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Clinical comparison of concentrated growth factor(CGF) plus non-eugenol periodontal dressing versus non-eugenol periodontal dressing alone in wound healing following gingival depigmentation: A spilt mouth randomized controlled trial

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Abstract

Introduction: Concentrated growth factor is 100% blood derived, cross linked fibrin glue with platelets and growth factors. It is a newer form of autologous platelet concentrate with an extra fibrin matrix and more growth factors than that observed with PRF. The application of CGF membrane shows better healing and lesser inflammatory cells. The use of CGF membrane will be helpful in protecting the raw wound region of depigmented sites, improving patient comfort, and better healing.

Objectives

1. To evaluate and compare healing of depigmentation wounds in both the surgical sites by visual analog scale and healing index.
2. To evaluate and compare the amount of inflammatory concentrate underneath the surgically depigmented sites by epithelization test.

Methodology: 1. It is a randomized split-mouth study. 10 participants with twenty sites were selected and randomly assigned equally into ten sites each.

2. Following depigmentation, Group A (Test group) received CGF membrane + periodontal dressing and group B (control group) received only periodontal dressing.

3. The individuals were evaluated for visual analog scale and healing index on 3rd and 5th day.

4. Epithelization test was done on the 5th day.

Results: Healing was better in test group than control group and pain, evaluated by the visual analogue scale was lesser in the sites where CGF was used.

Conclusion: Using CGF beneath a non eugenol pack in depigmented sites gave better results than using a periodontal pack alone.

Keywords: Gingival hyperpigmentation, non-eugenol periodontal dressing, concentrated growth factor, CGF membrane, CGF bandage, wound healing.

Introduction

In today's contemporary world, facial cosmetic concerns have created a demand for esthetics in the periodontal practice. The most frequently pigmented region of the oral cavity is gingiva. The colour variation in the gingiva mainly depends on the thickness of the gingival epithelium, blood supply, amount of the keratinization, and number of the melanin pigmented cells.[1] Melanin pigmentation determines the overall colour of gingiva even though other pigments such as carotene, oxyhemoglobin, reduced haemoglobin as well as exogenous factors (drugs, heavy metal, genetics) may be responsible for pigmentation of gingiva.[2]

Demand for cosmetic therapy of gingival melanin pigmentation is common. Gingival depigmentation has been carried out using various nonsurgical and surgical procedures. Different treatment modalities which have been reported include bur abrasion, scraping, partial thickness flap, cryotherapy, electrosurgery, gingivectomy with free gingival autografting, chemical agents, such as 90% phenol and 95% alcohol and lasers are also used.[3]

One of the conventional and the most popular for depigmentation is the surgical removal of undesirable pigmentation using scalpel. Gingival epithelium along with the connective tissue layer is removed creating a connective tissue bed and the healing takes place by secondary intention. The new epithelium which is formed is denuded of melanin pigmentation thus providing patient beneficial results.[4]

Covering the exposed connective during the initial post-surgical phase decreases the tendency of post-operative bleeding and prevents surface trauma thus facilitates healing.

Traditionally, periodontal dressing has been used as a material of choice by clinician owing to its mechanical properties.[5]

The present case study presents an attempt to evaluate early wound healing clinically and histologically with concentrated growth factor (CGF) membrane as periodontal bandage after depigmentation.

The newest platelet concentrate, concentrated growth factor is 100% blood derived, cross linked fibrin glue with platelets and growth Factors such as VEGF, PDGF, IGF-I and TGF-1. Compared to PRF, CGF contains a denser and richer GF-fibrin matrix. Furthermore, CGF has a 3D fibrin network in which growth factors are closely bound to one another. This provides the slow release of growth factors, which helps with wound healing. [6,7]

Material And Methods

Study design: A randomized split-mouth interventional study was conducted in Terna Dental college, Navi

Mumbai, India. 8 healthy participants were recruited who had an esthetic concern due to gingival hyperpigmentation and were needed for depigmentation procedure. Clearance was obtained for the clinical procedure and for the procurement of biopsy before the commencement of the study. Ethical clearance number TDC/EC/11/2020.

The inclusion criteria included systemically healthy study participants with an age range of 20–30 years. The plaque index score[8] of <1 and gingival index score[9] <1, thick biotype, and >2 mm of attached gingiva.

