Chapter

Platelet-Rich Plasma in Trauma Patients

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Abstract

Platelet-rich plasma (PRP) was mixed with thrombin and excess calcium resulting in activated platelets trapped within the fibrin network; within the matrix, platelets secrete bioactive substances that diffuse into the surroundings tissues. PRP is prepared from the patient's own blood, a variety of manufacturing techniques in vastly different cell counts, and growth factor concentrations. The clinical use of PRP is treatment of soft tissue diseases and injuries, treatment of burns, hard-to-heal wounds, tissue engineering, and implantology in dentistry. An essential criterion for PRP is for it to be autologous, for the donor of the blood, and the recipient of the PRP to the same person. Most of the literatures suggest that PRP does not appreciably impact bone healing or induce bone formation. PRP might augment recruitment of osteoblast progenitors to injection sites or in sites expected to experience delayed healing. In this capacity, PRP might be utilized to initiate repair of an otherwise poorly healing bony lesion. PRP stimulates bone repair in fractures. Early through late healing process is compromised with fractures, including reduced cell proliferation, delayed chondrogenesis, and decreased biomechanical properties. In this chapter, the importance of the PRP in oral and maxillofacial surgery in trauma patients is studied

Keywords: platelet-rich plasma, trauma, oral surgery

1. Introduction

Today, regenerative therapy is the most preferred treatment because it is a method that meets the expectations of the patient close to the ideal. With the progress of technology, new materials about growth factors are entering our lives. Tissue engineering is currently working hard to develop regenerative materials. The health sector and tissue engineering benefit from each other in this respect.

First-generation platelet concentrate platelet-rich plasma (PRP) was used as a biomaterial to speed up the process of healing of the tissues. PRP contains high concentrations of platelets and growth factors in the low-volume plasma. These growth factors stimulate cell proliferation, matrix formation, and angiogenesis [1].

In 2001, platelet-rich fibrin (PRF), a second-generation platelet concentrate product, was developed in France, which was first developed for use in oral and maxillofacial surgery [2]. PRF preparation technique is based on the principle of collecting platelets and growth factors in the fibrin matrix by centrifuging venous

blood from the patient. There are many forms of PRF materials such as P-PRF, L-PRF, A-PRF, I-PRF, and T-PRF used in oral and maxillofacial surgery.

2. Platelets

Platelets are cytoplasmic fragments of mature megakaryocytes in bone marrow. They are responsible for tissue regeneration by clotting, at the onset of wound healing, and by growth factors released from alpha granules. They are isolated from peripheral blood vessels [3].

Because of their short lifespan, the megakaryocytes should produce about $1.5–4 \times 10^{10}$ platelets per day to keep the platelet count in the normal blood count at $1.5–4.5 \times 10^{5}$ per microlitre (μL) of blood [4].

In 1960s, the interaction between platelets and endothelial cells supporting capillary endothelin integrity was revealed [5, 6]. Initial work by Folkman and colleagues used autologous PRP-augmented media to feed microvascular endothelial cells to enhance vascular integrity preservation in organs subjected to perfusion for transplantation. It has been determined that human platelet lysate (HPL) was prepared by repeated freezing/thawing cycles throughout the 1980s, and cell lines and primer fibroblasts were promoted by fresh blood or old platelet concentrates [7–9].

Platelets are quite active in terms of metabolism. Growth factors were released by platelet function with the phenomenon of "activation of macrophages by an increase in connective tissue healing, bone regeneration and repair, mitogenesis of fibroblasts, and angiogenesis of the wound area" by stimulating cell proliferation [10, 11].

After the resulting tissue damage, the platelets appear and the basal membrane of the collagen capillaries and the subendothelial microfibrils directly change shape. The alpha granules in the platelets engage the cell plasma membrane and release protein contents around with activation [11].

If the defects are small, platelet clotting is sufficient, and large wounds may require blood clots. The blood clot is activated from intrinsic and extrinsic pathways. "Intrinsic pathway" begins when there is a change in tissue damage or in blood. The "extrinsic pathway" begins with blood contact with factors other than blood, such as damaged tissue. Although they start differently in two ways, they converge on the next steps and share the reaction series. Coagulation in the presence of calcium and thrombin occurs by fibrinogen polymerization of fibrinogen monomers. The fibrin clot also provides a matrix environment for migration of fibroblasts and other tissue-forming cells, including endothelial cells, other than hemostasis [12].

