PRGF VS CGF in management of labial dehiscence around immediate implants (Comparative study)

Clinical trial registration: NCT05595772

Document Date: July 30, 2022

Introduction and Review

With the increase in esthetic demand, dental implants have become an indispensable part of modern dental practice. However, with the increasing practice of dental implants; the esthetic outcome is considered as important as the functional and biological outcome. **(Haas et al., 2002)**

Immediate implants have been evolved as the first treatment option in cases of the failed tooth to decrease the time of treatment plan. Immediate implantation at the time of tooth extraction has been associated with significantly higher patient satisfaction (95%) compared to early (84%) or delayed (80%) implant placement. **(Hof M. et al., 2015)**

To obtain an effective esthetic outcome with a single implant-supported restoration in the anterior region, it is crucial to preserve and maintain intact the bone anatomy, as well as the overlying soft tissues. The challenge in treatment is when the labial bone plate presents with a dehiscence type defect stemming from etiologies such as chronic inflammation from a mid-facial vertical fracture affecting the periodontal attachment or severe trauma and chronic infection**.** **(Sarnachiaro GO et al., 2016) (Fürhauser, R. et al., 2017)**

The compromised esthetic result is anticipated when a 1- to 2-mm vertical deficiency in soft tissue is noted. For defects ≥ 2mm, soft tissue augmentation should be considered before implant insertion. The keratinized gingival (KG) width on the mid-buccal side of the socket: ≥ 2, 1 to 2, and <1 mm were defined as adequate, compromised, and deficient, respectively. **(Juodzbalys et al., 2008)**

The extraction sockets were divided into four groups: Class I, intact soft tissue wall and bone walls; Class II, intact soft tissue wall with the destruction of at least one bone wall; Class III, the recession of all soft tissue walls by ≤5 mm; and Class IV, the recession of at least one soft tissue wall by >5 mm **(Cheng et al., 2021)**

It was advocated that the resorption of the socket walls that occurs following tooth extraction must be considered to ensure proper implant placement**.** Surgical techniques including the use of bone grafting materials as well as using different types of barriers to fill the space around the implants were proposed to maintain hard and soft tissue architecture and to regenerate lost bone in areas of dehiscence and bony defects **(Gaia Pellegrini et al., 2013) (Araujo et al., 2005**.**)**

One of the most popular techniques is guided bone regeneration (GBR), which entails placing a membrane over the defect to create a secluded space into which osteogenic cells can migrate and remain undisturbed over the exposed part of the implant. Guided bone regeneration (GBR) is frequently used in combination with the installment of titanium implants. The application of a membrane to debar non-osteogenic tissues from interfering with bone regeneration is a key principle of GBR **(Elgali I et al., 2017) (Vijayalakshmi R et al., 2012)**

Membrane materials possess several properties which are amenable to modification. A large number of membranes have been introduced for experimental and clinical verification .third-generation membranes have evolved, which not only act as barriers but also as delivery devices to release specific agents such as antibiotics, growth factors, adhesion factors, etc., at the wound site on a time or need basis to orchestrate and direct natural wound healing in a better way **(Sam G. et al., 2014)**

Numerous studies have explored the suitability of biocompatible materials in regenerative medicine. Platelet concentrates are originated from centrifuged blood and are named according to their biological characteristics, such as platelet-rich plasma, platelet-rich fibrin, and concentrated growth factor **(Ding, Z et al., 2021)**

Platelet concentrates have emerged as innovative autologous blood products that escalate tissue healing and regeneration in regenerative therapy. A common characteristic of these products is their higher than baseline platelet concentration, which ameliorates wound healing and tissue repair. Indeed, because these concentrates are autologous, all the biocompatibility issues are avoided **(Chou T-M et al., 2020)**

Platelets have been identified as a manufacturer of high quantity of growth factors, such as Platelet-Derived Growth Factor (PDGF), Transforming Growth Factor-B1 (TGF), TGF-B2, Fibroblast Growth Factor (FGF), Vascular Endothelial Growth Factor (VEGF), Insulin-like Growth Factor (IGF) that invigorating cellular proliferation, matrix remodeling and neo-angiogenesis **(Pakyari, M et al., 2013)**

Four major categories of products can be simply defined, based on their leukocyte content and fibrin architecture: pure platelet-rich plasma, such as Cell Separator PRP or Anitua' PRGF; leukocyte- and platelet-rich plasma (L-PRP), such as PCCS or Ace PRP; pure platelet-rich fibrin (P-PRF), such as Fibrinet PRFM; and leukocyte- and platelet-rich fibrin (L-PRF), such as Choukroun's PRF. **(Chou T-M et al., 2020)**