The exclusion criteria included the presence of gingival recession, thin gingival biotype, individuals on antibiotic or anti-inflammatory drugs for past 3 months, underwent periodontal surgery in past 6 months, individuals with a habit of smoking/tobacco chewing and pregnant and lactating mothers.

On fulfilling the criteria, the individuals were informed about the surgical procedure along with the application of concentrate growth factor membrane and the benefit that can be obtained from it. A signed informed consent was obtained from all the 8 individuals. All the relevant hematological tests were done and found satisfactorily within physiological limit.

Patients with hyperpigmented gingiva reporting to the outpatient department of the Department of periodontology were selected. Only those diagnosed with moderate pigmentation using the Dummett Index[10] were recruited for the study. (Fig.1)

Fig.1: Preoperative view of pigmentation

Following the depigmentation procedure, the groups were divided in the following way:

Group A: (Test group) received CGF membrane + periodontal dressing.

Group B: (Control group) received only periodontal dressing.

After taking the ethical clearance and patient's consent, the site was anesthetized with 2% lignocaine with adrenaline 1: 200,000. A split-thickness flap was reflected and excised maintaining the gingival architecture. The pigmented epithelium was thus excised exposing the underlying connective tissue. (Fig.2) The gingiva was covered with a CGF membrane on the test side while the control site was covered with periodontal dressing only.

Fig. 2: Depigmentation by surgical removal of undesirable pigmentation using scalpel and immediate postoperative following depigmentation

Postoperatively, amoxicillin 500 mg, TID for 3 days, and analgesic ibuprofen, 400 mg BD for 3 days were prescribed. The individuals were refrained from brushing for 3 days following the procedure and were instructed to rinse mouth with 0.2% chlorhexidine Digluconate mouthwash. On the 3rd day, the individuals were recalled, and the periodontal pack was removed.

The clinical and histological parameters were evaluated following the surgical procedure. The visual analog scale (VAS)[12] and healing index (HI)[13] were evaluated at 3rd and 5th day and epithelialization test at 5th day.[14] The histological analysis was carried out on the 5th day through punch biopsy from the depigmented gingival epithelium.

Also on the 5th day, toluidine blue test was performed for evaluating the degree of epithelization. On the same day, punch biopsies were taken from the test and control sites to evaluate the degree of inflammation microscopically.[15-17]

Preparation of concentrated growth factor membrane

During the surgery, 9 ml of blood was withdrawn from the antecubital vein of the patient and transferred to silica-coated plastic vacutainers without anticoagulants. Centrifugation was done for 30 s acceleration, 2 min at 2700 rpm, 4 min at 2,400 rpm, 4 min at 2700 rpm, 3 min at 3000 rpm, and 36 s deceleration to prepare CGF.[11] The CGF thus formed was removed from the tube using a sterile tweezer, separated from the red blood cells base using scissors. It was compressed between two sterile glass slides to form a membrane. (Fig.3 and 4)