3. Wound healing

Wound healing is a complex but a controlled mechanism regulated by growth factors and extracellular matrix.

Healing stages are:

1. hemostasis,

2. inflammation,

3. proliferation (granulation and contraction), and

4. remodeling (maturation) [13].

3.1 Hemostasis

Platelets behave like workers who close the damaged gas and water lines and seal damaged blood vessels. Blood vessels react to injury by vasoconstriction, but this spasm ends loosely. Thrombocytes secrete vasoconstrictor substances to facilitate this process, but this is not the main role. The primary role of platelets is to form clots. Adenosine diphosphate (ADP) leaks from damaged tissues. Platelets adhering to type 1 collagen, which is activated by ADP, thus become active. They are viscous glycoproteins that secrete and cause platelet aggregation [14]. At the same time, thrombocytes secrete factors that interact with and stimulate intracellular coagulation by intrinsic thrombin production, which initiates fibrinogen to fibrin. Platelets also secrete platelet-derived growth factors, known as one of the initiating factors for the healing process.

3.2 Inflammation

Inflammation is clinically associated with pain, swelling, temperature, and erythema, occurring between the first and fourth days after injury. Neutrophils perform their first defense against infection by phagocytosing existing debris and microorganisms. When the neutrophils digest bacteria and debris, they complete their task and die.

In wound repair, communication between soluble proteins and cells is ensured. These soluble proteins are growth factors and cytokines released by the cell. The role of the extracellular matrix in wound healing is activation of platelets, epithelial migration, and interaction with cells through receptors called integrins that lead to the movement of fibroblasts [15].

Macrophages secrete bacterial phagocytes and extracellular enzymes, to break down necrotic tissues and form the second line of defense. Secreted extracellular enzymes and matrix metalloproteinases (MMP) are calcium and zinc sources for the active site. MMP is responsible for necrotic tissue removal and repair of damaged tissue. MMP metalloproteinases are inactivated by tissue inhibitors (TIMPs) and uncontrolled activities are counterbalanced. Macrophages, fibroblast growth factor, epidermal growth factor, transforming growth factor-beta (TGF-β) and interleukin 1, etc. stimulate proliferation by secretion of cytokines and growth factors [16].

3.3 Proliferation

Proliferation begins after the injury of tissues and continues until the size of the wound and the systemic condition of the patient is up to 21 days in acute injuries. Characteristically, “angiogenesis,” “collagen deposition,” “granulation tissue” formation, “wound contraction,” and “epithelialization” are seen at this stage.

Cells are introduced into the proliferation phase: macrophages, fibroblasts, pericytes, endothelial cells, and keratinocytes.

Fibroblasts are responsible for the secretion of collagen. In case of a damaged home, “plumber” cells are pericytes that renew outer layers of capillaries and endothelial cells that “glue.” This process is called angiogenesis. Keratinocytes play the role of “roof plumber” and are responsible for epithelization.

3.4 Remodeling

Similarly, collagen tissue must be rearranged to provide greater tensile strength in wound repair. In addition, the density of cells and capillaries is reduced. The

main cells involved in this process are fibroblasts. Remodeling can last up to 2 years after wounding [17].

4. Three therapeutic improvements through the wound healing mechanism: primary, secondary, and tertiary healing

4.1 Primary wound healing

Primary wound healing is called healing if the cleaved cleft is closed without any complications. Within 24 h, the minimal space existing between them is filled with fibrin and makes fibrinous adhesion.

4.2 Secondary wound healing

The healing form of granulation tissue in open wounds is called "secondary wound healing." Initially wounded with clots and exudates, the wound is filled by fibroblasts 4–5 days after injury. In this type of healing, the wound surface is covered with scar tissue after 30–40 days following injury.

4.3 Tertiary wound healing

In case of infection, in the over-devitalized tissues and in the presence of a foreign body, the improvement observed by closing the wound after a few days is called "delayed primary healing" (tertiary wound healing).