Plasma rich in growth factors (PRGF), a subtype of P-PRP (pure platelet-rich plasma), is a supernatant enriched in plasma and platelet-derived morphogens, proteins, and growth factors. PRGF represents a complex pool of active mediators that may stimulate and accelerate tissue regeneration, which is generally safe to use and economical to obtain. Autologous PRGF has been approved for clinical use by the European Community and the U.S. Food and Drug Administration **(Anitua et al., 2014) (Dohan Ehrenfest et al., 2009)**

The drawback of PRP is its complex preparation process: several procedures are needed to segregate it and it has to be activated by thrombin and calcium chloride. **(Chen, X et al., 2018)**

CGF (concentrated growth factor), the third-generation platelet concentrate presented by Sacco in 2006 carries more growth factors and has a firmer fibrin structure than first-generation PRP and second-generation PRF (platelet-rich fibrin) **.** Sacco's membrane (CGF) shows a complex three-dimensional architecture which makes it a biomaterial rich in fibrin platelets, leukocytes, and growth factors - very satisfactory both for patient and operator **(Dohan et al., 2006) (Chen, X et al., 2018)**

In comparison with previous generations of platelet enrichment, the preparation of CGF membranes does not need additional reagents to generate platelet activation or fibrin polymerization and is less likely to develop immune responses or cross infections **(W. M. Talaat et al., 2018)**

Aim of the study

- Assess the effectiveness of PRGF and CGF in the management of buccal dehiscence and marginal bone level around the immediate implant.

- Compare the effectiveness of PRGF Vs CGF.

Patients and Methods

Patient selection

this study will be conducted on 20 patients indicated for immediate implant placement in the maxillary anterior region. After approval from the ethical committee, the entire patients will be recruited from the outpatients' clinic of the Oral Medicine, Oral Diagnosis, and Periodontology Department. Faculty of Dentistry, Minia University.

Inclusion criteria:

1. Selected patients of both sexes are 20-40 years old.
2. Patients are systemically healthy based on questionnaire dental modification of
Cornell index.
3. Gingival health according to the new classification system (2017)
4. The recipient site of the implant is free from any pathological conditions.
5. Class II extraction socket according to Chang's classification system
6. Adequate interocclusal space to accommodate the available restorative components.
7. Adequate native/apical bone to achieve primary implant stability.

Exclusion criteria:

1. Pregnant female.
2. Parafunctional habits such as bruxism and clenching Patients suffering from periodontitis.
3. Smokers.

Ethical regulation and Informed consents

All patients will undergo an immediate implant placement and the complete treatment plan will be explained to all patients including detailed steps, risks, and
expected results. Verbal and written informed consent will be obtained from all patients before the commencement of the study. All steps will be examined and approved by the appropriate ethics committee and have therefore been performed following the ethical standards laid down in the Declaration of Helsinki and the research ethics committee of the Faculty of Dentistry, Minia University.

Pre-surgical phase

1. All selected patients will be screened by comprehensive periodontal examination
and full periodontal charts will be obtained. A preoperative cone-beam computed
tomography (CBCT) will be performed for each patient who met the inclusion
criteria before the surgery to determine bone height and width and decide the
implant length and diameter to be placed and to evaluate the underlying bone
condition.

Randomization

The study will use simple randomization to allocate patients into 2 groups, each
group will be included 10 patients.

Group A: (concentrated growth factor group)

ten patients indicated for immediate implant in the maxillary anterior region (class II socket), will be a candidate for immediate implant placement with CGF combined with xenogeneic bone graft

Protocol for CGF preparation:

10 ml venous blood samples will be drawn from the patients and placed in a centrifuge tube without anticoagulants. Then the tubes will be placed in the centrifugation device in an opposing balanced manner and rotated in four sequential steps. The first step at 735 g (2249 ≈ 2200) for 2 min., the second one at 580 g (1998 ≈ 2000) for 4 min., the third one at 735 g (2249 ≈ 2200) for 4 min. and the fourth one at 905 g (2495 ≈ 2500) for 3 min. The result was a clot that was collected using a straight tweezer and ready to be used

Group B: (platelet-rich in growth factor group)

Ten patients who indicated immediate implant in the maxillary anterior region (class I or class II socket), will be a candidate for immediate implant placement with PRGF combined with xenogeneic bone graft.

