The Saudi Dental Journal 36 (2024) 328–333

Contents lists available at ScienceDirect

The Saudi Dental Journal

journal homepage: www.ksu.edu.sa
www.sciencedirect.com

Original Article

# Single-flap approach versus without concentrate growth factor in the treatment of periodontal supra-osseous defects: A randomized controlled clinical trial

Naglaa El-Wakeel *, Lobna Mohamed Abd-elaziz

*Oral Medicine and Periodontology Department, Faculty of Dentistry, Al-Azhar University (Girls Branch), Cairo, Egypt*

ARTICLE INFO

*Keywords:*
Randomized controlled trial
Concentrate growth factor
Supra bony defects
Surgical periodontal therapy
Minimally invasive flap

ABSTRACT

*Objectives:* We aimed to compare treatment outcomes of periodontal supra-bony defects using single flap (SFA) plus concentrate growth factor versus SFA alone.
*Methods:* 32 supra-bony periodontal defects were randomly assigned to test and control groups. Outcome variables were clinical attachment level (primary outcome). Probing pocket depths, gingival recessions, bone gain, post-surgical pain using visual analogue scale and wound healing index were recorded as secondary outcomes. Clinical and radiographic assessments were recorded at baseline and 6 months after treatment, whereas pain score and wound healing index were recorded within 10 days after surgery.
*Results:* Test group showed a significant improvement in all tested parameters compared to control group (P-value $\leq 0.05$). Better patient centered outcomes (wound healing and pain scores) were highly achieved in the test group compared to controls.
*Conclusion:* The tested combined approach offers better periodontal and patient centered treatment outcomes in management of periodontal supra-bony defects.

## 1. Introduction

Periodontitis is a common chronic inflammatory disease that can cause damage to the tissues that support the teeth. The clinical signs of periodontitis include pocket formation, loss of attachment, and alveolar bone destruction Therefore, periodontal therapy primarily aims to regenerate the damaged or lost periodontal tissues (Miron et al., 2021).

Regeneration of infra-bony defects has been achieved with a variable degree of success using open flap debridement and a combination of bone grafts, membranes, and biological mediators. On the other hand, supra-bony periodontal defects (SDs) represent a challenge for predictable regeneration due to the lack of bony walls support to the muco-periosteal flap to ensure wound stability along with the paucity of sources for cells capable of promoting periodontal regeneration (Iorio-Siciliano et al., 2021).

Conventional access flap surgery, involving the reflection of two buccal and palatal/lingual flaps, is still the primary surgical procedure for periodontal pocket reduction despite its drawbacks, such as post-surgical recession, patient discomfort, and dentin hypersensitivity. The single flap approach (SFA) was developed to overcome these drawbacks and treat intraosseous defects. Its main advantages come from repositioning and suturing to the undetached papilla, which allows the best wound healing, limited surgical trauma, better tissue esthetics, and minimal bone loss compared to the conventional approach (Mathala et al., 2021,).

Concentrate growth factor (CGF) is an advanced second-generation platelet concentrate obtained by differential continuous centrifuging of autologous blood, it has a variety of autologous growth factors of crucial importance in tissue regeneration. It has been reported that CGF promotes- not only the proliferation and osteogenic differentiation of mesenchymal stem cells in vitro -but also the excellent healing of bone defects of critical sizes in vivo (Kobayashi et al., 2016) Its higher leukocyte content, growth factors, and flexible fibrin mesh increase the angiogenic, osteogenic, and antimicrobial ability of these bioproducts in tissue regeneration (Nityasri et al., 2018).

With advances in biologics, CGF was suggested to be a promising approach to treating gingival and bony defects (Nityasri et al., 2018; Qi et al., 2020). Although SFA has proven effective in treating various

Peer review under responsibility of King Saud University. Production and hosting by Elsevier.
* Corresponding author at: Faculty of Dentistry, Al-Azhar University (Girls Branch), Al-Mokhayam El Dayem St., Nasr City, Cairo 1178, Egypt.
*E-mail address:* naglaelwakeel@gmail.com (N. El-Wakeel).

https://doi.org/10.1016/j.sdentj.2023.11.015
Received 31 July 2023; Received in revised form 12 November 2023; Accepted 14 November 2023
Available online 15 November 2023

periodontal defects, its efficacy in periodontal regenerative therapy, however, requires further verification. (Mathala et al., 2021; Simonelli et al., 2021; Windisch et al., 2022). Therefore, we aimed to assess if combining the beneficial effects of CGF and SFA could achieve better post-treatment periodontal and patient-centered outcomes in managing periodontal supra-bony defects.

## 2. Material and methods

### 2.1. Study design

In this double blinded, randomized, controlled clinical trial, Patients were recruited from outpatient clinics of oral medicine, and Periodontology department, Faculty of Dentistry, Al-Azhar University (Girl's branch), from June 2022 until September 2022. The Faculty Research Ethics Committee approved the study protocol, and the study was carried out by the Declaration of Helsinki, according to the CONSORT statement. The grouping and methodology are presented in a flow chart (Fig. 1). Each participant signed written informed consent after receiving full information about the study before participation. This study was registered in clinical trail.gov (identifier NCT05730153).

