APPLICATION OF AUTOGENOUS PLATELET-RICH PLASMA IN PERIODONTOLOGY

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ABSTRACT

INTRODUCTION: Autogenous platelet-rich plasma (PRP) is a platelet-rich substance obtained after specific processing of peripheral blood.

AIM: The purpose of the present study is to describe and examine the autogenous platelet-rich plasma and its application in periodontology.

DISCUSSION: In the last decade, PRP has gained wide popularity and is used in a variety of fields of medicine. The implementation of PRP is basically a regenerative procedure using an autogenous graft. Therefore, it is believed that there is no danger of genetic interference, sensitization, or any kind of disease transmission. Platelet-rich plasma therapy is a safe and effective option with no known risks or side effects. In the last decade or two, the amount of published studies focused on the joined use of barrier membranes and bone repair materials with PRP has increased. One of the main benefits of using PRP to administer damaged tissues is that it activates and releases growth factors, which can enhance collagen and elastin formation by fibroblasts, boost blood supply and metabolism in the affected area, as well as help promote angiogenesis (the formation of new blood vessels). In this way, PRP therapy can effectively restore lost tissue.

CONCLUSION: The presented study shows that the implementation of autogenous PRP is an innovative method for periodontal regenerative therapy based on the fact that regenerative therapy methods show different success rates and different long-term results, depending on the materials that are used.

Keywords: *guided tissue regeneration, autograft, platelet-rich plasma, periodontology*

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INTRODUCTION

Autogenous platelet-rich plasma (PRP) is a platelet-rich substance obtained after specific processing of peripheral blood. Peripheral blood comprises plasma and formed elements—erythrocytes, platelets, and leukocytes. α-granules, dense granules and lysosomes are the three different granules found in platelets. When platelets trigger and degranulate, α-granules release various growth factors. Nowadays,

it is well known that growth factors benefit cell proliferation, migration, and metabolic activity, as well as have an effect on chemotaxis and the production of extracellular matrix proteins. Consequently, bioactive materials, such as autogenous PRP, are increasingly being used in the field of periodontal regenerative therapy alongside established biomaterials such as barrier membranes and bone repair materials.

AIM

The purpose of the present study is to describe and examine the autogenous PRP and its application in periodontology.

MATERIALS AND METHODS

PubMed and Google Scholar databases were used to obtain related articles on the topic. All the observed articles were published from 1972 to 2022. Different keywords and their combinations were used to formulate the search such as: "guided tissue regeneration", "periodontal regeneration", "platelet-rich plasma", "autograft".

RESULTS AND DISCUSSION

Periodontitis is a plaque-induced inflammatory process of periodontal tissues (gingiva, periodontal ligament, cementum, and alveolar bone), occurring with loss of attachment (1,2). The goal of periodontal therapy consists in the elimination of periodontopathogenic microorganisms and complete regeneration of the lost tooth-supporting structures—alveolar bone, cement, and periodontal ligament (1,3,4).

Indications for guided tissue regeneration (GTR) are two-walled and three-walled bone pockets ≥4 mm deep, grade 1 or 2 furcation involvement, and Miller grade 1 and 2 gingival recessions (5).

Contraindications for performing GTR are some systemic diseases, poor oral hygiene, horizontal bone loss, single-wall bone defects, grade 3 furcation involvement, and Miller grade 3 and 4 gingival recessions (5).

Modern regenerative methods include the use of various types of biomaterials, such as barrier membranes, bone repair materials, growth factors, and various combinations between them. (1,6,7,8,9).

In the last decade, PRP has gained wide popularity and is used in a variety of fields of medicine—dentistry, maxillofacial surgery, dermatology, orthopedics, aesthetic and plastic-reconstructive surgery, neurosurgery, etc. (10,11,12). Today, PRP is increasingly being used as a means of preserving the volume of available tissues after tooth extraction (12) because the results obtained with PRP are equivalent to the results obtained with other time-proven techniques (13,14,15). There are a number of studies that show the benefits of using PRP in order to improve implant stability during the period after the second and before the sixth weeks after loading (16).

Autogenous PRP

Autogenous PRP is a platelet-rich substance obtained after specific treatment of venous blood (17,18). The concentration of thrombocytes in PRP (exceeds 1000 x 109/L) is 4 to 7 times higher compared to reference values from peripheral blood (140–440 x 109/L) (19).

Peripheral blood includes plasma and different types of cells—erythrocytes, platelets, and leukocytes.

Erythrocytes

Erythrocytes are the main part of the formed elements of blood. They originate from the erythropoietic tissue in the bone marrow. They pass through several stages of development—proerythroblast, basophilic erythroblast, polychromatophilic erythroblast, oxyphilic erythroblast. Erythrocytes are anucleated and have a diameter of 7–8 micrometers. They have the shape of a double concave disc. They contain about 70% water, 25% hemoglobin, and 5% other substances. One of their main functions is the transportation of oxygen and carbon dioxide within different parts of the human body. They also take part in the regulation of the ion composition in the blood, the acid-alkaline balance in the blood, etc. Platelet-rich plasma products prepared by centrifugation usually contain a minimal number of erythrocytes (20).

