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Concentrated Growth Factor (CGF) in Alveolar Bone Grafting Procedures: Dilemma or a Reality? - A Detailed Review

Dr. Mohammadi Begum [α], Dr. Jayaprakash Thirumala Reddy [σ], Dr. Sujan Kumar K V [ρ] & Dr. Madhav Naik P [ω]

Abstract- Alveolar bone grafting is considered to be one of the most challenging task in the management of cleft lip and palate patients as it is expected to bridge the gap between the alveolar segments and provide the solid base for the un-erupted tooth/teeth to erupt through it, besides effectively healing the Oro-antral fistula if any passing through the cleft into the nasal cavity. Although the traditional approach is to use autogenous bone graft from iliac crest, which has its own side-effects like pain, morbidity, additional surgery, etc. However with the advent of Tissue engineering technique, it has become possible to overcome most of these challenges by using a tissue friendly yet innovative material by name CGF (Concentrated Growth Factor) which in reality is the latest version of platelet-rich plasma having in it abundant of growth factors thereby serving the purpose of a regenerative medicine, wherein three factors are important to stimulate the bone regenerative effect: 1) Scaffold 2) Growth factors and 3) Autologous cells. All these are found to be present in sufficient quantity in CGF which was first introduced by Sacco in 2006 followed by Corigliano in 2010.

Keywords: concentrated growth factors, platelet-rich plasma, autologous bone, alveolar bone grafting, osteogenic potential.

I. Search Strategy

A secondary research based upon the library referencing from the year 2000 to 2018 through online search using key words as concentrated growth factors, platelets, wound healing, osteogenic potential, platelet-rich plasma, alveolar bone grafting, etc.

II. Introduction

Concentrated growth factor is considered to be an updated and latest version of platelet-rich plasma (PRP) found to be exhibiting remarkable wound healing potential in open surgical wound sites, where its application has proven to give both soft tissue and hard tissue healing potantial by virtue of its wound healing and osteogenic potential. Such desirable clinical and biotechnological potential of this group of platelets is found to be of immense use in different craniofacial surgical procedures including alveolar bone grafting in cleft lip and palate individuals wherein the golden standard of treatment is to use cortical bone from the iliac crest. Although the conventional method has its good bone induction and conduction property to bridge the gap in the cleft-alveolar segments, yet in most of the cases would result in several side-effects like surgical site morbidity and altered gait of the individuals post-surgery creating a new surgical site to treat the existing one.

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III. History and Background

Bone defects involving the Oral and maxillofacial anatomical regions have been treated for long time by using variable platelet-concentrates, which differ from each other by their preparation methods to induce and accelerate the bone formation when mixed with bone grafts and barrier membranes. These concentrates are found to be abundantly rich in growth factors which are in reality the "PROTEINS" involved in regulating the complex process of wound healing. Since the growth factors are located in the blood plasma and platelets, these platelet-concentrates are commonly used to accelerate the tissue repair and regeneration of clefts of the alveolar region. Platelet's regenerative potentiality was introduced in the year 1974 by Rose et al who described the presence of growth factors in the blood-plasma.[1] It was also reported that based upon their methods of preparations and evolution of their clinical applications periodically, the platelet-concentrates have been grouped into various generations.

a) First-generation of platelets

Includes PRP (Platelet-rich plasma) and PRGF (Platelet-rich in growth factor) which were introduced by Marx and Anitua respectively. The method of preparation involved addition of calcium and bovine thrombin to achieve stability which in turn made it technique sensitive for all the clinical applications.

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b) Second-generation of platelets

Involved PRF (Platelet-rich fibrin) introduced by Choukroun. The method of preparation involved using venous blood from the patient's veins and centrifugating the same to produce a fibrin-rich gel with aggregated platelets obtained in the middle of the tube, just between the red corpuscles at the bottom and platelet poor plasma at the top.

c) Preparation of CGF

Its method of preparation is similar to PRF but the centrifugation speed differs. Its preparation uses 2400 rpm to 2700 rpm to separate all the cells in the venous blood. As a result a block is obtained which is rich in fibrin having a thicker, larger and denser amount of growth factors compared to PRF. This makes CGF better in bone regenerative capacity improving its versatility.[3-5] After centrifugation the CGF was obtained in three parts, the upper white Part (PPP), the lower red Part (RBC) and the middle "buffy coat" Part (interface between white and red part). The results showed that platelets and leukocytes were localized in the buffy coat, whereas the erythrocytes were present only in the red part of CGF. The in vitro cumulative release of growth factors revealed the presence of PDGF-AB, TGF-β1 and IGF-1 having a constant kinetic release, reaching the maximum accumulation at day 3rd and 6th respectively. VEGF and BMP-2 had a slow kinetic release reaching the maximum accumulation at day 8th. TNFα and BDNF had a faster kinetic release reaching the maximum accumulation at day 1st and 3rd respectively. These findings have largely supported the clinical use of CGF for its enhanced healing and osteogenic-effects.[6,7] According to Professor Rodella[8] at University of Brescia-Department of Biomedical Sciences and Biotechnologies, CGF shows higher tensile strength, more growth factors, higher viscosity and higher adhesive strength than PRF. Therefore it is recommended that surgeons can use the CGF as a barrier membrane to accelerate soft tissue healing or be mixed with bone graft to accelerate new bone formation. CGF doesn't require any chemical or allergenic additives such as bovine thrombin or anticoagulants into it. Therefore it is usually free from any viral disease transmission.[9-11]

IV. Materials and Methods

A secondary research based on hand – search and online search using the key terms was done for the articles from 2000 to March 2018 involving discussion about the platelets (CGF) and their osteogenic capabilities.

