CASE REPORT Open Access

Concentrated Growth Factor as an alternative membrane material in periodontal regeneration: A case report

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Abstract

The risk of further periodontal breakdown increases with a deep intrabony defect. Non-surgical periodontal therapy could pose a challenge and surgical intervention is mainly required to manage the defect. Autologous platelet concentrates such as concentrated growth factor (CGF) may improve surgical outcome due to its enrichment with growth factors. Nevertheless, the outcomes of using CGF as a biomaterial in periodontal regenerative therapy is inconclusive. This case report describes the regenerative management of an intrabony defect on all the first molars of a 24-year-old Malay lady diagnosed with Generalised Periodontitis, Stage III, Grade C. A guided tissue regeneration strategy was utilised on all the first molars except on tooth 46, which was treated with xenografts and a biologic adjunct of CGF. Patient was recalled regularly every week up to two months following the procedure, followed by a three-month interval review. The results showed promising outcomes with an average of 4 mm probing pocket depth reduction and 79.1% radiographic bone fill for both regenerative strategies. The utilisation of biologic adjuncts such as CGF, could offer a viable alternative to collagen membrane in periodontal regeneration without compromising clinical results.

Keywords: *Concentrated Growth Factor, guided tissue regeneration, membrane, periodontitis, xenograft*

Received:
7 June 2022
Revised:
10 August 2022
Accepted:
8 November 2022
Published Online:
28 February 2023

How to cite this article:
Mohd Noh, N. Z., Salehuddin, N. Q., Ali, S. N., Mohamad, I. H., & Ariffin, F. (2023). Concentrated Growth Factor as an alternative membrane material in periodontal regeneration: A case report. *IIUM Journal of Orofacial and Health Sciences*, *4*(1), 80–88. https://doi.org/10.31436/ijohs.v4i1.165

Article DOI:
https://doi.org/10.31436/ijohs.v4i1.165

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Introduction

In achieving a successful outcome following non-surgical periodontal therapy (NSPT), various factors play a pertinent role. These include operator, patient, instrument design and tooth anatomic or site factors. The presence of anatomic features, specifically intrabony defect and furcation involvement increase the risk of future periodontal breakdown as these limit complete removal of subgingival biofilm and deposits in the periodontal pocket (Jepsen *et al.*, 2011; Graziani *et al.*, 2017). It poses a dilemma to either proceed with non-surgical or surgical periodontal treatment in such cases. As recommended by the current clinical guidelines, periodontal regenerative surgery is recommended for deep intrabony defect and class II furcation involvement as favourable outcomes have been reported (Sanz *et al.,* 2020).

However, selection of cases for regenerative surgery is crucial as there are many factors that may also influence the clinical outcomes following the regenerative therapy. One of the critical factors is from the surgical perspective as the choice of flap design may influence the outcome of treatment. In comparison to conventional approach, papilla preservation flap design offers a benefit of preserving the interdental tissue over the defect (Cortellini *et al.*, 1995, 1999). This flap design provides a better flap closure and complete membrane coverage, consequently leading to superior clinical outcomes. In addition, the application of adjunct biologic agents such as enamel matrix protein and recombinant human growth factors has also been reported to significantly enhance better outcomes following regenerative therapy (Bosshardt, 2008; Suárez-López Del Amo *et al.,* 2015). Another alternative adjunct regenerative material which is gaining traction is concentrated growth factor (CGF). However, the results of using CGF as a biomaterial in regenerative therapy is inconclusive.

Therefore, this case report aims to discuss regenerative management of a periodontitis patient presented with intrabony defects with 1) guided tissue regeneration (GTR) and 2) xenografts with biologic adjunct of CGF strategies.

Case Report

A 24-year-old Malay lady was referred to the Postgraduate Periodontics Clinic for management of generalised deep periodontal pockets. The patient was fit and healthy with no known underlying systemic risk factors. Upon clinical examination, she was presented with a full mouth plaque score of 36.6% and gingival inflammation was observed mainly on her lower anterior teeth. Full mouth periodontal examination revealed deep probing pocket depth (PPD) ranging from 5 mm to 10 mm with bleeding on probing. Radiograph taken in July 2019 demonstrated periodontitis due to the presence of alveolar bone loss with prominent vertical bone loss affecting the mesial root surface of all the first molars (Figure 1). Based on clinical examinations and radiographic investigation, she was diagnosed with Generalised Periodontitis, Stage III, Grade C (Tonetti *et al.*, 2018).