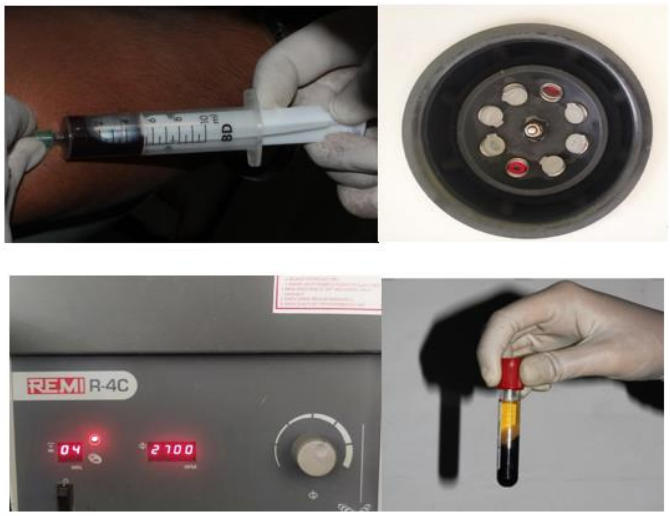


Fig.3: Preparation of CGF membrane

A. Blood withdrawn from antecubital vein
B. Centrifuged
C. The CGF membrane obtained

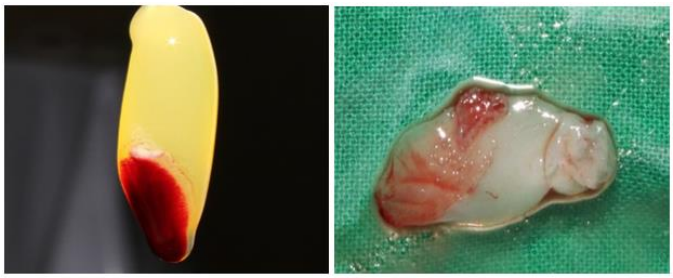


Fig. 4: Preparation of concentrated growth factor membrane

Fig.5: CGF membrane placement

Fig.6: Tin-foil placement

Fig.7: Non-eugenol periodontal dressing (Coe Pak) was given at both sites

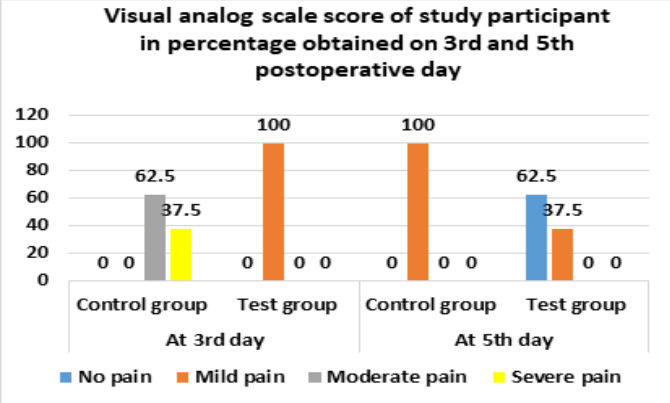
(Fig.8) 3rd day postoperative and 5th day postoperative

Statistical analysis

Statistical analysis was performed using Statistical package for social sciences (SPSS) software (IBM Corp) (v.21.0). Frequency and percentage distribution of the participants according to the scores was performed for all the parameters assessed. Independent samples t-test/Unpaired t-test was performed to assess significant differences between the control and test groups. A p value of less than 0.05 was considered as statistically significant at 95% confidence intervals in the study.

Visual analog scale:

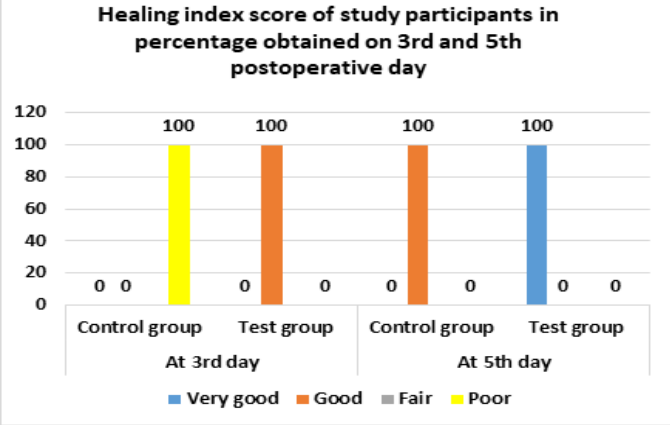
On the 3rd and 5th days postoperatively, VAS[12] was assessed. In our study, the frequency and percentage distribution of the VAS scores was performed and comparison of the VAS scores between 2 groups was done using, Independent samples t-test/Unpaired t-test. On the 3rd day, it was found that almost 62.5% of the participants had moderate pain and 37.5 % had severe pain in control group; whereas in test group all (100%) the participants had mild pain. On 5th day, it was found that almost 100% of the participants had moderate pain in control group; whereas in test group 62.5% showed no pain while 37.5% the participants had mild pain. This comparison showed statistically significant differences between the 2 groups. (p value <0.001). Thus, test group showed better results as compared to control group.



Graph 1

Healing index

The healing index was assessed as per the index given by Landry et al[13]. On the 3rd day, it was found that almost 100% of the participants had good healing in test group while all (100%) the participants had poor healing in control group. On 5th day, it was found that almost 100% of the participants had very good healing in test group while all (100%) the participants had good healing in control group. This comparison showed statistically significant differences between the 2 groups. (p value <0.001). Thus, test group showed better results as compared to control group.