### 2.2. Sample size

Using the G Power software version 3.1.9.7, the study included comparisons between two groups, at two-time intervals, thus ANOVA test will be suitable for comparison between the different outcomes. As this was the first trail that investigated the CGF in suprabony defects with no previous studies, the program settings were adjusted to the moderate value of the effect size (f) = 0.3 and power settings with (1-β = 0.90) at a significance probability level of $p \leq 0.05$. According to this, a minimum total sample size of 32 samples was considered sufficient and according to sample size calculations, there is a 90 % chance of correctly rejecting the null hypothesis of no significant effect of the interaction with 16 samples for each group.

### 2.3. Participant's eligibility

Patients with periodontitis, age range from 18 to 60 years, were recruited. Full medical and dental histories were taken followed by oral clinical examination to evaluate patients' eligibility.

#### 2.3.1. Inclusion criteria

Class III patients with single interdental supra-bony periodontal defects at a minimum of two single-rooted or multi-rooted adjacent teeth. Periodontal defects selected for intervention were those with pocket depths ≥ 5 mm after finishing the non-surgical treatment phase.

#### 2.3.2. Exclusion criteria

Patients with systemic illness, abnormal blood picture or coagulation function, prolonged antibiotic, or anti-inflammatory treatment within 4 weeks prior to treatment, former or current smokers, pregnant or lactating females, history of periodontal treatment in the last 6 months, bad oral hygiene, or *para*-functional habits, and grade II and III tooth mobility and teeth with furcation involvement.

### 2.4. Patient grouping, randomization, and calibration

Eligible patients were randomly assigned at the time of surgery using computerized generated tables into two groups as follows:1-Test group treated with SFA open debridement + CGF. 2- Control group treated with SFA alone. A single operator (LA) performed all surgeries. Before surgery, a single examiner (ZA) evaluated 5 pairs of SDs for clinical parameters and another single examiner (GS) evaluated 5 pairs of SDs for radiographic parameters on CBCT, both examiners were blinded to the study groups, Kappa Value (≥85 %). The follow-up visits were performed by the same clinician (KA)who was blinded to the study protocol.

### 2.5. Radiographic and periodontal examination

#### 2.5.1. Radiographic assessment

Linear measurements of bone loss around affected teeth for treatment were taken as follows: On the window of CBCT sagittal cut, a line

