukocytes and cytokines from the fibrin mesh which lasts for more than 7 days [19]. PRF is completely autogenous and expensive graft which should be used immediately [20] after its preparation because any delay can cause the fibrin to polymerize through diffusion, leaving behind only a small poorly formed clot in the test tube [21]. PRF can be simply prepared, as well as faster without any additives and anticoagulants like bovine thrombin, highly biocompatible with no autoimmune reactions against PRF [12]. The occurrence of infection in the PRF site could not be predicted because it has an anti-inflammatory effect which acts as an immune regulation node [21].

**Disadvantages of PRF**

There are two main disadvantages of PRF that limit its usage: (1) its preparation, as the clinical benefit of PRF depends on the time interval between blood collection and centrifugation as PRF is prepared without adding any anticoagulants like bovine thrombin [22]. (2) PRF should be used immediately after preparation because shrinkage may occur, causing dehydration of PRF decreasing its integrity, growth factors release, and also it has leukocyte content that alters the biological effects of PRF, especially its anti-inflammatory and anti-infection characteristics [10].

**PRF Preparation Protocol**

Dr. Choukroun has invented the first way for PRF preparation in 2000 [23]. It was totally prepared without adding any anticoagulants during blood centrifugation or
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Bovine thrombin during gelling [12]. This PRF preparation protocol has to be followed properly to obtain the proper quality and quantity of the platelets, leukocytes, fibrin-matrix, and growth factors. For PRF preparation, there is some equipment needed. This equipment includes PC-02 table centrifuge and a blood collection kit [23]. The blood collection kit consists of a 24-gauge butterfly needle and 9 ml-blood collection tubes. After that, the blood specimen is taken from the patient without adding any anticoagulants in 10 ml tubes, then this specimen undergo immediate centrifugation at a speed of 3,000 rpm for 10 minutes [22]. During the centrifugation process, when the blood gets in contact with the test tube wall, the platelet gets activated leading to the initiation of the coagulation cascade. When centrifugation finishes, we get a product which consists of three layers. The first layer on the top is the platelet poor plasma layer. The second layer on the middle of the product is PRF clot, while the third layer on the bottom is RBCs [23]. After that, the fibrin clot obtained after centrifugation is discarded from the tube and the attached RBCs is detached from it and removed. For preparing PRF in the form of a membrane, the fibrin clot is squeezed from the fluids present. For the success of PRF preparation, centrifugation should start immediately after the blood specimen is collected. If centrifugation is not done immediately after blood specimen collection, a small blood clot will be formed with irregular consistency due to diffuse polymerization of fibrin [22].

Evidence for the Role of PRF in Periodontal Regeneration

PRF is characterized by its biocompatibility and ability to release growth factors and cytokines which increase the healing of hard and soft tissues [4]. So, PRF is used in implant and plastic periodontal surgery procedures to enhance bone regeneration and soft-tissue wound healing [23]. PRF was primarily used in implant surgery for enhancing the healing properties of the bone [24]. PRF can promote the healing of intrabony defects by different mechanisms. In Table 1, the literature has conducted

Table 1. Previous studies on the PRF role in periodontology.

<table>
<thead>
<tr>
<th>Conclusion</th>
<th>Year</th>
<th>No. of pt.</th>
<th>Type of study</th>
<th>Author</th>
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<tbody>
<tr>
<td>The classical principles for PRF preparation by Dr. Choukroun are considered the best due to its simplicity, inexpensiveness, high successful results in periodontal tissue regeneration.</td>
<td>2014</td>
<td>Review article</td>
<td>Chandran and Sivadas [25]</td>
<td></td>
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<td>PRF can stimulate the release of p-ERK and also can promote the release of osteoprotegerin which promotes osteoblasts to proliferate and then bone formation.</td>
<td>2010</td>
<td>20 Case report</td>
<td>Chang et al. [26]</td>
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<td>PRF has the ability to promote periodontal tissue regeneration. The mechanism of this action depends on growth factors released from PRF such as transforming growth factor and platelet-derived growth factor. Also, PRF promotes the mesenchymal stem cells to differentiate into odontoblastic cells. The mechanism of this action depends on regulating the expression of alkaline phosphatase and osteoprotegerin.</td>
<td>2010</td>
<td>6 Case report</td>
<td>Huang et al. [27]</td>
<td></td>
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<td>This case report has concluded that PRF can be added to alloplastic graft material for use in treatment of periodontal intrabony defect. The results have shown that this technique can increase the level of attached gingiva, decrease the depth of the pocket, bone formation in the site of the intrabony defects.</td>
<td>2013</td>
<td>1 Case report</td>
<td>Panda et al. [28]</td>
<td></td>
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<td>PRF can be used as a grafting material in the bone-added osteotomy sinus floor in implantology after sinus lifting. This technique has led to the bone formation at the sinus floor at a period ranges from 2 to 3 months and sufficient bone formed within 1 year.</td>
<td>2008</td>
<td>20 Case report</td>
<td>Diss et al. [29]</td>
<td></td>
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<tr>
<td>By comparison between PRP and PRF in their ability for osteoblasts proliferation and differentiation, PRF was more able than PRP, so it is preferred to be used with implants as a graft material.</td>
<td>2003</td>
<td>Review article</td>
<td>Sanchez et al. [30]</td>
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<td>Intrabony defects can be treated well with good results and accepted bone fill by using PRF with conventional open flap debridement which gives better results than conventional open flap debridement only.</td>
<td>2011</td>
<td>42 Case report</td>
<td>Sharma et al. [31]</td>
<td></td>
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<tr>
<td>PRF contains platelets which release various growth factors that are capable of modulation of cell proliferation. In periodontology, PRF stimulates osteoblasts and periodontal ligament cells to proliferate and differentiate, so PRF has a great role in periodontal regeneration.</td>
<td>2009</td>
<td>10 Case report</td>
<td>Tsai et al. [32]</td>
<td></td>
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</table>
various studies on the PRF role in periodontology and periodontal regeneration.

**Conclusion**

Dr. Choukroun has discovered the first protocol for PRF preparation which is simple, safe, and inexpensive. PRF release different growth factors like transforming growth factors and platelet-derived growth factors. These factors stimulate osteoblasts and other periodontal tissue cells to proliferate and differentiate. In cases with intra-bone defects, PRF can be added with alloplastic graft for bone fill in sites of the defect which can appear radiographically within 3 months. So that PRF is capable of periodontal tissues regeneration in different periodontal conditions.

**List of Abbreviations**

PRF Platelet-rich fibrin  
PRP Platelet-rich plasma

**Conflict of interest**

The authors declare that there is no conflict of interest regarding the publication of this article.

**Funding**

None.

**Consent for publication**

Informed consent was obtained from all the participants.

**Ethical approval**

Not applicable.

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