Guided Bone Regeneration Using a Platelet-Rich Fibrin Membrane and Sticky Bone Graft: Case Reports

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Abstract

Bone reconstruction is sometimes necessary before the implant placement. As a result, various clinical procedures such as Plasma Rich in Growth Factors (PRGF) have been described for preserving or increasing bone volume.

We present here six patients, mean age of 58.2 years ± 8.9, with volumetric bone defects on the maxilla that have been treated using PRGF protocol in oral implantology.

A CBCT was prescribed before and after the surgery. Measurements of the ridge were divided into 3/3 from the top to its base. On the day of surgery, the patient’s venous blood was collected and placed in a System V® centrifuge, allowing the platelets to be separated in Fraction 1 (F1) rich in fibrin, and Fraction 2 (F2) rich in platelets. After the removal of the stitches 2 to 3 days after surgery.

Mean residual crestal width was 3.7 mm ± 0.8 (range: 3 mm to 5 mm), mean residual vestibular height was 6.2 mm ± 2.9 (3 mm to 11 mm) and mean residual palatal height was 8.7 mm ± 2.1 (6 mm to 11 mm). An average of 5 implants per patients (1 to 8) have been placed. At six months follow-up, the average height gain was 5.7 mm ± 2.1 (2 to 8) for the vestibular wall and 3.3 mm ± 1.2 (2 to 5) for the palate wall. The average gain in crestal width was 4.2 mm ± 0.8 (3 to 5).

PRGF form mixed with a filling allograft biomaterial, and a membrane resulting from the same PRGF protocol, represents a promising treatment of bone defects in implantology.

Keywords: Plasma-Rich in Growth Factors; PRGF; Sticky-Bone Graft; Implants

Introduction

Since the work on osseointegration and its clinical application [1] in implantology, a bone reconstruction is sometimes necessary before the implant placement [2]. As a result, various clinical procedures have been described for preserving or increasing bone volume. However, these procedures do not always allow the expected bone volume to be obtained.

Recently, autologous platelet concentrates have been proposed in the treatment of bone defects [3]. Their major interest lies in the fact that they would concentrate an amount of growth factors necessary for tissue regeneration [4]. These biological mediators, once released on the implant site, would act on chemotaxis, proliferation, cell differentiation and synthesis of the extracellular matrix by osteoblasts, all thus promoting healing and tissue regeneration [5].

Since the first autologous platelet concentrate in 1994 by Tayapongsak [6], Choukroun [7] and Anitua [8] have tried to improve the concept. Plasma Rich in Growth Factors (PRGF) is a 100% autogenic technique [8]. It results in the release on the implant site of various inflammatory mediators; coagulation factors, fibrinogen and fibrinolysis inhibitors involved in hemostasis; and metalloproteinase’s which degrade the matrix and allow its renewal and participate in angiogenesis [3]. Their major interest lies in the fact that they would concentrate an amount of growth factors necessary for tissue regeneration [4]. These biological mediators, once released on the implant site, would act on chemotaxis, proliferation, cell differentiation and synthesis of the extracellular matrix by osteoblasts, all thus promoting healing and tissue regeneration [5].

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In France, PRGF is indicated in post-extractive alveoli [10], implant surgery [11], gingival recessions [12], reduced risk of osteoradionecrosis and osteochimionecrosis [13,14] and the treatment of bone defects [15]. For this last indication, PRGF can be used in different formulas, pure or combined with a bone filling material [16]. Studies have evaluated the benefit of platelet concentrates in the treatment of periodontal defects [17]. However, despite numerous studies carried out on PRGF [18], few have explored its application with a filling material in the treatment of bone defects in oral implantology.
We present here the six-month-clinical and radiological outcomes of six patients requiring implant prosthetic rehabilitation with volumetric bone defects that have been treated using PRGF mixed with a filling material, and a membrane resulting from the same PRGF protocol.

**Materials and Methods**

**Patients**

This retrospective case series includes detailed reports of all patients with partial or complete edentulosity with or without extraction, with volumetric bone defects in the maxilla, consulting for an implant prosthetic rehabilitation at the oral surgery department of Bordeaux University Hospital and a private practice, France, who were treated using PRGF mixed with a filling material, and a membrane resulting from the same PRGF protocol between February 2018 to November 2019.