5. Platelet-rich plasma (PRP)

Platelet-rich plasma (PRP) was first developed in the early 1970s, but it was used rarely. PRP was mixed with thrombin and excess calcium resulting in activated platelets trapped within the fibrin network; within the matrix, platelets secrete bioactive substances that slowly diffuse into the surroundings tissues. PRP was introduced to the dental community by Whitman and colleagues, who hypothesized that the activation of platelets and the subsequent release of growth factors would enhance surgical healing [10]. PRP is now commonly applied to surgical sites and injuries to promote wound healing. PRP is rich in growth factors (PRGF), platelet-rich fibrin matrix (PRFM), and platelet-rich fibrin (PRF) [18].

The natural blood clot contains 95% of red blood cells, 5% of platelets, and 1% of white blood cells; thrombocyte-rich plasma obtained by centrifugation of blood tissue contains 4% of red blood cells, 95% of platelets, and 1% of white blood cells. Platelet concentrates in plasma are called "platelet-rich plasma." The goal of using platelet-rich plasma is to accelerate healing. High levels of platelets and growth factors also include all components of clotting factors. At least 5 ml of plasma is required for platelet-rich plasma to be clinically effective in order to have 10^6 μl of platelets. The platelet-rich plasma should be prepared in nonclotted form and should be used within 10 min from the start of coagulation [19, 20].

"Platelet-rich plasma" is administered by "injection" to the site of interest or by mixing with "grafts." "Platelet-rich plasma" has a long storage period, but should be used quickly when used. It takes up to 7 days in the region where the growth factors are applied [21].

1. Preparation of platelet-rich plasma

Nowadays, there are many preparation methods. These are as follows:

a. Preparation with standard blood bank procedures:
   - It can be prepared in Aferez units
   - It can be prepared from whole blood donors

2. It can be prepared with the aid of a test tube with 20–60 cc of blood.

3. It can be prepared using commercially available automatic preparation devices [22, 23].

4. PRP is subjected to a process known as differential centrifugation. It is prepared clinically by "PRP method" or "buffy coat method" [22, 23].

In the PRP method, an initial centrifuge (3000 rpm for 3 min) at low speed separates red blood cells (RBC), and then a second centrifuge (4000 rpm for 3 min) is applied at high speed to concentrate the platelets. In the initial centrifuge, the venous blood is centrifuged in tubes containing citrate dextrose. Acid citrate dextrose is an anticoagulant agent.

After the initial centrifugation, the whole blood is divided into three layers:

1. A top layer (platelet poor plasma) containing mostly "platelets" and "white blood cells (WBCs)" is of 40%.

2. An intermediate layer is rich in white blood cells known as the buffy coat and is of 5%.

3. A lower layer consisting mostly "red blood cells" is of 55% [23].

For the production of pure PRP (P-PRP), the top layer and the cover of the intermediate layer known as the buffy coat are transferred into an empty sterile tube. For the production of leucocyte-rich PRP (L-PRP), the top layer known as "PPP" is transferred to the entire layer of the "buffy coat" and a few "red blood cells." By the second centrifuge, the "red blood cells" and the PRP are separated. The PRP obtained after the second centrifugation is activated with thrombin and calcium chloride to prepare a PRP gel. PRP gel contains high amounts of platelets and natural fibrinogen. It takes approximately 30 min to prepare PRP with this technique. Prepared PRP should be used within 6 h.

6. Things to be aware of when preparing PRP

- In acid citrate dextrose (ACD-A), tubes should be obtained with whole blood by venipuncture.
- Blood should not be chilled at any time before platelet separation or platelet separation.
- Whole blood must first be centrifuged at "low speed."
- Supernatant containing platelets (floating on top of the precipitate) should be transferred into another sterile tube (no anticoagulant).
- Tube should be centrifuged at a higher speed (hard spin) to obtain platelet concentrate.

- At the end of centrifugation, bottom 1/3 of the tube consists of PRP and the top 2/3 consists of PPP. At the bottom of the tube platelet, pellets are observed.

- It is necessary to suspend platelet pellets in a minimum amount of plasma (2–4 ml) by removing the PPP and gently shaking the tube [24, 25].