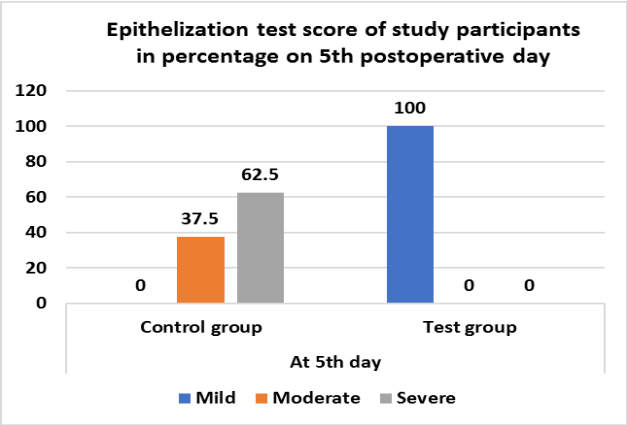
Graph 2

Epithelization test

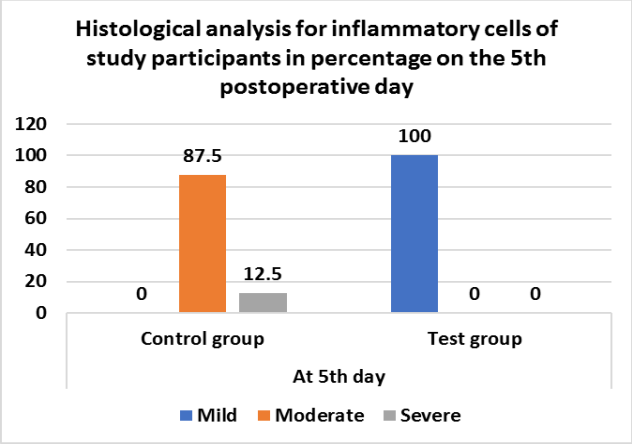
On the 5th day after surgery, both the test and control site was stained with toluidine blue. The degree of staining corresponds to the extent of inflammatory concentrate below. Thus, this test helped us to determine

the degree of inflammation in the test and control sites. In the control sites 37.5% of the patients picked up moderate staining whole 62.5% of patients picked up severe staining as compared to the test sites, which picked up mild staining for 100% of patients. Thus, in the control sites, toluidine blue score clearly shows the presence of more inflammatory cells. (Fig.9)

Fig. 9: Staining with toluidine blue



Graph 3



Graph 4

Histologic Report

At 5th day after the surgical procedure, a section of tissue from the test and control sites of lateral incisor region was taken through punch biopsy from all the treated sites. Eosin and Hematoxylin stained slides were prepared and evaluated at 10x magnification. Sections of CGF treated sites showed mild inflammatory infiltrate in the connective tissue. The control sites, demonstrated chronic inflammatory cell infiltrate consisting of lymphocytes in the connective tissues. The test sites showed a distinct parakeratinized stratified squamous epithelium with fibrous connective tissue with negligible inflammatory cell infiltrates. (Fig.10)

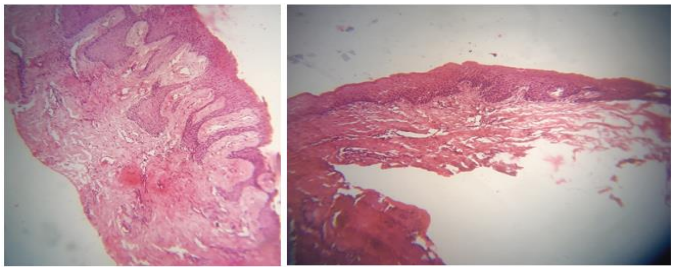


Fig.10: Histological analysis at 5th day a) at control site b) at test site

Results

The application of CGF bandage at depigmented sites, treated with surgical depigmentation, showed superior healing as compared with moderate healing at the sites that were covered only with periodontal dressing. The healing index showed better healing at the test site. The visual analog scale results demonstrated better lesser pain at test sites as compared to control sites. Toluidine blue test demonstrated more staining at control sites indicating more inflammation. Similarly, histological examination showed more inflammatory cells at control sites.