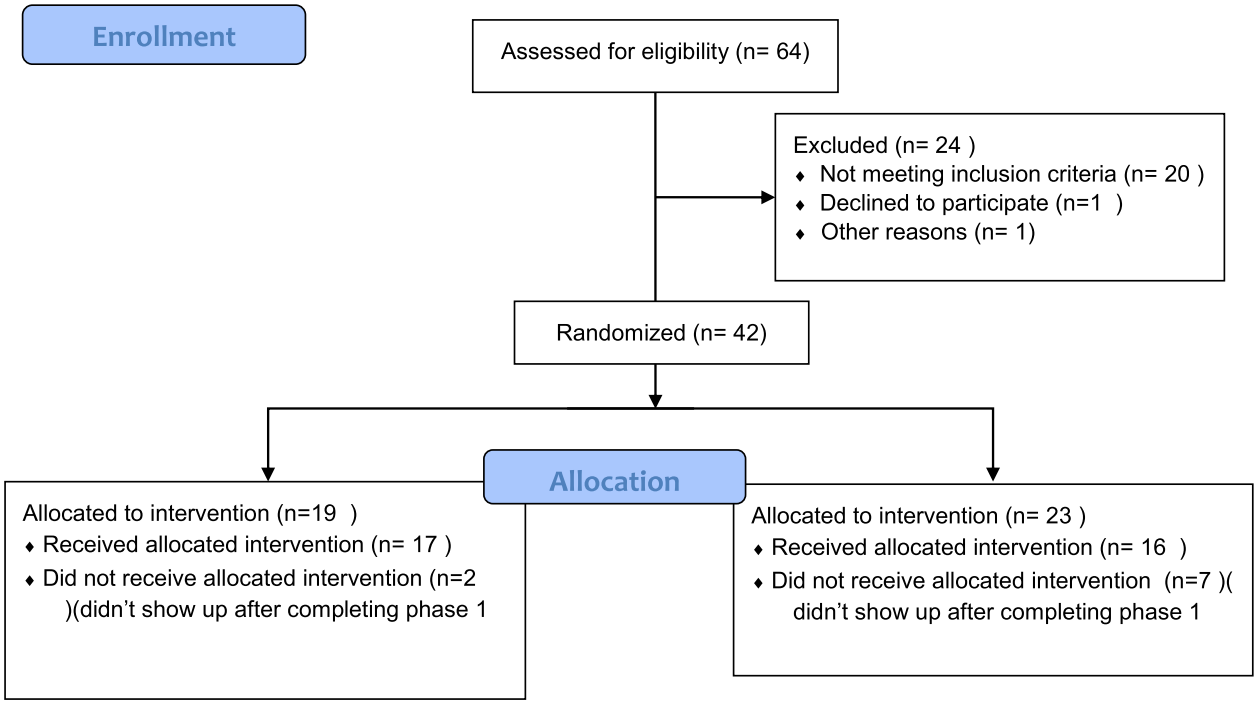


**Fig. 1.** CONSORT 2010 Flow Diagram.

was drawn from the cementoenamel junction of the two adjacent teeth surrounding the defect to crestal bone level mesial and distal around the defect. Measurements were recorded for each defect in both groups and the mean score was obtained at baseline and 6 months after surgery. Romexis 3D imaging software was used with an electronic measuring tool to the nearest millimeter. Radiographic examination for a specific area, using the low radiation mode offered by the CBCT (Planmecca Viso G7 pro). Data was acquired using 5.040 scanning time at 100 Kvp and 12.5 m as exposure with a voxel size of 150 Mm and Field of view of 10 cm*10 cm. Dimensions of the bone defects were measured under standard conditions (Same monitor without changes in contrast and resolution, same lightness of room, and equal distance from the monitor).

#### 2.5.2. Periodontal examination and presurgical protocol

After the initial clinical assessment, subjects received full mouth scaling and root planning (SRP) by hand and ultrasonic instruments, accompanied by oral hygiene instructions and motivation. Phase 1 therapy was re-evaluated after four weeks, and patients received surgical treatment when inflammation resolved.

### 2.6. Surgical procedures

#### 2.6.1. Flap design

We adopted the incision design modifications reported by (Trombelli et al., 2009, Simonelli et al., 2021). In the selected site, under local anesthesia and using 3.5 × magnifcation loupes (ExamVision, Sams, Denmark), gingival sulcular incision was done in the teeth next to the defect and the lateral extension of the flap was kept to a minimum while ensuring good access for proper defect debridement. To preserve the interdental papilla, a horizontal, butt-joint incision was performed 1–2 mm coronal to the bone crest (as detected through pre-operative bone sounding). Using a microsurgical periosteal elevator, a buccal mucoperiosteal envelope flap was elevated, leaving an undetached part of the interdental supra-crystal soft tissues. The root and the defect were debrided manually using area-specific curettes. After completing defect debridement, defects assigned to receive SFA + CGF were filled with the biomaterial between the roots inter-proximal below the undetached papilla and extending as far as we can get to cover the root surface buccally, while defects assigned to receive SFA alone were left to fill with a blood clot (Fig. 2). Using a resorbable suture (Vicryl ® 5.0, Ethicon, Sommerville, NY), the flap was repositioned using a horizontal internal mattress suture first at the base of the papilla and second between the most coronal part of the flap and the most coronal part of the papilla. suture removal was performed 14 days after surgery.

#### 2.6.2. CGF preparation for intervention group

Within the test group, 10 mL intra-venous blood sample was collected in two glass-coated plastic tubes with no anticoagulant addition. The tubes are once centrifuged in the following manner: 30-sec acceleration of the sample then for 2 min at 2700 rpm, 4 min at 2400 rpm, 4 min at 2700 rpm, 3 min at 3000 rpm, and 36-sec decelerations until the end. At the end of the procedure GF, and stem cell layer (CGF) were prepared (Saini et al.,2020). The CGF layer was separated using sterile surgical scissors and the clot was gently condensed into the defect (Fig. 2).

#### 2.6.3. Post-surgical instructions

No systemic antibiotics were given. Patients were instructed to abstain from oral hygiene procedures in the surgical area for two weeks and rinse twice daily with 0.12 % chlorhexidine (Antiseptic Kahira pharma & CHEM.IND.CO. Cairo-Egypt). Subjects were recalled for monthly maintenance visits for 6 months.

### 2.7. Treatment outcome

The primary outcome variable was Clinical Attachment Level (CAL) measured by the distance from the cementoenamel junction to the base of the pocket. Secondary outcomes were: 1- Probing Depths (PD) measured from marginal gingiva to the base of pocket;2- Gingival Recession; measured from CEJ to the most apical extension of the gingival margin. Measurements of CAL, PD, and GR were done at baseline and 6 months after surgery, at six sites per tooth by a manual periodontal probe (PCP-UNC 15®, HuFriedy, Chicago, IL, USA), but only the site with the greatest reading was subjected to the statistical analysis. 3-post operative pain using a visual analog scale (VAS)recorded 24 and 48 h after surgery (Myles PS et al., 2017) 4- Wound Healing Index (Debnath K et al., 2018) recorded 10 days after surgery, and 5- linear bone measurements were recorded at baseline and 6 months after surgery that measured from CEJ to the crest of alveolar bone.