Indications and contra-indications were evaluated through a comprehensive interview and clinical examination. The most important contraindications for PRGF procedure are bleeding disorders or hematological diseases which can be difficult to manage in the office. A CBCT was used to assess the bone defect in volume and bone quality. The treatment plan and the protocol using PRGF was explained to the patients who had to sign an informed consent for the treatment.

**Material**

The material necessary for the preparation of the PRGF is certified by BTI (Biotechnology Institute). Each collection kit for single use per patient contains at least: A fin needle to draw the patient’s blood; four collection tubes of 9 ml each, containing an 0.9 ml of anticoagulant (3.8% sodium citrate) to prevent non-specific activation of platelets; one PTD (Plasma Transfer Device) which allows to separate each fraction obtained after centrifugation; two fractionation tubes of 9 ml each, containing the fractions obtained after centrifugation; an activation syringe; five identification labels. It also contains a System V® centrifuge - a Plasmaterm H® which facilitates and accelerates the platelet activation syringe; five identification labels. It also contains a System V® centrifuge at low speed (580 g for 8 min), allowing the platelets to be separated from the white blood cells. The plasma thus has a double fraction [8,19].

- Fraction 1 (F1): Poor in platelets (Platelet-Poor Plasma) but very rich in fibrin. It represents less than 2 ml for a 9 ml tube.

- Fraction 2 (F2): Plasma very rich in platelets, 2 ml for a 9 ml tube.

The fractions F1 and F2 provide four different formulas. PRGF can thus be adapted to different therapeutic uses [16].

A fibrin membrane form from the F1 fraction is used as a biological membrane to protect the grafted sites. It would also allow total epithelialization of the soft tissues. The liquid form of the F1 fraction is used in oral surgery to activate the implant surface.

The coagulum is a solid form from the F2 fraction, similar to the coagulum, it is a PRGF-bone filling material mixture (endogenous or exogenous). This PRGF/biomaterials combination arouses major interest in oral surgery and implantology. Here we used as biomaterial, Biobank cs’ Cortico Spongious particulate allograft, granulometry 0.5 mm to 1 mm (Biobank-DPO, 2003, Lieusaint).

The various therapeutic formulas are developed while the surgeon is preparing the operating site. For some cases, it was first to treat the bone defect of the site to be implanted in a second step, and for others the implantation was done at the same time as bone reconstruction.

The following surgical protocol was conducted: (1) Periapical anesthesia 1/200,000 (Articaine) - (2) Soft tissue incision (3) Peel flap (4) In some cases, tooth avulsion and alveolar curettage - in other cases, implant drilling sequence and implant placement (5) Filling the bone defect using the PRGF-filling material mixture and covering the graft with a PRGF membrane (6) Sutures (apical horizontal mattress, glycolon 5/0) without traction to bring the two banks closer to the flap. A coronal suture is performed to maintain hermetic surgical embankment closure.

The PRGF mixed with the filling material was generally prepared in 10 min, and a membrane obtained in 25 min.

After each intervention, post-operative advices were given to patients with a drug prescription - Amoxicillin 1 g (1-0-1) over 7 days - Paracetamol 500 mg (1-1-1) over 3 days.

**Follow-up and outcomes**

Patients were seen 2 or 3 days after surgery to visually assess the development of wound healing at the operating site and to remove the stitches. Then, all the patients were regularly followed up to 6 months for the realization of the final prosthesis.

A second CBCT was performed 6 months later post-surgery to assess the gain of the bone volume relative to the width and height of the residual bone ridge.

CBCTs were performed using the same device (Planmeca ProMax 3D Mid Finland, 2017), before and after surgery. Measurements of the edentulous areas were performed using Romexis Planmeca software. The height of the ridge was divided into 3/3 from the top to its base, the base being either the floor of the nasal cavity or the floor of the maxillary sinus and was measured at the two walls (vestibular and palatal). The residual crestal width of the edentulous ridge was measured between the two walls (vestibular and palatal) at the level of the apical 1/3 and the basal 1/3 of the edentulous ridge (Figure 1).