Discussion

Gingival pigmentation which may not be a serious medical concern however, it can have an impact on a person's aesthetics and potentially affect their self-

confidence and psychological well-being. Although several depigmentation methods have been employed for managing this situation, there is limited literature specifically addressing the management of inflammation, healing procedures, and pain control after gingival depigmentation procedures. [4]

When it comes to gingival depigmentation procedures, the primary aim is to achieve satisfactory results in a cost-effective and comfortable manner, while minimizing pain, tissue loss, and damage to the attachment apparatus. While no procedure is completely devoid of potential side effects or risks.

Gingival depigmentation is also known as surgical stripping or split thickness epithelial excision. Conventional scalpel procedure includes surgical removal of the gingival epithelium using a scalpel, leaving the denuded connective tissue for healing by secondary intention. [3] This process is simple, easy, convenient and economical to perform with less efforts and time. With this technique healing is faster as compared to other surgical techniques. Also lower recurrence rate and cost, support surgical gingival stripping. However, this technique is associated with post-operative discomfort, some pain, intra- and post-operative bleeding as well as the need to place periodontal dressing. This technique is contraindicated in patients with thinner gingival biotypes and in narrow papillary areas. [18]

Traditionally it is believed that periodontal dressing applied after surgical depigmentation, decreases the wound infection risk, bleeding and formation of granulation tissue. This enhances tissue healing and reduce patients' pain and discomfort immediately post-surgery. [13] The use of periodontal dressings after surgical procedures, including gingival depigmentation, has been associated with certain drawbacks. One potential concern is that periodontal dressings may contribute to increased inflammation, which could potentially delay the wound healing process.[19]

Periodontal dressing is thought to cause allergic reactions, difficult to handle and manipulate and it leaves a rough surface after the application. Histological evidence shows inflammatory cell infiltration after application of periodontal dressing.[20]

Platelet-rich fibrin (PRF) is a second-generation platelet concentrate that has been extensively studied and used in the field of periodontology. PRF is derived from the patient's own blood and contains a high concentration of platelets, growth factors, and cytokines that promote tissue healing and regeneration. Aravindaksha et al., used PRF membrane as a palatal bandage on the donor site, after free gingival graft.[21] Also in a study by Debnath et al., PRF membrane was utilized as a bandage, after depigmention procedure, for adequate patient's relief. The study had positive results which can be because of the fibrin composition of PRF as well as the release of different growth factors over a long time period.

The latest in platelet concentrates, CGF (concentrated growth factor) is a novel method to produce a fibrin matrix enriched with concentrated growth factors. Concentrated growth factor is 100% blood derived, cross linked fibrin glue with platelets and growth factors. It is a newer form of autologous platelet concentrate with an extra fibrin matrix and more growth factors than that observed with PRF. Its clinical applications are being currently evaluated.[22]

CGF does not dissolve rapidly and the solid fibrin gel is gradually remoulded over the period of time. Dohan et al., have reported that CGF has a complex three-dimensional architecture, which is a platelet, leukocyte as well as growth factor-rich fibrin biomaterial. The

presence of platelets, as well as the dense fibrin network, make huge coagulation clusters as confirmed by scanning electron microscopy.[23]

A case series has already been done earlier. Hence, a randomised controlled trial was done to further evatuate the numerous benefits obtained using the CGF membrane as a bandage for coverage of the exposed gingival surface. There is less pain and discomfort to the patient and also visibly lesser inflammation at the surgical site. Due to the presence of growth factors like TGF-β1 and VEGF stimulation of cell proliferation, modelling of the matrix, and angiogenesis are enhanced.[24] Sohn et al., demonstrated an alternative centrifugation speed for making CGF allowing the isolation of a much denser fibrin matrix which is richer growth factors.[25] Rodella et al studied the agglutination of fibrinogen, factor XIII and thrombin results in a fibrin clot that has high cohesion, which reduces plasmin degradation, leading to higher fibrin tensile strength and stability. [26]

Hence it can be concluded that the CGF membrane application as a bandage in the present case study has been proven as an effective approach in protecting the exposed connective tissue of the depigmented sites, with better patient results, compliance as well as faster recovery.

Conclusion

Thus, the application of CGF membrane as a bandage in the present study has shown a successful approach to protect the raw wound area of depigmented sites with better patient comfort and faster healing than the use of a periodontal pack alone.

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