a) Inclusion criteria

All original researches, reviews, case reports on the POSITIVE outcome of the osteogenic properties of the CGF were included. Studies that dealt with craniofacial surgery for total or partial reconstruction of mandibles/maxilla, cleft lip and palate surgeries, distraction osteogenesis and Osseo-integration were also added in the search strategies.

b) Exclusion criteria

Studies involving gene therapy, etc.

c) Research Dilemma

Therefore the need of the hour is to use this material which can help in efficient wound healing and also provide osteogenic impulse so that second surgical site can be avoided which would be beneficial to the patient in terms of pain, morbidity and cost.

d) Advantages of CGF

It is accepted that CGF is capable of better regenerative-capacity and higher versatility. The fibrin block is thick and dense with a very high concentration of fibrinogen, factor XIII and thrombin. The activated form of XIII (XIIIa) cross links the fibrin clot to increase the stability, strength, and protection against plasmin mediated degradation. Mixing this combination with autogenous or other fillers makes it user-friendly material to handle and fill even the larger bone defects improving the overall bone regenerative effect.[12] Sohn in 2009[3] reported that CGF has multipurpose use associated to its higher levels of active proteins which can support healing, growth and cell morphogenesis. CGF provides sufficient stability to implant- root interface during healing process providing necessary bone formation around the implant which would be capable of absorbing the functional load during healing. With the help of Resonance Frequency-Analysis (RFA) which is considered to be very important tool for assessing the Osseo-integration process and also tracks the changes in the stability not only during the implant placement but also during the healing and later periods, the active role played by CGF and other growth factors containing products during Osseo-integration and bone healing was reported. In a sum up of all its advantages, CGF appear to show superior potential for tissue-regeneration in the clinical and biotechnological applications including sinus and alveolar ridge augmentation.[13-19]

e) Possible mode of action by CGF

The various research studies have shown that the improved regenerative effect of CGF when used to treat the bone defect could be attributed to its biologic constituents which are active in presence of chemotactic and mitogenic PDGF (Platelet Derived Growth Factor) which are basically involved in tissue regeneration process. Unlike PRP, CGF does not dissolve rapidly following its application on the surgical site. However it was found that the thick fibrin-matrix is remodeled slowly like a natural blood-clot. Thus prolonging the duration of growth factors activity which in turn is found to be effective for growth factor synergy, enhancing the cell proliferation and osteogenic differentiation.[20,21]

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V. Discussion

CGF, therefore is considered as the latest progeny of the platelets containing the abundant number of growth factors, leucocytes and fibrin-matrix in it. The growth factors released are responsible for aiding in tissue regeneration (both hard and soft tissue) which is the reason that it can provide immediate wound healing and repair of the surgical site by outgrowing the number of growth factors.[22-27] The greater advantage of this latest PRP is in it being an AUTOGENOUS preparation, which not only improves the tissue healing but also enhances the clinical outcome of the surgical procedure at a considerable short period of time.[28-30]It is also reported that the presence of growth factors in CGF are considered to be a class of natural biological mediators that regulate the key cellular events in the tissue repair, including cell proliferation, differentiation and extracellular matrix synthesis. Release of biological factors responsible for tissue repair occurs through platelet activation and de-granulation. These factors are PDGF (Platelet-Derived Growth Factors), VEGF (vascular-endothelial growth factors), IGF (Insulin-Like Growth Factors), TGF (Tissue-Growth Factor), BDGF (Brain-Derived Growth Factor) and BMP (Bone-Morphogenetic Protein).[31-33] Recent studies have reported that when CGF is used alone or mixed with bone allograft increased the bone growth process by accelerating the healing of the soft tissue and facilitating periodontal ligament repair in both the animal and human studies. Furthermore, the findings suggested that CGF along with CD34 positive cells has played an effective role in vascular maintenance, neo-vascularization and angiogenesis when used at the surgical wound site. This was all attributed to the presence of the growth factors in CGF which in turn would enhance the lost or the damaged tissue regrowth at the local site of application.[34-36] Although it is suggestive that the best bone grafts are loaded with the desirable qualities of Osteo-conduction, Osteo-induction and Osteo-genesis, it is the autogenous bone which is still considered the "gold standard" since it has all the three characteristics without any associated immune response. However it was found that CGF when used along with the autogenous bone could harness the osteogenic effect to achieve longer and better osteogenesis. This property is also found to be helpful in providing a complete root coverage for denuded roots in orthodontic cases as well.[37-39] Additionally it is reported that use of CGF and other platelet- concentrates during bone grafting offers the advantages in terms of formation of a dense fibrin clot which primarily plays an important mechanical role, secondly it promotes cellular migration, particularly of endothelial cells which are necessary for neo-angiogensis, vascularization and survival of the graft. Finally the presence of leukocytes and cytokines in the fibrin network play a significant role in the self- regulation of inflammatory and infectious phenomenon within the grafted material.[40]

VI. Conclusion

CGF with its well-known tissue-regeneration capability can be the next material of choice to be used for its beneficial wound healing and osteogenic property at the Cranio-maxillo-facial surgical wound site and therefore can he recommended to be used in augmenting the bone in alveolar bone grafting procedures alone or in combination with other graft materials for the best clinical outcome. Besides providing relief to the patient in terms of reduced wound healing time and an excellent opportunity to avoid another surgical procedure of harvesting bone from the iliac crest, its versatility and regeneration potentials should be given a fair chance to help the patients suffering from cleft lip and palate so that the burden of care giving is taken care by the clinicians. Although CGF has proven to be effective in Osseo-integration and bone healing further investigations and research at the clinical and histopathological levels should be encouraged to understand its role played at different levels for the benefit of mankind.

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