Figure 1. Panoramic radiograph of the patient illustrates generalised bone loss with vertical bone loss on the mesial root surface of all the first molars.

With consent, she was managed initially with professional mechanical plaque removal involving scaling and root debridement (SRD), which was completed in two consecutive days. An adjunct combination of antibiotic comprising of 500 mg amoxicillin and 400 mg metronidazole was prescribed to the patient for a week. She was called two weeks later for a compliance review and chairside brushing was conducted. During her periodontal review five months later, her gingival condition has improved as compared to the baseline visit. A good oral hygiene was maintained with full mouth plaque score of 22.6% and a marked improvement in reduction of PPD was observed, with the only deepest PPD of 6 mm to 8 mm were observed on the mesial surface of all the first molars.

After considering all factors, regenerative therapy was proposed for all the first molars and agreed by the patient. The regenerative therapy was completed in four different sessions. After assessing the planned surgical sites, the modified papilla preservation technique (MPPT) of flap design was employed for regenerative management on the mesial surface of all the first molars as the interdental space width was ranging between 4 mm to 5 mm. After local anaesthesia was administered using mepivacaine hydrochloride (2% Scandonest), intrasulcular incision was performed around the surgical site (tooth 16, 26, 36 and 46) and its adjacent teeth on buccal, lingual or palatal and interdentally. Horizontal incision was made approximately at the level of buccal cemento-enamel junction (CEJ) of the respective tooth (Figure 2). Full thickness mucoperiosteal flap was elevated and the interdental papilla was elevated and reflected to the palatal or lingual site through the interdental space (Figure 3).

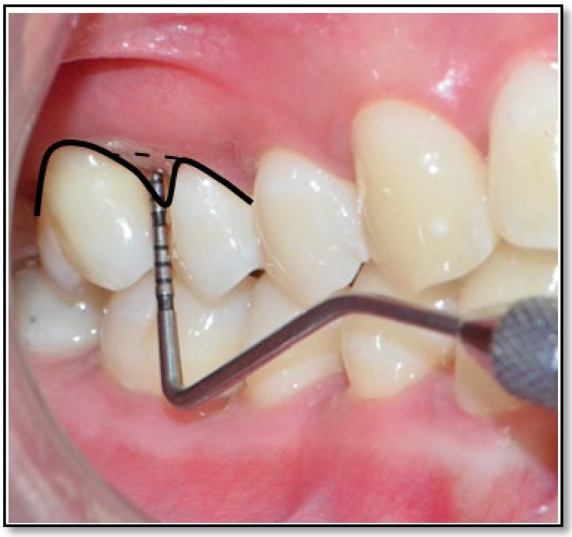

Figure 2. Surgical plan involving MPPT design. A horizontal incision was performed at the level of buccal CEJ on tooth indicated for regeneration.