Protocol for PRGF preparation:

30 ml venous blood will be collected from the patient then deposited in 5 mL tubes containing sodium citrate anticoagulant. Then the tubes will be centrifuged at 580 G (2270 rpm) for 8 minutes at room temperature. After centrifugation, the blood sample will be layered into the following four distinctive layers:
1) 0.5 mL Plasma poor in growth factors (PPGFs) =F1 in the uppermost part of the tube

2) 0.5 mL Plasma with growth factors (PGFs) = F2

3) 0.5 mL (PRGF) = F3 located immediately above the red blood cell portion in the tube

4) Red blood cell concentrate layer

From all tubes, The 500 µL PPGF will be eliminated and the PRGF will be separated with 500 µL pipettes and transported to an independent dish then activated using 50 µL of 10% calcium chloride for every 1 ml of preparation and mixed with xenogenic bone graft then it will be incubated for 40 minutes in 37℃ to produce easy to handle gelatinous layer (PRGF) fibrin mixed with the xenogenic bone.

Surgical Phase

1. The surgical site will be prepared by scrubbing the surgical site using Betadine: Povidone-iodine, 7.5% (0.75% available iodine) the Nile Comp. for Pharmaceuticals and Chemical Industries, Alexandria, Egypt
2. Nerve block or infiltration anesthesia will be administrated Articaine (4%) with epinephrine (1:100,000 or 1:200,000)
3. Atraumatic extraction of the tooth or remaining root using periotome, then sequential implant drilling accompanied by copious irrigation will be carried out. then cover screw attached to the implant top by the aid of its driver
4. A sample of venous blood will be withdrawn from the patient and centrifuged without delay according to the preparation protocol of each group.
5. Then the membrane loaded with the bone graft will be applied and condensed around the dental implant filling the gap between the fixture and the walls of the socket.
6. Finally, Tension-free Closure of the wound was achieved using 4/0 vicryl sutures.

Postoperative instructions

1. Routine verbal and written postoperative instructions for periodontal surgery will be given to all patients including ice compression on the surgical site during the first 4 h, a liquid and/or soft food diet for 3 days.
2. As with all surgical procedures, patients will be informed to contact our clinic if any problems will be developed during the postoperative period.
3. The postoperative medications prescribed will be (Amoxicillin+ clavulanic acid*625mg for 7 days) every 8 h or clindamycin** 300 g every 12 h for 7 days for patients allergic to penicillin, and (Ibuprofen*** 600 mg every 12 h for 5 days).
4. The sutures will remain in situ for 2 weeks.

Clinical assessment:

All patients included in the present study will be followed carefully and monitored to motivate the patient for oral hygiene instructions and maintenance of good oral
hygiene.

*Augmentin®, GlaxoSmithKline
** Dalacin C®, Pfizer
*** Brufen®, Abbott

Radiographic evaluation

A periapical film with the paralleling technique will be used immediately after the implant placement

And after 9 months CBCT imaging will be used to evaluate:
1- Bony density
2- Marginal bone level.

Statistical analysis:

-All data will be tabulated and analyzed by statistical method.

References

Anitua, E., Pascual, C., Antequera, D., Bolos, M., Padilla, S., Orive, G., & Carro, E. (2014). Plasma rich in growth factors (PRGF-Endoret) reduces neuropathologic hallmarks and improves cognitive functions in an Alzheimer's disease mouse model. *Neurobiology of aging*, *35*(7), 1582–1595.

Araújo, M. G., & Lindhe, J. (2005). Dimensional ridge alterations following tooth extraction. An experimental study in the dog. *Journal of clinical periodontology*, *32*(2), 212–218.

Balasubramaniam, A. S., Raja, S. V., & Thomas, L. J. (2013). Peri-implant esthetics assessment and management. *Dental research journal*, *10*(1), 7–14.

Chang, L.-C., & Cheng, Y.-M. (2021). The Effect of Different Socket Types on Implant Therapy While Using Flapless Ridge Preservation. *Applied Sciences*, *11*(3), 970.

Chen, X., Wang, J., Yu, L. *et al.* Effect of Concentrated Growth Factor (CGF) on the Promotion of Osteogenesis in Bone Marrow Stromal Cells (BMSC) *in vivo*. *Sci Rep* **8,** 5876 (2018).

Chou, T. M., Chang, H. P., & Wang, J. C. (2020). Autologous platelet concentrates in maxillofacial regenerative therapy. *The Kaohsiung journal of medical sciences*, *36*(5), 305–310.