### 2.8. Statistical analysis

Statistical analysis was performed using ANOVA to compare parametric data, followed by a Post Hoc test for multiple comparisons between different groups. Statistical analysis for non-parametric data was performed by Kruskal-Wallis, followed by the Mann-Whitney Test for pairwise comparisons between groups. P-value $\leq 0.05$ was considered statistically significant (95 % significance level). The Shapiro-Wilk test was used for testing the normality of data. The following equation calculated the percentage of change:

$$Percentage\ of\ change\ (\%) = \frac{Baseline\ value - the\ value\ after\ time}{baseline\ value}$$

The negative value of the percentage change means the baseline value changed to a higher value after time t. In contrast, the positive value of

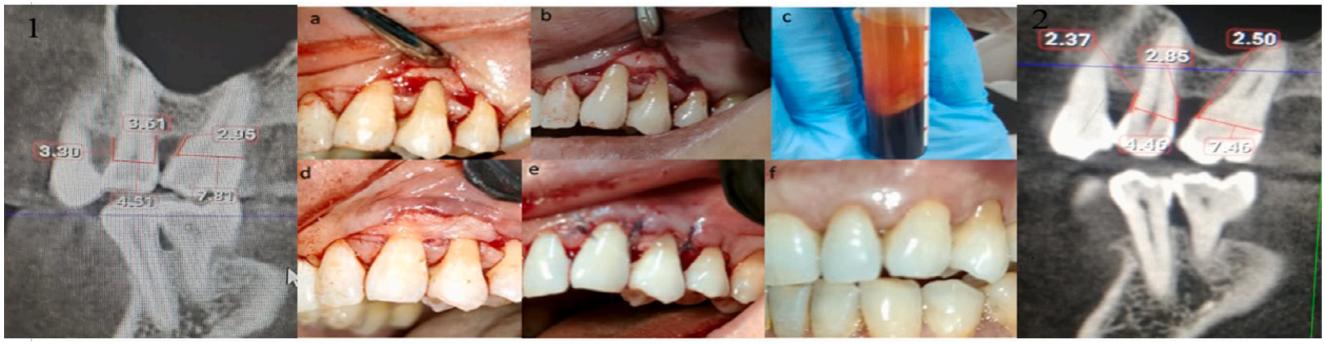


**Fig. 2.** (1) CBCT sagittal cut showing measurement of supra bony defect before treatment. (a) a horizontal, butt-joint incision was performed 1–2 mm coronal to the bone crest. (b) a buccal mucoperiosteal envelope flap (SFA) was elevated, and the defect was debrided manually. (c) CGF preparation. (d), defects were filled with CGF between the roots inter-proximal below the undetached papilla and extending to cover the root surface buccally. (e) a horizontal internal mattress suture. (f) 21-day healing. (2) CBCT sagittal cut showing measurement of supra bony defect 6 months after treatment.

the percentage change means the baseline value changed to a lower value after time t. Statistical evaluation was performed using the SPSS statistical package (version 25, IBM Co. USA).

## 3. Results

### 3.1. Demographic data

Most patients were females (64.3 % and 57.1 % for control and test groups). The mean age was 38.14 ± 10.70 years, and 36.50 ± 11.29 years for the control and test groups respectively (Table 1).

### 3.2. Clinical parameters assessment

**At baseline;** PD, CAL and GR values showed a non-significant difference between the 2 groups before treatment**. PD** mean values for control group were 7.68 ± 0.66, which decreased significantly to 5.82 ± 0.96 (P-value 0.001). Test group pre and post treatment values were7.74 ± 0.53 and 3.80 ± 0.12 respectively (p- value 0.000). As for **CAL**; before and after treatment values for control group were 6.17 ± 0.18 and 5.01 ± 0.73 (P- value 0.000). For test group these values were 6.45 ± 0.36 and 3.75 ± 0.13 (P- value 0.000). PD and CAL after treatment intergroup comparison showed a significant reduction in favor to test group.

**GR**; the mean baseline value for the control group was (2.46 ± 0.52 mm), increased to (2.87 ± 0.35 mm) after treatment (p-value = 0.019) while the test group showed a non-significant reduction after treatment (p-value = 0.716).The test group showed a significant reduction after treatment compared to the controls (p-value = 0.716) (Table 1).

### 3.3. Radiographic assessment

Within the control group, mean bone loss values before treatment were (3.40 ± 0.33 mm), and non-significantly increased to (3.75 ± 10.62 mm) after treatment (p-value = 0.189). For the test group, mean values for pretreatment and after treatment were (3.63 ± 0.36 mm) and (3.05 ± 0.30 mm) receptively, this decrease was statistically significant (p-value = 0.008).

The inter-group comparison showed a non -significant difference between the two groups before treatment (p-value = 0.547) and a significant difference between the two groups after the treatment (p-value = 0.001) (Table 1).