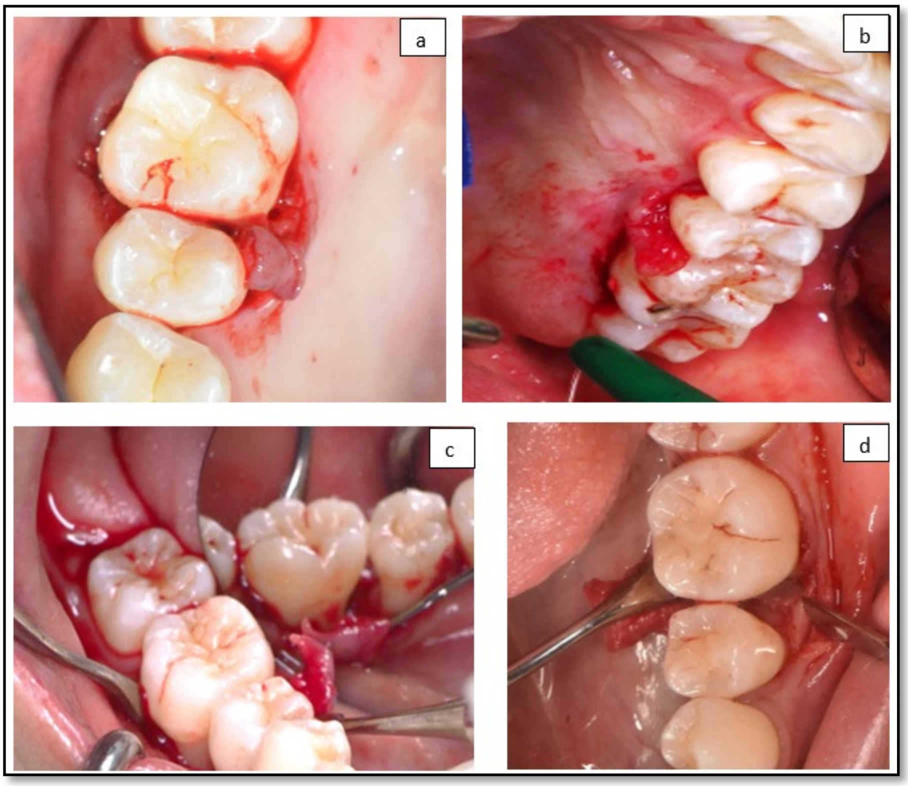

Figure 3. Papilla reflection from the buccal to palatal or lingual site of the tooth a) 16, b) 26, c) 46 and d) 36.

After the removal of chronic inflammatory tissue and the localised SRD was done, all four sites (tooth 16, 26, 36 and 46) were presented with a three-wall bone defect about 5 mm to 6 mm in depth. Prior to the placement of xenografts (i.e., Geistlich Bio-Oss® and OsteoLemb) on the mesial bone defect of the tooth, collagen membrane (i.e., OsteoBiol®, PericardLemb) was measured and covered the intrabony defect of tooth 16, 26 and 36. The xenografts were then packed to the mesial bone defect under the collagen membrane (Figure 4).

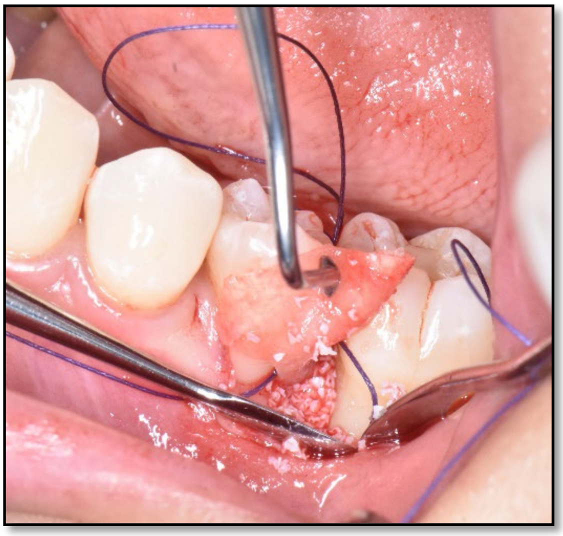

Figure 4. Placement of xenograft under the collagen membrane on tooth 36.

During regenerative procedure on tooth 46, fortunately blood could be drawn from the patient. About 10 mL blood was collected into serum vacutainers (BD vacutainer®, USA) and immediately centrifugated with a centrifugation machine (Table Top Centrifuge Kubota 2420, Tokyo, Japan) using alternate speed to fabricate the CGF. The alternate speed was set following the protocol used by other studies: 30 seconds acceleration, two minutes at 2700 rpm, four minutes at 2400 rpm, four minutes at 2700 rpm, three minutes at 3000 rpm, 36 seconds deceleration and stop (Kim *et al.,* 2014; Takeda *et al*., 2015; Durmuslar *et al*., 2016) (Figure 5). The CGF was later compressed with a PRF box® to form a CGF membrane. Then, Geistlich Bio-Oss® was packed into the mesial bone defect and covered with the adjunct of CGF membrane prior to flap approximation (Figure 6).