There are also several factors that influence platelet concentration, such as the size of the platelets, the biological differences between individuals, and the hematocrit variability. It is more critical after the second centrifuge because the process of separating red blood cells intended for the first centrifugation may not be fully realized and erythrocytes may be present in the transferred volume. The remaining erythrocytes form a pellet at the base of the tube. Approximately, 20% of the platelets remain adsorbed on erythrocyte globules [26].

Another issue to be aware of is the impossibility of obtaining platelet-rich plasma from a non-anticoagulated blood. Platelets are responsible for the initiation of hemostasis and healing. Since platelets do not have platelets in the serum, it is not possible to obtain platelet-rich plasma from the serum, only anticoagulant platelets are possible.

Clinically, acid citrate dextrose or citrate phosphate dextrose is frequently used for anticoagulation. Citrate phosphate dextrose, acid citrate dextrose, has similar properties but has been suggested to be 10% less effective in protecting thrombocyte vitalites in studies. EDTA is not recommended because it will damage the platelet membrane.

Dual centrifugation technique is necessary to prepare platelet-rich plasma. Not enough platelets can be obtained with a single centrifugation and a mixture of both platelet-rich plasma and thrombocyte poor plasma cannot be separated completely [26].

7. Mechanism of action of platelet-rich plasma

Growth factors alone do not increase bone production. Platelets increase in the area applied with platelet-rich plasma. The increase in platelets also increases the growth factors numerically. PRP also contributes to bone regeneration by increasing the number of stem cells in a small number. Marx used a combination of bone graft and platelet-rich plasma in mandibular defects and attributed the contribution of platelet-rich plasma to bone regeneration to the function of growth factors in the environment [27].

Platelet-rich plasma is the basis for the activation of defense mechanisms by the activation of macrophages and the formation of a nonspecific immunoreaction with the leukocytes and interleukins involved.

The platelet-rich plasma has antimicrobial properties against microorganisms such as "*Escherichia coli*," "*Staphylococcus aureus*," "*Candida albicans*," and "*Cryptococcus neoformans*" [28].

8. Duration of action and storage of platelet-rich plasma

The duration of action of PDGF and TGF-β in the platelet-rich plasma was investigated and a reduction in cell growth stimulating activity between 4 h and 3 days after venous blood ingestion was reported [29]. It is recommended to use PRP within the first 6 h after its preparation to keep the prepared biomaterials at a minimum level of contamination and to minimize disease transmission risks [30, 31]. It has been suggested

that the degranulation of platelets and the release of growth factors are within the first 3–5 days; therefore, the effect of platelet-rich plasma is also 7–10 days [32]. Although the direct effects of platelets and growth factors are lost, bone regeneration is expected to continue, since the lifespan of active osteoblasts is approximately 3 months [33, 34].

9. Classification of platelet-derived blood concentrates

9.1 Pure platelet-rich plasma (P-PRP)

Using only the upper part of the yellowish layer to inhibit the presence of leukocytes, resulting biomaterial leads to a lower platelet count. Because it is possible to prepare clinically, it is a low-cost application [33, 35].

9.2 Leukocyte and platelet-rich plasma (L-PRP)

Blood in sterile tube containing no anticoagulants is subjected to initial centrifugation. All of the poor plasma and buffy coat layers from the cell and a portion of the bottom layer containing the red blood cells are transferred to a new tube. At a high speed, a second centrifugation is carried out and the poor plasma layer from the cell is withdrawn by pipetting. Coagulation is achieved by adding thrombin or calcium chloride as the activator. L-PRP, which takes time to prepare by hand, also has low density [35].

9.3 Pure platelet-rich fibrin (S-PRF)

The "P-PRP," "L-PRP," and "P-PRF" biomaterials all contain too much tombocytes from physiological values. It is reported in the literature that biomaterials with platelet content 2.5 times more than the number of platelets present are most effective [36].

9.4 Leukocyte and platelet-rich fibrin (Choukroun's PRF) (L-PRF)

L-PRF is a platelet concentrate containing all components of blood. There is no need for any anticoagulant agents in the preparation of L-PRF, so it can be regarded as a second-generation platelet concentrate. It is used in oral, maxillofacial, otorhinolaryngology, and plastic surgery. In the technique of preparing L-PRF, platelets and leukocytes are obtained with high efficiency. With the activation of L-thrombocytes, thrombocyte and leukocyte growth factors are embedded in the fibrin matrix [37–44]. In the biomaterial prepared, leukocytes act as an infection-preventive cells and immunomodulator [45, 46].