### 3.4. Pain score (VAS)

After surgery by 24 h, control group patients who reported scores 3, 6, and 7 were (6.7 %, 40 %, and 53.3 %) respectively. On the second day after surgery 33.3 % of patients reported a score of 6 while 66.7 % reported a score of 7) (P value = 0.008). For test group, patients reported scores 3 and 4 on the first day were 40 % and 60 % respectively. After 48 h, 40 % reported a score of 2, 46.7 % reported a score of 3, and 13.3 % reported a score of 4() (P value = 0.001). There was a significant difference between the two groups at the two time intervals (P-value = 0.000) for both time intervals (24 and 48 h). (Table 2).

### 3.5. Wound healing index (WHI)

In the control group, 53.3 % of patients recorded a score of 2, and 46.7 % recorded a score of 3, however, 100 % of patients recorded a score of 1 in the test group, a significant difference between the two groups (P-value = 0.000) (Table 3).

## 4. Discussion

This study reports the improved clinical, patient centered, and radiographic outcomes of CGF plus SFA in the management of periodontal SDs after 6 months. Open flap debridement is considered the most effective treatment modality for managing SDs. According to recent clinical practice guidelines, the presence of deep bleeding periodontal pockets after phase I and II periodontal therapy requires surgical intervention (Sanz et al., 2020). SFA is less invasive technique with a basic principle of elevating a single mucoperiosteal flap -either buccal or lingual/palatal side- to access the defect and repositioning the flap to the undetached interproximal papilla. SFA reported improved periodontal clinical outcomes when compared to the double flap approach in the treatment of infra-bony defects (Trombelli et al., 2018, Trombelli et al.,

**Table 1**
Descriptive statistics and P-value results for all variables at different time intervals.

| | Control | | | Test | | |
|---|---|---|---|---|---|---|
| | Before | After | P-value* | Before | After | P-value* |
| Sex (in %) | | | | | | |
| Male | 35.7 % (5) | | | 42.9 % (6) | | |
| Female | 64.3 % (9) | | | 57.1 % (8) | | |
| P-value** | **0.832$^{NS}$** | | | | | |
| Age | | | | | | |
| Mean (SD) | 38.14 (10.70) | | | 36.50 (11.29) | | |
| P-value** | **0.968$^{NS}$** | | | | | |
| GR | | | | | | |
| Mean (SD) | 2.46 ± 0.52 | 2.87 ± 0.35 | **0.019$^{S}$** | 2.33 ± 0.49 | 2.40 ± 0.51 | **0.716$^{NS}$** |
| P-value** | **1.000$^{NS}$** (α) | | | **0.000$^{S}$**(β) | | |
| PD | | | | | | |
| Mean (SD) | 7.68(0.66) | 5.82(0.96) | **0.001$^{S}$** | 7.74(0.53) | 3.80(0.12) | **0.000$^{S}$** |
| P-value** | **0.473$^{NS}$** (α) | | | **0.007$^{S}$** (β) | | |
| CAL | | | | | | |
| Mean (SD) | 6.17(0.18) | 5.01(0.73) | **0.000$^{S}$** | 6.45(0.36) | 3.75(0.13) | **0.000$^{S}$** |
| P-value** | **0.052$^{NS}$**(α) | | | **0.000$^{S}$**(β) | | |
| Bone loss | | | | | | |
| Mean (SD) | 3.40 ± 0.33 | 3.75 ± 10.62 | 0.189$^{NS}$ | 3.63 ± 0.36 | 3.05 ± 0.30 | 0.008$^{S}$ |
| P-value** | **0.547$^{NS}$** (α) | | | **0.001$^{S}$**(β) | | |
| % of change | **−10.34 %** | | | **16.01 %** | | |
| P-value** | **0.000$^{S}$** | | | | | |

- S = statistically significant (P-value ≤ 0.05). NS = non-significant (p-value > 0.05).
* P-value for Intra-group comparison (Before vs. After). ** P-value for Inter-group comparison (Control vs. Test) α = P-value for comparison between control and test groups before the treatment.
β = P-value for comparison between control and test groups after the treatment.

**Table 2**
Comparison of Pain Perception Score (VAS) distribution between the two groups after different time intervals.

| | Control | | | Test | | | P-value* |
|---|---|---|---|---|---|---|---|
| | **Score 3** | **Score 6** | **Score 7** | **Score 2** | **Score 3** | **Score 4** | |
| After 24 h | 6.7 % | 40 % | 53.3 % | 0 % | 60 % | 40 % | **0.000[S]** |
| After 48 h | 0 % | 33.3 % | 66.7 % | 40 % | 46.7 % | 13.3 s% | **0.000[S]** |
| P-value** | **0.008[S]** | | | **0.001[S]** | | | |

* P-value for Intra-group comparison (after 24 h vs. After 48 h).
** P-value for Inter-group comparison (Control vs. test).