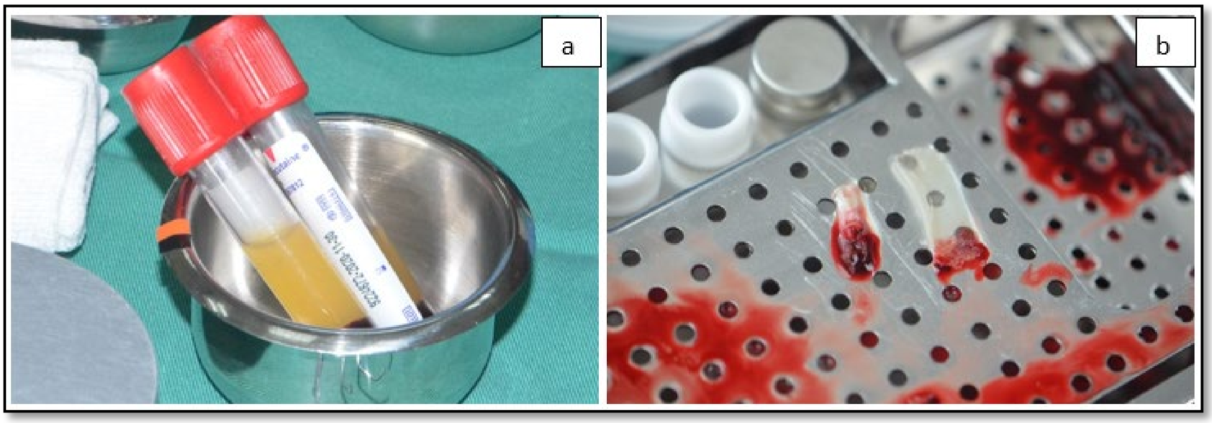

Figure 5. Blood was drawn and centrifuged to form a) CGF gel and compressed to form b) the CGF membrane.

Figure 6. Placement of CGF membrane prior to the flap approximation on tooth 46.

All sites were secured with Laurel sutures for flap approximation and Coe-Pak™ periodontal dressing was applied. Patient received post operative care and instructions as proposed by Cortellini and Tonetti (2000). She was recalled weekly up to two months for a review where professional prophylaxis was performed as necessary. She was then followed-up regularly for every three months up to one-year post operative.

During her recent periodontal review in March 2022, she was presented with periodontal stabilisation. Periodontal probing was performed and the previous deep PPD on all the first molars have healed to disease-free PPD, with an average of 4 mm probing pocket depth reduction. Radiographic examination revealed that all treated defects have been filled to almost similar height of the alveolar crest on the distal side of the adjacent tooth and the angular bony defects have been eliminated. The average percentage of radiographic bone fill was 79.1%. Moreover, intact lamina dura could be noticed, indicating stabilised bone formation. The comparison between pre-operative and post-operative radiographs were shown in Figure 7. The patient is satisfied with her current periodontal conditions and is now under supportive periodontal treatment phase.

Discussion

In comparison to NSPT, periodontal surgery, mainly regenerative therapy, offers a superior benefit in managing deep intrabony defect and class II furcation involvement. There are various regenerative strategies, including GTR, enamel matrix derivatives (EMD), bone substitutes, growth factors and combination of the strategies (Nibali *et al.,* 2020). Regenerative therapies resulted in a greater clinical attachment level gain of 1.34 mm as compared to open flap debridement alone in the presence of deep intrabony defect (Nibali *et al.,* 2020). In addition, superior clinical outcomes of furcation closure or class I conversion is achieved on class II furcation-involved molars with regenerative therapies in comparison to open flap debridement (Jepsen *et al.*, 2020).