9.5 Advanced platelet-rich fibrin (A-PRF)

For L-PRF preparation, centrifugation for 12 min at a speed of 2700 rpm is required, but at a slower speed such as 1500 rpm for A-PRF preparation, longer time such as 14 min is required. Studies have shown that the number of viable cells, including platelets, is higher in A-PRF. Clinically, it will be beneficial for increasing amounts of growth factor and cytokine release. Reported that the levels of growth factors (TGF, PDGF-AB, VEGF) released from A-PRF are less than those of L-PRF when compared to that of L-PRF [47].

9.6 Injectable platelet-rich fibrin (I-PRF)

One of the latest developments in PRF technology is the production of injectable PRF (I-PRF). For preparation of I-PRF, blood samples are taken in plastic tube without anticoagulant and centrifuged at 2400–2700 rpm at about 700°C for 2–3 min [48].

9.7 Titanium platelet-rich fibrin (T-PRF)

During PRF preparation, different products are obtained using different materials for blood processing. Medical titanium tubes to produce PRF and 111333, named this material T-PRF [49]. In one study, it was observed that T-PRF samples had a fairly regular network than L-PRF samples [49]. In addition, the T-PRF fibrin network was observed to cover the wider area of the L-PRF fibrin network and the fibrin was thicker in the T-PRF specimens. T-PRF was obtained by centrifugation of 20 ml of blood at 2800 rpm for 12 min in medical titanium tubes in a human study. T-PRF membranes were found to have positive effects on palatal mucosal wound healing [49].

9.8 Concentrated growth factor (CGF)

The most important different CD34 stem cell content from the thrombocyte-rich plasma and fibrin of the concentrated growth factor is the content. CGF-CD34 is the name of the layer containing platelets, leukocytes, growth factors, and cytokines by separating the autologous blood into its components by centrifugation at four different rpm at the same time. Concentrated growth factor does not cause any infection or immunological reaction as it is prepared from the own blood of the person, and no chemicals are used during the process. CGF causes less inflammation, bleeding, and pain than other materials. Due to the stem cell content of CD34, regeneration capacity is higher than other biomaterials [50].

10. In vitro applications of thrombocyte-rich plasma

Although the clinical use of PRP and PRF is widespread in oral and maxillofacial surgery, the mechanism of cellular action has not yet been clearly elucidated. Although in vitro studies have been carried out on dental-derived cells, there is no comprehensive study describing the mechanism of action of stem cells. A limited number of in vitro studies do not provide a convenient and reliable basis for clinical practice.

Thrombin-activated plasma stimulate “adhesion,” “migration,” and “myofibroblastic differentiation” of human gingival fibroblasts [51]. In another study, PPP and 50% PRP resulted in the greatest increase in cellular proliferation and differentiation at various concentrations, the proliferation of osteoblast and periodontal connective tissue cells in platelet-rich plasma and platelet-poor plasma, and the effect on calcium formation [52].

Functions of the platelet-rich plasma are obtained from periodontal ligament tissue and pulp of human tooth root cells [53]. Colony formation and cellular proliferation of dental cells reduced platelet-rich plasma at concentrations of 0.5 and 1% [53].

Thrombocyte-rich fibrin regulates cell proliferation in a cell-type-specific manner, and that the thrombocyte-rich fibrin can promote cell proliferation [54].

In vitro studies of “platelet-rich plasma” have shown that the “PDGF-AB” and “TGF-β” factors are in high concentrations in platelet-rich plasma preparations and that the platelet—the proliferation [55, 56]. In another study of the same

researchers, it was observed that the fibrinogen used with growth factors in platelet-rich plasma effectively increased wound healing in periodontal tissues.

11. Clinical studies on platelet-rich plasma

Contrary to in vitro studies, there is extensive literature in clinical trials. Thrombocyte-rich plasma in dentistry is used to increase tissue regeneration in periodontal disease, to accelerate healing of alveolar plugs after tooth extraction, and to accelerate osseointegration around dental implants [48, 56, 57].