**Table 3**
Comparison of wound healing score distribution between the two groups.

| | Control | | | Test | | | P-value |
|---|---|---|---|---|---|---|---|
| | **Score 1** | **Score 2** | **Score 3** | **Score 1** | **Score 2** | **Score 3** | |
| Wound healing score | **0 %** | **53.3 %** | **46.4 %** | **100 %** | **0 %** | **0 %** | **0.000[S]** |

2020, 2021). Till now, limited data are available regarding the use of SF design in the treatment of periodontal osseous defects although these limited data have reported favorable promising results (Mathala et al.,2021, Windisch et al., 2022).

Over time, the use of biologics has become more popular in periodontal treatment. The second and third-generation platelet concentrates protocols are now simpler, less expensive, and faster. These concentrates contain an entire physiological fibrin matrix with a high concentration of growth factors that stimulate tissue generation, angiogenesis and bone cell proliferation. (Caruana et al., 2019; Tavelli et al., 2020). GFC offers a denser, highly cross-linked three-dimensional fibrin scaffold structure than A-PRF and I-PRF (Lei et al., 2020), this allows for sustained release of the contained growth factors, such as platelet-derived growth factor (PDGF), transforming growth factor (TGF)-β1, TGF-β2, fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF), brain-derived growth factor (BDGF) and insulin-like growth factor (IGF) (Tavelli et al., 2020). An in vitro study investigated the growth factor release kinetics in CGF. It showed that TNF-α and BDGF exhibit accelerated release, reaching their highest concentration on the 1st and 3rd day, respectively. Similarly, PDGF-AB, TGF-β1, and IGF-I display constant kinetic release, reaching their maximum concentration on the 3rd and 6th day, respectively. VEGF and BMP-2 express slow late release, reaching their maximum levels on the 8th day (Yu and Wang., 2014). Thus, CGF prolongs the duration of growth factor activity and synergy causing enhanced cell proliferation and osteogenic differentiation (Schär et al., 2015).

In this study, we hypothesized that preserving an undetached wall of gingiva on the palatal/lingual side, along with an undetached coronal papilla and the mesial and distal roots, would create a contained defect that offers better stability for both the blood clot and the CGF, resulting in a higher chance of successful periodontal regeneration. This theory is partly based on Simonelli et al. (2021). They found that preserving the papilla using either single or double flaps had a positive effect in correcting (SDs) surgically.

In accordance with earlier data, our results showed significant PD and CAL reduction in both groups compared to pretreatment levels (Mathala et al., 2021, Windisch et al., 2022). The test group showed a significant reduction than the control group in these periodontal parameters. Recent data from systematic review supports the belief that biological agents can prevent the apical migration of epithelium in periodontal defects (Tavelli et al., 2020). Biological agents have higher angiogenic and wound healing abilities when applied without barrier membranes that otherwise might jeopardize the blood supply and chemotaxis of critical cells for periodontal regeneration (Nevins et al., 2013). Although this review focused on the intra-bony defect, the same concept can be applied to the horizontal bony defects as well, mainly when used with a technique that gives better stability to the soft tissues like SFA.

In our work and in accordance with earlier data, SFA alone caused a significant increase in GR after treatment (Simonelli et al., 2021). However, others showed that SFA didn't significantly cause any change in GR measurements (Mathala et al., 2021). In our test group, CGF caused no significant change in levels of GR. Farina et al., proposed that combining the SFA with specific added procedures/technologies can control the post-surgical increase in GR. Furthermore, GR of less than 1 mm after surgery was considered a success (Farina et al., 2015).

It was shown that no or only very limited bone gain can be expected after treatment of SDs (Yilmaz et al., 2003). However, others believed that the combined effects of SFA plus CGF would be beneficial in slight bone gain in SDs (Xu, et al., 2019). We didn't expect much bone formation, thus we used the CBCT to detect the slightest change. In our work a slight, yet no significant decrease in bone loss 6 months after SFA alone was reported, although earlier reports showed that SFA alone is capable of a significant reduction of bone loss in SDs (Mathala et al., 2021). Our results supply the first evidence of bone gain in 6th month after the test intervention. Our findings support earlier case reports and animal studies that reported bone regeneration after CGF application in bone defects (Park et al., 2016, Sureshbabu et al., 2019).

The need for high-level evidence on the effects of different periodontal treatment approaches on soft tissue regeneration and post-operative complications was recently highlighted (Chen et al., 2021). In agreement with earlier reports, our study reported excellent wound healing events in the test group compared to the controls (Nityasri et al., 2018, Elayah et al., 2022). This is supported by the effectiveness of CGF in soft-tissue regeneration. Moreover, CGF is an efficient surgical hemostatic substance-as through the polymerization of the fibrinogen molecules- the fibrin block includes a 3D polymer network of interwoven fibers that entrap multiple platelets. This environment is essential for cell–cell, and protein– protein interactions to create tissue symmetry (Rodella et al., 2011). Our reported healing effects could be attributed to the synergistic effect of the flap design plus the CGF application.