**Results**

Six patients aged between 41 and 65 years old (mean age of 58.2 years ± 8.9) underwent implant placement with mixed PRGF treatment, including four women (Table 1). All were healthy and two smokers. All edentulousness were at the maxilla.

Patients with partial edentulosity (N=3) exhibited mostly two-dimensional bone resorption of the crest after dental avulsions. Among patients with complete edentulosity (N=3), two previously suffered from type 2 and grade 3 or 4 periodontitis [20], which led to the loss of several teeth and required the extraction of very fragile residual teeth (terminal mobility), after a long periodontal treatment. One patient presented with very advanced caries of the abutment teeth of a full bridge causing its loss.
Mean residual crestal width was 3.7 mm ± 0.8 (range: 3 mm to 5 mm), mean residual vestibular height was 6.2 mm ± 2.9 (3 mm to 11 mm) and mean residual palatal height was 8.7 mm ± 2.1 (6 mm to 11 mm). All implants placed in all the patients had 3.5 mm of diameter and 11 mm of length.

An average of 5 implants per patients have been placed. At 2 to 3 days post-surgery, inflammation in the operated area was clinically observed in none of the cases.

**Patient treatment**

As an example of the six patients treated, a 60-year-old man, a smoker, presented with stage 2 and grade A periodontitis with vertical and horizontal resorption in the maxilla. The treatment based on periodontal hygiene was first carried out a few months before, and the implantation was done at the same time as bone reconstruction.

The X-ray shows the general state of the maxilla with bone resorption and fragile teeth (Figure 2). After the extraction of residual teeth, 8 implants were immediately placed (Figure 3), followed by the placement of the PRGF-Biobank mixture (cs®Cortico Spongious particulate allograft, granulometry 0.5 mm to 1 mm, BIOBANK-DPO, 2003, Lieusaint), and covering of the graft with the PRGF membrane (Figure 4). The healing was evaluated 3 days post-operative (Figure 5).

Transient prosthesis was placed on the third day after surgery (Figure 6), and the final prosthesis was inserted 6 months later (Figure 7).

It should be noted that for this case, given the significant resorption of the sub-sinus areas, we performed at the same day of surgery two elevations of the sinus floor (left and right). The mandible was also rehabilitated with conventional implants at a later time.

At six months follow-up, the average height gain was 5.7 mm ± 2.1 (2 to 8) for the vestibular wall (Figure 8) and 3.3 mm ± 1.2 (2 to 5) for the palatine wall (Figure 9). The average gain in crestal width was 4.2 mm ± 0.8 (3 to 5) (Figure 10).

During follow-up, no complications of an inflammatory or infectious type were noted in the short, medium and long terms until the final prosthesis. The keratinized gum was very favorable.

**Discussion**

In this paper, we reported six various cases of the use of PRGF-
filling material mixture and the covering of the operating site. Indeed, after activation, the platelets secrete numerous proteins which can influence certain aspects of wound healing such as chemotaxis and mitogenesis of stem cells and osteoblasts, angiogenesis for capillary growth, bone matrix formation and collagen synthesis [22]. And the absence of neutrophils would prevent degradation of the matrix by enzymes such as the matrix metalloprotease. PRGF would stimulate fibroblasts, so it would improve the proliferation of connective tissue, hence the good healing of the gum. Even if the absence of inflammation was only visual, the use of PRGF seemed to have the potential to reduce tissue inflammation after surgery [23]. This was despite the findings of Masuki et al. [24] who showed that the PRGF preparation had lower concentrations of growth factors (TGF-β, PDGF and VEGF) compared to the A-PRF and PRP preparations which would have higher levels of growth factors. Thus, PRGF may contain sufficient concentrations of growth factors to insure adequate healing. In addition, it contains less leucocytes limiting inflammation process.