Prior to the regenerative therapy, patient's periodontal condition was stabilised with the first and second steps of the therapy (Sanz *et al.,* 2020). After considering various factors, regenerative therapy was proposed to the patient as various studies had reported a long-term survival of regenerated tooth. Cortellini and colleagues (2004) reported that the survival of regenerated teeth was greater than 96% up to 16 years following the procedure. This corroborates the finding by a recent longitudinal study that evaluated their patients according to several site-specific and patient-related factors for 21 to 26 years after the GTR therapy (Cieplik *et al.,* 2020). Even though regenerative therapy may ensure the longevity of tooth, both studies emphasised that the outcomes were greatly influenced by smoking and diabetic status, and compliance to periodontal maintenance and monitoring. This shows that patient selection for regenerative therapy is crucial to ensure a good clinical outcome and tooth survivability.

As mentioned earlier, papilla preservation technique offers an advantage in preserving the interdental tissue over the defect (Takei *et al.,* 1985). Cortellini and his team (1995, 1999) has introduced a modification on Takei's technique, which consists of modified papilla preservation technique (MPPT) and simplified papilla preservation technique (SPPT) design. Since the interdental space width on the indicated teeth was more than 2 mm, MPPT flap design was employed for this patient. From a recent systematic review and meta-analysis, it was suggested that EMD or GTR combined with papilla preservation flaps shall be considered as treatment of choice in managing deep intrabony defect of 3 mm and more (Nibali *et al.,* 2020).

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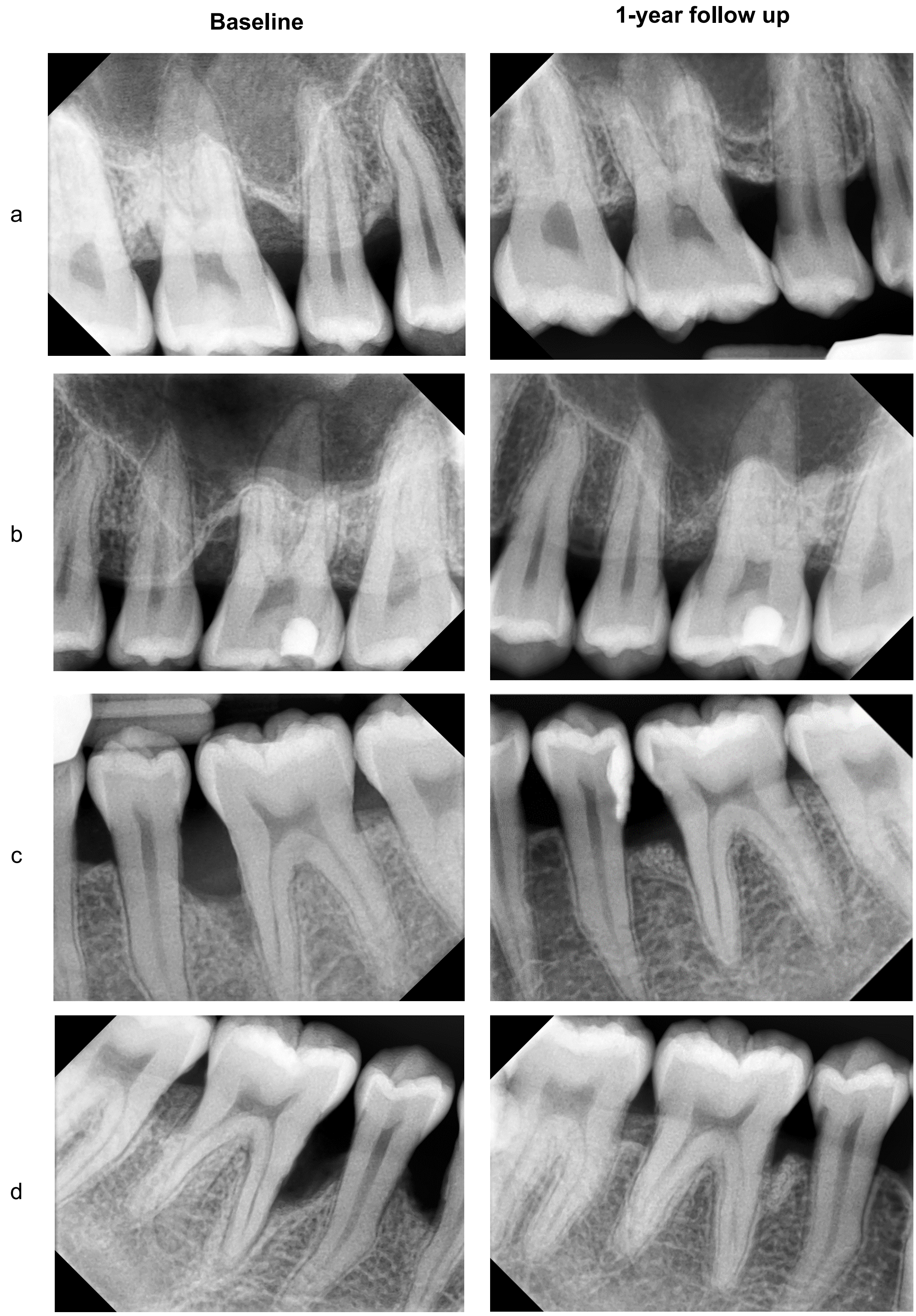