Less post operative pain after test intervention was an important finding in our work. The role of CGF in reducing postsurgical complications such as edema and pain was earlier reported (Naik B et al., 2013, Alaa et al., 2021). Findings related to the effect of SFA on pain reduction after surgery are sparse, Mathala et al., 2021, reported a better patient satisfaction outcome after SFA compared to the double flap approach.

## 5. Conclusions

The clinical and radiographic findings of the combined use of CGF with SFA are consistent with regeneration and satisfactory healing, further, being a simple, easily accessible, and cost-effective approach, it

could be recommended for the management of periodontal supra-bony defects. More studies are needed with more extended post-operative period and using other regenerative aids.

## 6. Funding information

The study was self-funded by the authors.

## 7. Ethical approval

The study was approved by the faculty of dentistry (girls branch), Al-Azhar university ethical committee (code P-PD-22-9**).**

## 8. Informed consent

Informed consent was obtained from all study participants.

## 9. Author statement

Naglaa El-Wakeel, the corresponding author of manuscript entitled (Single-flap approach versus without concentrate growth factor in the treatment of periodontal supra-osseous defects: A randomized controlled clinical trial), certify that the contributors' and conflicts of interest statements included in this paper are correct and have been approved by all co-authors.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sdentj.2023.11.015.

## References


Alaa, Z., Makki Anoud, M. Alsulami, Arwa S. Almatrafi, Moroj Z. Sindi, Shahinaz N. Sumbawa .2021.The Effectiveness of Advanced Platelet-Rich Fibrin in comparison with Leukocyte-Platelet-Rich Fibrin on Outcome after Dentoalveolar Surgery", International Journal of Dentistry,:2021; 2029.

Caruana, A., Savina, D., Macedo, J.P., Soares, S.C., 2019. From platelet-rich plasma to advanced platelet-rich fibrin: Biological achievements and clinical advances in modern surgery. Eur. J. Dent. 13 (2), 280–286.

Chen, J., Wan, Y., Lin, Y., Jiang, H., 2021. Considerations for clinical use of concentrated growth factor in maxillofacial regenerative medicine. J. Craniofac. Surg. 32 (4), 1316–1321.

Debnath, K., Chatterjee, A., 2018. Treatment of horizontal defect with and without platelet-rich fibrin matrix: A randomized comparative clinical study. J. Indian Soc. Periodontol. 22 (5), 406–413.

Elayah, S.A., Liang, X., Sakran, K.A., Xie, L., Younis, H., Alajami, A.E., Tu, J., Na, S., 2022. Effect of concentrated growth factor (CGF) on postoperative sequel of completely impacted lower third molar extraction: a randomized controlled clinical study. BMC Oral Health 22 (1), 368.

Farina, R., Simonelli, A., Minenna, L., Rasperini, G., Schincaglia, G.P., Tomasi, C., Trombelli, L., 2015. Change in the gingival margin profile after the single flap approach in periodontal intraosseous defects. J. Periodontol. 86 (9), 1038–1046.

Iorio-Siciliano, V., Blasi, A., Stratul, S.I., Ramaglia, L., Octavia, V., Salvi, G.E., Sculean, A., 2021. Healing of periodontal suprabony defects following treatment with open flap debridement with or without an enamel matrix derivative: A randomized controlled clinical study. Clin. Oral Investig. 25 (3), 1019–1027.

Kobayashi, E., Flückiger, L.B., Fujioka-Kobayashi, M., Sawada, K., Sculean, A., Schaller, B., Miron, R.J., 2016. Comparative release of growth factors from PRP, PRF, and advanced-PRF. Clin. Oral Invest. 20, 2353–2360.

Lei, Q.i., Lu, L., Yue, H.u., Li, J., Li, J., Ningning, C., Fangxing, Z.u., Chaoji, S., Lei, Z., 2020. Concentrated growth factor promotes gingival regeneration through the AKT/Wnt/β-catenin and YAP signaling pathways. Artif. Cells Nanomed. Biotechnol. 48 (1), 920–932.

Mathala, V.L., Konathala, S.V.R., Gottumukkala, N.V.S.S., Pasupuleti, M.K., Bypalli, V., Korukonda, R., 2021. Single-flap versus double-flap approach for periodontal pocket reduction in supraosseous defects: a comparative study. J. Periodont. Implant Sci. 51 (4), 239–253.

Miron, R.J., Moraschini, V., Fujioka-Kobayashi, M., Zhang, Y., Kawase, T., Cosgarea, R., et al., 2021. Use of platelet-rich fibrin for the treatment of periodontal intrabony defects: a systematic review and meta-analysis. Clin. Oral Invest. 25 (5), 2461–2478.

Myles, P.S., Myles, D.B., Galagher, W., Boyd, D., Chew, C., MacDonald, N., Dennis, A., 2017. Measuring acute postoperative pain using the visual analog scale: The minimal clinically important difference and patient acceptable symptom state. Br. J. Anaesth. 118 (3), 424–429.