First time, 88 mandibular bone defects were treated with autogenous bone graft, some with autogenous bone graft, and some with platelet-rich plasma. As a result of the study, it was observed that platelet-rich plasma significantly increased bone regeneration [27]. After tooth extraction, many complications can occur. There are studies showing that the graft site is covered with thrombocyte-rich plasma and local conditions such as "dry socket" and "abscess" formation are prevented, and conditions are improved. It has been reported that high aftertouch growth factor concentration increases tissue regeneration [58–62]. There are also studies in the literature, which show conflicting results with other studies suggesting that the platelet-rich plasma administered after tooth extraction does not have a significant effect. There are also observations that thrombocyte-rich plasma does not increase bone regeneration alone, as is the case with osseointegration at dental implant placement and studies that give positive platelet-rich plasma to accelerate new bone formation.

There are reports of positive results associated with thrombocyte-rich fibrin in sinus augmentation therapy prior to placement of the dental implant [62–66]. Co-use of deproteinized bovine bone (Bio-Oss) and thrombocyte-rich fibrin is only compared with Bio-Oss use; combined use of maxillary bone atrophy has been reported to give better results [67, 68].

Contradictory results have also been observed in the use of platelet-rich plasma in periodontal surgery. There are studies reporting increased tissue regeneration when applied with platelet-rich plasma graft materials [68, 69] while some studies suggest no improvement in healing process after thrombocyte-rich plasma implantation [70, 71]. The same conflicting results exist in the literature for thrombocyte-rich fibrin. Thrombocyte-rich fibrin in the third molar withdrawal of the mandible did not increase bone repair.

It has been demonstrated that the application of "thrombocyte-rich plasma" is effective in the "bison-linked osteonecrosis (BRONJ)" treatment of the jaw. The application of surgical debridement procedures in conjunction with autologous thrombocyte-rich plasma was reported that increased bone and soft tissue regeneration, increased neovascularization, and reduced tissue inflammation [71–76]. According to some investigators, thrombocyte-rich plasma regeneration capacity is a low biomaterial and may have a short-lived effect in the early phase of bone healing, flattening between the third and sixth months of treatment.

11.1 Use of platelet-rich plasma in surgical sockets

Thrombocyte-enriched plasma to the suction ports and stitch area of 170 patients after withdrawal of third molar teeth and alveolar osteitis was prevented with less pain and more intense bone formation [48].

In 20 patients with "periodontal defect" and "vertical root fracture" in two groups as thrombocyte-rich plasma and autogenous bone graft applied, only autogenous bone graft was applied. As a result, epithelialization of the group with autogenous bone grafting with thrombocyte-rich plasma and bone healing was faster [77].

11.2 Use of platelet-rich plasma in jaw reconstructions

"Autogenous bone graft" and "platelet-rich plasma" combination in "mandibular reconstruction" significantly improves bone healing [78]. Patients who underwent "partial mandibulectomy" combined "autogenous bone graft" and "thrombocyte-rich plasma" for reconstruction. After 6 months, they found that the biopsy bone they had received was sufficient and they applied the implant after 1 year [79].

11.3 Use of platelet-rich plasma in distraction osteogenesis

Implants in patients were done by injecting "mesenchymal stem cells" and "platelet-rich plasma" into the distraction range to obtain three-dimensional bones in the distraction osteogenesis of the mandible and to shorten the consolidation period. They reported that platelet-rich plasma was effective at the end of the study [80].

Injected mesenchymal stem cell and thrombocyte-rich plasma derived from bone marrow were used for "achondroplasia" and "congenital pseudoarthrosis. As a result of the study, they reported that short-term minimally invasive procedure is an advantage of increasing bone regeneration [81].

11.4 Use of platelet-rich plasma in individuals with alveolar cleft

Patients with alveolar congenital defects were using bone and tibia-derived grafts plus thrombocyte-rich plasma and reported that the corresponding region was rapidly restored according to the patient group, who had never used thrombocyte-rich plasma [82].