Platelets

Platelets are a major cellular component of PRP products. These cells are anucleated shaped elements derived from megakaryocytes in the bone marrow and range in size from 0.5 to 3 μm in diameter. The shape of platelets varies. Megakaryocytes go through controlled cell fragmentation to produce platelets. This process results in the production of 5,000

to 10,000 platelets. At rest, platelets circulate in the blood for 7 to 10 days. At the end of this period, the spleen and Kupffer cells are responsible for the destruction of these cells. On an electron microscope, platelets have a three-layered membrane that is the source of phospholipids needed for the clotting process. Other main functions of platelets are production of biologically active substances, which are important for regeneration processes and normal functioning of the endothelium, and production of vasoconstrictors (21,22,23).

Platelets contain RNA, mitochondria, a canalicular system, and various types of granules. The main types of granules in platelets are lysosomes, dense granules, and α-granules. Lysosomes consist of glycosidases, proteases and cationic proteins. Dense granules contain ADP, ATP, serotonin, histamine, and calcium. α-granules contain coagulation factors (fibrinogen, factor V), adhesion molecules (vitronectin, thrombospondin, von Willebrand factor), protease inhibitors (C1 inhibitor, plasminogen activator inhibitor-1), and a number of growth factors. During activation and degranulation of platelets, the contents of their intracellular granules are released (21,22,23).

Platelet-Derived Growth Factor (PDGF)

The PDGF is a mitogenic factor and has five isoforms (AA, AB, BB, CC, DD). They stimulate the proliferation of osteoprogenitor cells, cells of the fibroblast line, and endothelial cells. In guided tissue regeneration, they have been found to stimulate cementoblasts. They are also potent chemotactic factors for fibroblasts, neutrophils, smooth muscle cells and osteoblasts. They activate transforming growth factor β (TGF-β), stimulate neutrophils and macrophages, mitogenesis of fibroblast and smooth muscle cells, collagen synthesis, collagenase activity, and angiogenesis (24,25,26).

Transforming Growth Factor β1 (TGF β1)

While PDGF is considered to have a predominantly mitogenic effect among other growth factors, the main activity of TGF-β is related to the synthesis and preservation of the extracellular matrix. It has three isoforms—TGFβ1, TGFβ2, and TGFβ3 (27).

It is associated with stimulation of fibroblast chemotaxis and proliferation, as well as collagen synthesis. Thanks to it, wounds heal without cicatrix. A number of authors have analyzed the pleiotropic effect of TGF-β. It exerts an opposite effect in wound healing, where it is a chemoattractant for neutrophils and macrophages and sparks keratinocyte migration when epithelialization has commenced. This growth factor stimulates the formation of granulocytic tissue by attracting fibroblasts, stimulates angiogenesis and collagen synthesis. Subsequently, it promotes wound contraction, inducing the transition of cells into myofibroblasts (25). With regard to fracture healing, the addition of TGF-β to a demineralized bone matrix has proven to work as a stimulant for the consolidation process (28).

Vascular Endothelial Growth Factors (VEGFs)

Vascular endothelial growth factors are released from platelets within the hemostatic response to an open wound (29). They trigger angiogenesis, vasodilation, and boost microvascular permeability. They are essential for the regulation of endothelial cell proliferation. They activate the formation of metalloproteinase, which leads to the degradation of types 1, 2, and 3 interstitial collagens (30,31).

Insulin-Like Growth Factor (ILGF)

Insulin-like growth factor is discharged during platelet degranulation and in term is found ubiquitously in circulating blood (32). It has mitogenic potential for several mesodermal cell types and promotes the formation of collagenases and prostaglandin E2. It benefits DNA creation of bone cells and collagen type 1 production. Insulin-like growth factor stimulates osteoblastic proliferation and differentiation (32,33).

Fibroblast Growth Factors (FGFs)

Fibroblast growth factors participate duly in proliferation, differentiation, angiogenesis, and cell migration. They have a mitogenic effect on osteoblasts (34).

Epidermal growth factors (EGFs)

Epidermal growth factors encourage the proliferation of both epidermal and epithelial cells, as well as fibroblasts and embryonic cells. They are a chemoattractant for both fibroblasts and epithelial cells. They induce reepithelialization and angiogenesis (34).

