An Overview on the Use of Concentrated Growth Factor (CGF) and Poly Lactic-co-Glycolic Acid (PLGA) in Periodontal Regeneration

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Abstract: Alveolar bone loss as a result of periodontitis and physiological alveolar bone resorption following tooth extraction can be treated and minimized with clinical procedures such as periodontal regeneration and socket preservation. The use concentrated growth factor (CGF) has received an attention nowadays in clinical practice as source of growth factors. Meanwhile, poly lactic-co-glycolic acid (PLGA) microspheres is well known for its use in drug delivery due to its high porosity and interconnected pores. The objective of this review paper is to provide an overview on the current use of CGF and PLGA in periodontal regeneration in order to promote and obtain new bone formation and periodontal attachment.

1. Introduction

Conventional open flap debridement is a common practice in previous years in treating periodontal defect such as intrabony defect and furcation defect. With the evolution of knowledge and technologies, many surgical techniques and new materials have been introduced in order to provide better care for the patient and treatment outcome. These include the use of concentrated growth factor (CGF) and poly lactic-co-glycolic acid (PLGA).

CGF is the third-generation of platelet concentrate, containing more growth factors and harden fibrin structure as compared to first and second generation of platelet concentrate, which are platelet-rich plasma (PRP) and platelet rich fibrin (PRF) respectively. It is very much useful in periodontal and oral surgeries. Meanwhile, a wide range of PLGA based drug delivery systems have been reported for the treatment or diagnosis of various diseases and disorders. Therefore, a combination of CGF and PLGA is seen as a novel approach to induce bone regeneration and connective tissue attachment. Therefore, this review article aimed to provide a glance on the current use of CGF and PLGA in periodontal regeneration in order to promote and obtain new bone formation and periodontal attachment.

2. Concentrated growth factor

The invention of platelet concentrate provides an alternative effective measure to recombinant human growth factors to deliver high concentration of growth factors to the respected sites. Recombinant human growth factors are expensive, tend to suffer from instability and quick dilution due to solubility of the delivery vehicle. This will significantly reduce the half-life of the growth factors [1]. Therefore, the use of platelet concentrate may overcome those limitations of human recombinant growth factors.

2.1 Platelet concentrate generations

Nowadays, the use of patient's own blood that are rich in growth factors has gained an attention to facilitate the success of periodontal regeneration procedure as it is more cost saving as patient's own blood is drawn for its fabrication and thus minimizing the risk of cross contamination. The discovery of platelet concentrate using autologous source of blood started with the development of PRP followed by PRF in 2001.

CGF is the current generation of platelet concentrate product which was first introduced by Sacco in 2006 [2], [3]. CGF is produced using single centrifugation with alternate speed and this allows for isolation of larger and denser fibrin matrix compared to PRP and PRF that are rich in growth factors. It also results in clot with increase stability, strength and protection against plasmin degradation. Therefore, it can prolong the release of growth factors and action [4]. Following centrifugation, three layers were obtained in the vacutainers; which are red blood cell layer at the bottom, fibrin gel with platelets and growth factor at the middle and upper serum layer [5].

Various growth factors have been identified in the CGF. These include the platelet derived growth factor (PDGF)-AB, transforming growth factor (TGF), insulin-like growth factor

(IGF) -1, bone morphogenetic protein (BMP) -2 and vascular endothelial growth factor (VEGF). Borsani and colleagues observed that PDGF-AB and TGF- ß1 had constant release from the CGF throughout eight days of experimental period. Meanwhile, BMP-2 and VEGF had maximum accumulation by day eight and IGF-1 by day 6 [2]. Significant amount of concentrations of TGF-ß1, PDGF-BB and VEGF also had been observed by Masuki and colleagues. They concluded that CGF act as a reservoir for various growth factors required for healing [6].

2.2 CGF in periodontal management

The application of CGF may provide a constant supply of growth factors to further enhance healing. Bone stromal cells and osteoblast cells that have been treated with CGF also showed significant higher cell differentiation and proliferation [3], [7]. Similarly, application of CGF into human periosteal cells resulted in significant cell proliferation [6]. This shows that CGF provides a medium to augment better periodontal regeneration.

In the current practice, CGF has been fabricated to be used as a membrane in periodontal regeneration procedure. Many clinical studies have been conducted in order to investigate on the effectiveness of CGF in regenerative procedure. One of them was done by Qiao and colleagues where they used CGF on management of grade II furcation involvement. Significant improvement in periodontal clinical parameter was noted one year after surgery in a group of patients receiving bone graft with CGF [8].

Qiao and colleagues also had conducted a study on management of intrabony defect. A significant result was also noted in clinical parameter and hard tissue fill on radiograph in group treated with bovine porous bone mineral and CGF [9]. Significant gain in gingival thickness and keratinized gingival width on Miller class I and II recession was also noted with utilization of CGF combined with coronally advanced flap [10]. These in total show that application of CGF may provide better treatment outcome on hard and soft tissue regeneration.

3. Poly Lactic-co-Glycolic Acid

3.1 Properties of PLGA

PLGA is a copolymer of lactic acid and glycolic acid that is FDA-approved biodegradable polymer and safe to be used in living cells as it has great strength property and highly biocompatible [11]. It is a synthetic polymer that can be dissolved by a wide range of common solvents. It is a flexible material as it can be can be processed into any shape and size to encapsulate various agents such as drugs, vaccines, proteins and growth factors. Molecular weight of the monomers initial, ratio of lactic acid and glycolic acid, exposure time to water and storage temperature are among several factors that influenced the physical properties of PLGA [12]. It undergoes degradation by hydrolysis and the rate of degradation is also influenced by several factors such as the molecular weight, composition of lactic and glycolic acid and surrounding pH environment [11], [12].

3.2 PLGA and periodontitis

Current approach already focused on the use of PLGA in periodontal treatment, particularly used as barrier materials in guided tissue regeneration (GTR) procedures as the materials are being incorporated into the membrane. Yoshimoto and colleagues have constructed bilayer PLGA membrane and it was found that the use of bilayer PLGA membrane successfully inhibited connective and epithelial tissue invasion while promoting bone regeneration [13]. Besides that, PLGA also were constructed as a scaffold to be put into extraction sockets and better extraction bone socket preservation noted [13]–[15]. Apart from that, PLGA has also been incorporated into sutures due to its biocompatibility [16].

Local delivery of antimicrobials is one of the management in treating periodontal defect. PLGA microspheres have been fabricated as a carrier for doxycycline placed in the periodontal pockets in chronic periodontitis patients as an adjunct to non-surgical periodontal therapy and was observed to provide a sustained release of doxycycline up to twenty days after placement [17]. The usage of PLGA as scaffold for phenytoin, nifedipine and cyclosporine delivery in treating periodontal defect have also been investigated using Sprague-Dawley rats. It was found that PLGA loaded phenytoin resulted in significant new alveolar bone formation compared to other drugs and the control group [18]. These shows that the use of PLGA aids in enhancing the clinical outcome.

4. Conclusion

The application of CGF and PLGA have shown better clinical outcome in regenerative medicine and dentistry. This shows that both materials can serve as an alternative to current available materials that may further augment clinical outcome and has the potential to facilitate better periodontal regeneration.

5. References

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