Autogenous bone grafts, in five of 12 patients with alveolar cleft, and the remaining seven were combined with autogenous bone and thrombocyte-enriched plasma in the remaining seven and closed the scales. They reported that regeneration in patients who were closed by a combination of autogenous bone and thrombocyte-rich plasma in a computed tomography scan was better than the other group [83].

11.5 Use of thrombocyte-rich plasma in oriented bone regeneration technique

Lecovic et al. reported that the combination of thrombocyte-rich plasma and bovine peroneal bone mineral was effective in the treatment of intrabony defects in patients with chronic periodontitis, although no directed tissue regeneration was performed [84].

11.6 Use of platelet-rich plasma after peripheral nerve injury

Peripheral nerve injuries may occur after surgical operations in the maxillofacial region and after trauma to the maxillofacial region. "Microsutures," "fibrin-cyanoacrylate adhesives," "grafting," and "laser" applications are preferred in the treatment of injured nerve tissue. However, the regenerative capacity of the nerve tissue is limited and heals very slowly. The use of platelet-rich plasma was considered to speed up this process of healing. An animal study was conducted using rats, although there is no human study on the subject. After the sciatic nerves of the rats were cut bilaterally, the nerve was connected with "cyanoacrylate" on one side and "platelet-rich plasma" on the other side. The number of nerve fibers formed on the treated side of the biopsied platelet-rich plasma after 12 weeks was higher than the other side [85].

11.7 Use of platelet-rich plasma in soft tissue injuries

Platelet-rich plasma is also effective in soft tissue injury as it is effective in hard tissue repair. Two groups were formed in the study in which 59 patients with acute traumatic soft tissue injury were treated. Thirty-two patients were treated with routine wound care while the remaining 27 patients were treated with routine thrombocyte-rich plasma as well as with routine wound healing. As a result, wound healing was faster in the platelet-rich plasma group [85].

12. Conclusion

Platelet-rich preparations are a safe (PRP) and is a preparation of plasma that contains an increased concentration of platelets compared to blood. PRP is autologous: for the recipient of the PRP to be the same person. PRP is used for both soft and hard tissue and also used in clinical dentistry, because it accelerates bone formation and induces healing.

Many studies support the use of autologous PRP in clinical practice, including for soft tissue injuries, chronic diabetic ulcers; injuries to muscles, tendons, or ligaments; bone fractures; molar extractions; urologic, dental, ophthalmic, and plastic surgery procedures; and periodontal, sinus lift, and oral/maxillofacial surgeries. Since growth factors play crucial roles in soft and hard tissue regeneration, the proposed mechanism for the enhanced healing outcomes by PRP is through the release of critical growth factors by activated platelets [86, 87].

Bone lesions and defects may arise out of many kinds of traumas. Due to the high prevalence of trauma, bone is the most transplanted tissue.

The use of autologous grafts is a gold standard to the biomaterial filling of bone defects. However, the limitation of tissue available, risks of infection, and necrosis re-motivated the proposition on synthetic biomaterials, which by turn are not biologically functional and adapted to remodeling bone tissue.

The use of biological factors, such as PRP and bone morphogenetic proteins (BMP), has shown good results in bone reconstructions, since they are directly associated with the tissues. Platelet growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-b (TGF-b), fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF)-A, and insulin-like growth factor (IGF-1) regulate bone regeneration, proliferation, and differentiation of osteoblasts, for the therapeutic use.

The use of PRP in the treatment of bone lesions has shown significant results from 1990s. PRP also used as an alternative to fibrin glue or platelet gel is frequently employed in maxillofacial defects. The therapeutic benefits and the reparative power of PRP consist of one action faster than conventional treatments maximized by autologous growth factors and are free from immune complications.

PRP action with the concentration of bone marrow had better consolidation and greater bone quantity by area in the PRP group. The superior result obtained can be explained by the immediate recruitment of all proteins necessary to start the healing cascade, while the concentration of bone marrow demanded longer time to recruit these elements. Thus, it can be assumed that the monitoring for a period of time up to 4 weeks, this group might have had similar results of consolidation. However, there were no new studies that could confirm this hypothesis.

Several studies reporting the association of PRP and artificial bone grafts showed improvement in the quality of healing. However, only PRP was used, and the short-term and/or long-term results, were positive but not significant. PRP could be beneficial and contribute to the morphological and functional improvement in chronic tendinopathy [86, 87].