Guided bone generation is a well-established technique for increasing absorbed alveolar ridges. The success criteria being the stability of the graft, the maintenance of the regeneration space, the sutures without tension [25], the PRGF-filling material mixture would, by its consistency, allow the mechanical stability of the graft even in bone defects important [26]. We have seen this in all cases of total toothlessness that we have treated. Indeed, filling with the PRGF-material mixture (sticky bone) adheres by sticking to the surface of the crest to be reconstructed. This phenomenon further stabilizes the whole graft thus promoting healing. This was confirmed in our various clinical cases as the healing was optimal for both bone and soft tissue. The randomized clinical trial carried out by Anitua [4] showed the effectiveness of PRGF in the regeneration of tissues in the post-extractive alveoli for implant placement [4]. The membrane resulting from the PRGF protocol also seems to support healing by covering the operating site. Indeed, in our clinical cases, the PRGF-material mixture, although adhering well to the recipient bone surface, the covering of the whole graft by the PRGF membrane, rather than the natural flap, played the role of a protective cushion of the site, thus promoting the isolation of the graft and the while facilitating the migration of the epithelium above. A randomized study evaluated the efficacy and safety of PRGF and autologous bone by demonstrating the regeneration of mandibular post-extractive alveoli over a 12-week period [27]. Also, in the control group, very little connective tissue and mature bone were observed. Bone regeneration of mature bone was greater in quantity and quality in patients treated with PRGF. This result was later corroborated by an animal study [28].

The appearance of the attached gum shows good epithelialization. Two studies report an improvement in the healing of soft tissues, and very thick keratinized tissue from the 15th day. These results would be explained by the strong presence of angiogenic growth factors and mitogens in endothelial cells. However, the limited studies in the literature do not allow conclusions to be drawn. Recently, Aprajita et al. [29] used a PRF-filling material mixture, rather suggesting that it would be beneficial to combine an autologous platelet concentrate with a membrane to improve the healing.

Whatever the form of use, liquid, coagulum or membrane, these preparations, rich in growth factors would accelerate the mucosal and bone healing, while reducing the risk of infection. A priori, the bacteriostatic effect of PRGF is not due to the absence of leukocytes. The same effect is found in other platelet-rich plasma and leukocyte protocols [26].

These clinical results would be explained by the fact that platelets are a rich source of growth factors [21]. Indeed, after activation, the platelets secrete numerous proteins which can influence certain aspects of wound healing such as chemotaxis and mitogenesis of stem cells and osteoblasts, angiogenesis for capillary growth, bone matrix formation and collagen synthesis [22]. And the absence of neutrophils would prevent degradation of the matrix by enzymes such as the matrix metalloprotease. PRGF would stimulate fibroblasts, so it would improve the proliferation of connective tissue, hence the good healing of the gum. Even if the absence of inflammation was only visual, the use of PRGF seemed to have the potential to reduce tissue inflammation after surgery [23]. This was despite the findings of Masuki et al. [24] who showed that the PRGF preparation had lower concentrations of growth factors (TGF-β, PDGF and VEGF) compared to the A-PRF and PRP preparations which would have higher levels of growth factors. Thus, PRGF may contain sufficient concentrations of growth factors to insure adequate healing. In addition, it contains less leucocytes limiting inflammation process.

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These results suggest that strengthening the concentration of growth factors by applying PRGF to an operating site would favor its evolution as other studies have claimed. Moreover, a meta-analysis by Del Fabbro et al. [30] concludes that the use of autologous platelet concentrates such as PRF, PRP or PRGF may be an advantage in certain clinical cases. Larger studies are needed to evaluate the interest of this protocol compared with another existing protocols using other growth factors (PRF, PRP) [30], or with a conventional protocol without using healing factors. However, the results observed in these clinical cases are interesting.

Conclusion

In the series of various clinical cases presented here, we used the PRGF protocol mixed with allograft biomaterial in patients presenting different clinical indications and origins of bone defect. The healing of soft and hard tissues was clinically interesting. The use of autologous platelet concentrate of the PRGF type seems to be a supplement in bone reconstruction surgery. However, between the different platelet concentrate protocols, the qualities of some are presented as being optimal. It is likely that these protocols all have different and interesting qualities for the healing of soft and hard tissues, all the more so because their opinions differ on the use of platelet concentrate associated or not with a bone filling material. A randomized comparative study between these different autologous platelet concentrates would be interesting.

References