Naik, B., Karunakar, P., Jayadev, M., Marshal, V.R., 2013. Role of Platelet rich fibrin in wound healing: A critical review. J. Conserv. Dent. 16 (4), 284–293.

Nevins, M., Kao, R.T., McGuire, M.K., McClain, P.K., Hinrichs, J.E., McAllister, B.S., et al., 2013. Platelet-derived growth factor promotes periodontal regeneration in localized osseous defects: 36-month extension results from a randomized, controlled, double-masked clinical trial. J. Periodontol. 84 (4), 456–464.

Nityasri, Aromal, S., Pradeep Kumar, Y., Kalaivani, V., Pandian, R. 2018. Role of Concentrated Growth Factor) in periodontal regeneration. Journal Dental Health Oral Disord Ther. 9(2), 350-2.

Park, H.C., Kim, S.G., Oh, J.S., You, J.S., Kim, J.S., Lim, S.C., et al., 2016. Early bone formation at a femur defect using CGF and PRF grafts in adult dogs: A comparative study. Implant Dent. 25 (3), 38793.

Rodella, L.F., Favero, G., Boninsegna, R., Buffoli, B., Labanca, M., Scarì, G., et al., 2011. Growth factors, CD34 positive cells, and fibrin network analysis in concentrated growth factors fraction. Microsc. Res. Tech. 74 (8), 772–777.

Saini, K., Chopra, P., Sheokand, V., 2020. Journey of platelet concentrates: A review. Biomed. Pharmacol. J. 13 (1).

Sanz, M., Herrera, D., Kebschull, M., Chapple, I., Jepsen, S., Beglundh, T., et al., 2020. Treatment of stage I-III periodontitis—The EFP S3 level clinical practice guideline. J. Clin. Periodontol. 47 (S22), 4–60.

Schär, M.O., Diaz-Romero, J., Kohl, S., Zumstein, M.A., Nesic, D., 2015. Platelet-rich concentrates differentially release growth factors and induce cell migration in vitro. Clin. Orthop. Relat. Res. 473 (5), 1635–1643.

Simonelli, A., Minenna, L., Trombelli, L., Farina, R., 2021. Single flap approach with or without enamel matrix derivative in the treatment of severe supraosseous defects: a retrospective study. Clin. Oral Invest. 25, 1–8.

Sureshbabu, N.M., Selvarasu, K., Jayanth Kumar, V., Nandakumar, M., Selvam, D., 2019. Concentrated growth factors as an ingenious biomaterial in regeneration of bony defects after periapical surgery: A report of two cases. Case Reports Dent., 7046203

Tavelli, L., McGuire, M.K., Zucchelli, G., Rasperini, G., Feinberg, S.E., Wang, H.L., Giannobile, W.v., 2020. Biologics-based regenerative technologies for periodontal soft tissue engineering. J. Periodontol. 91 (2), 147–154.

Trombelli, L., Farina, R., Franceschetti, G., Calura, G., 2009. Single flap approach with buccal access in periodontal reconstructive procedures. J. Periodontol. 80, 353–360.

Trombelli, L., Farina, R., Minenna, L., Toselli, L., Simonelli, A., 2018. Regenerative periodontal treatment with the single flap approach in smokers and nonsmokers. Int. J. Periodont. Restor. Dent. 38, 59–67.

Trombelli, L., Farina, R., Vecchiatini, R., Maietti, E., Simonelli, A., 2020. A simplified composite outcome measure to assess the effect of periodontal regenerative treatment in intraosseous defects. J. Periodontol. 91, 723–731.

Trombelli, L., Simonelli, A., Quaranta, A., Tu, Y.K., Li, H., Agusto, M., Jiao, X.J., Farina, R., 2021. Effect of flap design for enamel matrix derivative application in intraosseous defects. JDR Clin. Transl. Res. 6 (2), 189–194.

Windisch, P., Iorio-Siciliano, V., Palkovics, D., Ramaglia, L., Blasi, A., Sculean, A., 2022. The role of surgical fap design (minimally invasive fap vs. extended fap with papilla preservation). Clin. Oral Invest. 26, 1811–1821.

Xu, Y., Qiu, J., Sun, Q., Yan, S., Wang, W., Yang, P., 38; Song, A. 2019. One-Year Results Evaluating the Effects of Concentrated Growth Factors on the Healing of Intrabony Defects Treated with or without Bone Substitute in Chronic Periodontitis. Medical Science Monitor. 25, 4384–89.

Yilmaz, S., Kuru, B., Altuna-Kiraç, E., 2003. Enamel matrix proteins in the treatment of periodontal sites with horizontal type of bone loss. J. Clin. Periodontol. 30 (3), 197–206.

Yu, B., Wang, Z., 2014. Effect of concentrated growth factors on beagle periodontal ligament stem cells in vitro. Mol. Med. Rep. 9 (1), 235–242.