In treatment of tendinopathy, PRP plays an important role. Physical therapy and a program of activities after injection of PRP, adopted in most studies, demonstrate better results in tendon lesions [88].

Platelet-rich plasma is a blood-derived product used for local healing. Interest in their activity over the last two decades has increased significantly in different disciplines. It is widely accepted that these materials stimulate soft and hard tissues to mimic the physiological healing process. The reason is that it contains high amounts of blood components such as fibrinogen, platelets, etc.

These biomaterials have been proposed for various uses in oral and maxillofacial surgery. Most studies in the literature: improvement of alveolar sockets after shrinkage, osseointegration of dental implants, sinus lifting procedures, improvement of periodontal bone defects, etc., examine the effects on the case. It has also been observed that platelet concentrations increase cell migration and neovascularization in vitro studies.

In addition to having many advantages of platelet-rich plasma, there are also disadvantages: increased risk of malign transformation as the PDGF release increases in chronic wounds, and the lack of factor V of the bovine thrombin used for anticoagulants and immunological reactions.

The activity of the platelet concentrates is expected with the high amounts of active growth factors and cytokines they contain. Nowadays, the preparation of these platelet concentrates is very different from each other. When platelet concentrates are compared, thrombocyte-rich fibrin is thought to have a higher regenerative potential than thrombocyte-rich plasma.

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Bone defects caused by infection, tumor, trauma, metabolic disease, or massive osteolysis due to prosthesis still remain a major clinical concern. Unfortunately, the self-repair capacity of the critically bone defected is extremely limited and this condition generally requires bone grafting. Osteoinductivity, osteoconductivity, and osteogenesis are optimal bone graft substitute. Allografts or xenografts have unique osteoconductive properties and rarely cause disease transmission. Because of these limitations, synthetic bone grafts are being used. Osteoinductive growth factors, autogenic bone marrow, and mesenchymal root cells promote osteogenesis while demineralized bone matrix (DBM) and platelet-rich plasma (PRP) induce formation of progenitor cells from surrounding tissues. However, each of these substitutes has its own significant limitations and none of them meets full expectations to serve as bone substitute in instance of bone defect.

Both PRP and DBM are osteoinductive substitutes that have shown satisfactory results for fracture healing. A number of growth and differentiation factors are liberated, including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), transforming growth factor-1 (TGF-1), insulin-like growth factor-1 (IGF-1), hepatocyte growth factor, platelet factor-4, fibroblast growth factor (FGF), trombospondin-1, osteonectin, and fibronectin via activation of platelets. These factors play an important role in intracellular matrix formation, osteoid production, and the collagen synthesis involved in fracture healing. DBM is an organic collagen matrix that includes various types of bone morphogenetic proteins (BMP), which are responsible for its osteoinductive properties. PRP can be prepared easily with two-step centrifugation of autogenous blood, and DBM can be obtained commercially.

Through positive impacts of PRP and DBM based on these findings, the present study evaluated the impact of individual and combined applications of PRP and DBM on fracture healing of critical bone defects. Allogeneic PRP would

have beneficial effect on treatment of segmental bone defects, comparable to DBM. Possibility of agonistic or additive osteoinductive effects of DBM and PRP combination was also investigated [89].

Despite the large number of clinical trial studies, there is little evidence of the cellular effect of blood derivatives. The lack of standard protocols leads to the lack of reliable clinical results. Frequent and unnecessary application of blood-derived products, especially in the maxillofacial region, results in both an increase in procedures and a significant increase in costs to clinicians and patients. The indications of the protocols for the application and preparation of blood derivatives should be made absolutely widespread and systematic in order to clarify the benefits for patients of blood derivatives. This can be achieved through a collaborative work between clinical and in vitro researchers. Further research on thrombocyte-rich plasma and thrombocyte-rich fibrin activity on dental cell biology, more clinical application of platelet concentrates, and greater use in the oral and maxillofacial region may provide a stable basis for more predictable outcomes.

Conflict of interest

We declare that there is no conflict of interest with any financial organization regarding the material discussed in the chapter.

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