Ding, Z., Tan, Y., Peng, Q., Zuo, J., & Li, N. (2021). Novel applications of platelet concentrates in tissue regeneration (Review). Experimental and Therapeutic Medicine, 21, 226.

Dohan Ehrenfest, D. M., Rasmusson, L., & Albrektsson, T. (2009). Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). *Trends in biotechnology*, *27*(3), 158–167.

Dohan, D. M., Choukroun, J., Diss, A., Dohan, S. L., Dohan, A. J., Mouhyi, J., & Gogly, B. (2006). Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part I: technological concepts and evolution. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics*, *101*(3), e37–e44.

Elgali, I., Omar, O., Dahlin, C., & Thomsen, P. (2017). Guided bone regeneration: materials and biological mechanisms revisited. *European journal of oral sciences*, *125*(5), 315–337.

Fürhauser, R., Mailath-Pokorny, G., Haas, R., Busenlechner, D., Watzek, G., & Pommer, B. (2017). Immediate Restoration of Immediate Implants in the Esthetic Zone of the Maxilla Via the Copy-Abutment Technique: 5-Year Follow-Up of Pink Esthetic Scores. *Clinical implant dentistry and related research*, *19*(1), 28–37

Haas, R., Polak, C., Fürhauser, R., Mailath-Pokorny, G., Dörtbudak, O., & Watzek, G. (2002). A long-term follow-up of 76 Bränemark single-tooth implants. *Clinical oral implants research*, *13*(1), 38–43.

Hof, M., Pommer, B., Ambros, H., Jesch, P., Vogl, S., & Zechner, W. (2015). Does Timing of Implant Placement Affect Implant Therapy Outcome in the Aesthetic Zone? A Clinical, Radiological, Aesthetic, and Patient-Based Evaluation. *Clinical implant dentistry and related research*, *17*(6), 1188–1199.

Juodzbalys, G., Sakavicius, D. and Wang, H.-L. (2008), Classification of Extraction Sockets Based Upon Soft and Hard Tissue Components. Journal of Periodontology, 79: 413-424.

Pakyari, M., Farrokhi, A., Maharlooei, M. K., & Ghahary, A. (2013). Critical Role of Transforming Growth Factor Beta in Different Phases of Wound Healing. *Advances in wound care*, *2*(5), 215–224.

Pellegrini, G., Pagni, G., & Rasperini, G. (2013). Surgical Approaches Based on Biological Objectives: GTR versus GBR Techniques. *International journal of dentistry*, *2013*, 521547.

Sam, G., & Pillai, B. R. (2014). Evolution of Barrier Membranes in Periodontal Regeneration-"Are the third Generation Membranes really here?". *Journal of clinical and diagnostic research : JCDR*, *8*(12), ZE14–ZE17.

Sarnachiaro, G. O., Chu, S. J., Sarnachiaro, E., Gotta, S. L., & Tarnow, D. P. (2016). Immediate Implant Placement into Extraction Sockets with Labial Plate Dehiscence Defects: A Clinical Case Series. *Clinical implant dentistry and related research*, *18*(4), 821–829.

Talaat, W. M., Ghoneim, M. M., Salah, O., & Adly, O. A. (2018). Autologous bone marrow concentrates and concentrated growth factors accelerate bone regeneration after enucleation of mandibular pathologic lesions. *Journal of Craniofacial Surgery*, *29*(4), 992-997.

Vijayalakshmi, R., Rajmohan, C. S., Deepalakshmi, D., & Sivakami, G. (2012). Use of platelet rich fibrin in a fenestration defect around an implant. *Journal of Indian Society of Periodontology*, *16*(1), 108–112.

World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013 Nov 27;310(20):2191-4. doi: 10.1001/jama.

Moutamed, G. (2019). Boosting Effect of Concentrated Growth Factor on Osseointegration of Immediate Implant: A Histological Analysis in Dogs. *Egyptian Dental Journal*, 65(Issue 4 - October (Oral Surgery)), 3305-3314. doi: 10.21608/edj.2019.74761

Ihab S. Abd El-Hamid, Khaled A. Abdel–Ghaffar, Ola M. Ezzatt, Fatma H. El Demerdash, Noha N. EL-Zalabany, Marwan F. Antar. Socket Preservation Using Atorvastatin Loaded in Growth Factor Plasma Rich Fibrin Scaffold: A Randomized Clinical Trial. Nat Sci 2018;16(7):82-91]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). http://www.sciencepub.net/nature. 13. doi:10.7537/marsnsj160718.13.