Leukocytes

Other blood cells that are present in PRP products are leukocytes. White blood cells

include granulocytes (neutrophils, basophils, and eosinophils), lymphocytes and monocytes. Leukocytes play an important role in the entire consolidation of growth factors either by their own release or by enhancing platelets to discharge growth factors (35,36). Today, it has been proven that the higher the number of leukocytes in PRP, the greater the concentration of PDGF and VEGF in PRP (36). Some authors believe that the introduction of leukocytes in PRP induces positive anabolic influence on the cells and has a significant antimicrobial effect (36,37,38). Other authors claim that leukocytes, especially neutrophils, discharge damaging proteases and acid hydrolases (40).

Methods of Regenerative Therapy Involving Autogenous PRP

Guided tissue regeneration is the principle of restoring damaged or lost tissue. It involves using a barrier to prevent the growth of fast-growing tissues near a defect, and allowing cells that have the potential to regenerate desired tissues to grow slowly (40).

Over the years, clinical techniques and materials have been established for the regeneration of periodontal defects. The development of improved biomaterials for periodontal regeneration has significantly improved the results of its treatment. Barrier membranes, bone repair materials, various growth factors, and a combination of them are used today (41,42).

Nowadays, growth factors are known to benefit cell proliferation, as well as migration and metabolic activity, have influence on chemotaxis and the manufacturing of extracellular matrix proteins (43,44). Platelet-rich plasma works by degranulating platelet α-granules, which consist of several growth factors. Within the first minutes, their active separation begins. The growth factors immediately attach to the outlying surface of the cell membranes of the cells from the transplant or the cells of the flap, with the help of the transmembrane receptors. They, consecutively, play a role in activating an endogenous inner signaling protein that leads to a cascade of reactions leading to cell proliferation and collagen synthesis, as well as extracellular matrix formation and osteoid production (45).

The implementation of PRP is basically a regenerative procedure using an autogenous graft. Therefore, there is believed to be no danger of genetic interference, sensitization, or any kind of disease transmission. Platelet-rich plasma therapy is a safe and effective option with no known risks or side effects. It has been found to be successful in treating various conditions, without any lasting negative effects (46).

In the last decade or two, the amount of literature focused on regarding the joined use of barrier membranes and bone repair materials with PRP has increased (47). One of the main benefits of using PRP to administer damaged tissues is that it activates and releases growth factors, which can enhance collagen and elastin formation by fibroblasts, boost blood supply and metabolism in the affected area, as well as help promote angiogenesis (the formation of new blood vessels). In this way, PRP therapy can effectively restore lost tissue (44).

Platelet-rich plasma has the potential to influence osteoprogenitor cells in bone and bone repair material (autogenous bone), thus being used in different manipulations much like sinus lift, horizontal or vertical alveolar bone augmentation techniques, bone defects (being periodontal or peri-implant) (48,49,50,51).

Velich et al. (52) assessed the effectiveness of β-tricalcium phosphate (β-TCP) and hydroxylapatite bone repair materials and a PRP/β-TCP combination in the therapy of large mandibular defects. As a final result, they concluded that all the therapy approaches were effective and the PRP/β-TCP group displayed faster fresh bone development and bone reshaping in a period between 9 and 12 months.

Dori et al. (53) found no statistically significant differences in any of the clinical parameters between patients who received β-TCP/GTR combination therapy and those who did not receive PRP at the end of the first year. Additionally, there were no reported benefits for PRP treatment.

Throughout their empirical survey, Kovacs et al. (54) evaluated histologically the results of the utilization of β-TCP and PRP/β-TCP in bone defects after extraction of premolars in the canine mandible. The research found that the treatment group with PRP/β-TCP had reasonably more bone formation after 12 weeks. A separate experimental case with an analogous conception by Kovacs et al. (55) showed a reasonable contrast beneficial for the PRP/β-TCP set

of patients after 70 days and ruled out that the usage of PRP quickened β-TCP reshaping and resulted in bone creation more or less with the same quality as autogenous bone.

Yassibag-Berkman et al. (56) assessed the efficacy of β-TCP, PRP/β-TCP, and PRP/β-TCP/GTR in the treatment of 2-walled and 3-walled infraaxial faults. The results show an enhancement in the entire set of investigated parameters in comparison to the standard position of the bone defects.

A number of studies (57,58,59) have shown that during the first 12 months after regenerative therapy of infraosseous faults, favorable clinical outcomes were obtained with GTR in combination with bone-restorative materials with and without the addition of PRP. The data from the different methods is conflicting, so more research is needed to settle the debate.

CONCLUSION

The presented study shows that the implementation of autogenous PRP is an innovative method for periodontal regenerative therapy. According to reports in the literature, regenerative therapy methods show different success rates and different long-term results, depending on the materials that are used. Today, it has been proven that growth factors enhance cell proliferation, migration, and metabolic activity, as well as have an effect on chemotaxis and the production of extracellular matrix proteins. For this reason, many specialists prefer to combine the use of established regenerative materials with autogenous PRP to support a faster recovery process and a better treatment outcome.

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