Figure 7. Pre-operative and post-operative (one-year follow-up) intraoral periapical radiographs of tooth a) 16, b) 26, c) 36, and d) 46.

Recently, the application of platelet concentrates such as concentrated growth factor (CGF) has been widely applied in the clinical setting. CGF is a recent generation of platelet concentrate that was first introduced in 2005 by Sacco (Chen and Jiang 2020). It provides a high suspension of various growth factors such as platelet-derived growth factor (PDGF), transforming growth factor beta (TGF-β), insulin-like growth factor (IGF), epidermal growth factor (EGF) and vascular endothelial growth factor (VEGF) which are beneficial for healing (Rodella *et al.,* 2011; Borsani *et al.*, 2015). Its autologous nature also minimises the risk of cross-reaction and can serve as an alternative source of growth factors to the expensive recombinant human growth factors.

Since all sites were presented with a three-wall bone defect, a predictable outcome following GTR can be expected (Becker & Becker, 1993). In addition, there were higher bone gain and percentage of bone fill in three-wall bone defects due to its capacity to provide better blood clot retention and allow better repopulation of osteoprogenitor cells during regeneration (Cortellini *et al.,* 1993). As evidenced from this patient, tooth 46 that received CGF membrane revealed similar clinical and radiographic outcome to the other three sites that were managed with GTR strategy. However, to date, there is no study that compares between the GTR and CGF membrane alone in the regenerative management of periodontitis. On the other hand, the application of CGF as adjunct has shown promising results in regenerative therapies. Adjunct application of CGF with bone graft performed better than the sole use of bone graft in terms of probing depth reduction and bone fill one year after the surgery (Qiao *et al.*, 2016; Qiao *et al.,* 2017; Xu *et al.,* 2019). A finding by Lei and his colleagues (2020) revealed that the adjunct application of CGF during GTR therapy has resulted in similar clinical outcomes at six months of observation with the control without CGF. These studies therefore reinstate the potential of CGF in enhancing the clinical outcome.

Another interesting point is the application of CGF also influences post-operative pain. Besides optimising the growth factors, the regular, cross-linked fibrin matrix of CGF with increased stability, strength, and protection against plasmin degradation resulted in a significant amount of CD34 positive cells. CD34 positive cells, which are responsible for maintenance and growth of vascular tissues, accelerate wound-healing regeneration by enhancing their ability to stimulate angiogenesis (Rodella *et al.,* 2011; Mijiritsky *et al.,* 2021). Subsequently, earlier healing with pain reduction is observed, as revealed by studies investigating post-operative pain following the management of alveolar osteitis (Kamal *et al.*, 2020; Kamal *et al.*, 2020). This was also reported by the patient in this study as lesser pain was experienced on the site receiving CGF in comparison to the non-CGF sites.

Conclusion

Regenerative therapy is one of the treatment options that can be suggested to patients in managing intrabony defect. Even though resorbable GTR is the ideal regenerative technique, adjunct application of CGF membrane could be utilised as an alternative to collagen membrane in periodontal regeneration without compromising clinical outcomes.

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