Future Dental Journal

Volume 9 | Issue 2 Article 12

2023

Effect of Concentrated Growth Factor alone and mixed with Hyaluronic Acid on Osseointegration of Delayed Implant.

kholoud sobhy eldeeb kholoud eldeeb
Future university,Egypt, kholoud.eldeeb@fue.edu.eg

lobna mohammed abdelaziz
Al-Azhar University, lobnamohammed85@yahoo.com

shahira Elashiry
Cairo University, schahira@gmail.com

Eatemad Shoreibah
Al-Azhar University, eshoreibah@yahoo.com

Effect of Concentrated Growth Factor alone and mixed with Hyaluronic Acid on Osseointegration of Delayed Implant.

Cover Page Footnote

ACKNOWLEDGEMENT Many thanks to oral medicine and periodontology department, the Faculty of Dental Medicine, Al-Azhar University Girls' branch for their support in my work.

Effect of Concentrated Growth Factor alone and mixed with Hyaluronic Acid on Osseointegration of Delayed Implant.

Kholoud S. Eldeeb[1], Lobna M. Abdel[1]aziz[2], Shahira. Elashiry[3], Eatemad. Shoreibah[4]

ABSTRACT:

Purpose: The aim of current study was evaluating effect of concentrated growth factor alone and mixed with hyaluronic acid on osseointegration of delayed implant. **Subject and Methods**: A total of 12 patients, ranging in age from 20 to 45 years old, were divided into two groups in random manner. Group A: Dental implants were placed associating with concentrated growth factor. Group B: Dental implants were placed associating with concentrated growth factor and hyaluronic acid. Treatment changes were evaluated for each group and compared between groups. **Results:** In the mean of implant stability a statistically significant difference existed within group A as implant stability increased from base line immediately after implant insertion to follow up period after six months, also statistically significant difference existed in the mean of Implant Stability within group B as implant stability decreased from base line immediately after implant insertion to follow up period after six months. Also, there was statistically significant difference in the mean of Implant Stability between the two groups. **Conclusions:** Concentrated growth factor alone have positive effect on bone osseointegration.

Keywords: Osseointegration, Concentrated growth factor, Hyaluronic acid, Implant stability.

Introduction:

Paper extracted from master thesis titled “Effect of Concentrated Growth Factor and Hyaluronic Acid Apart or Combined on Osseointegration around Dental Implant.”

1- Teaching assistant at department of Oral Medicine, Periodontology, Oral Diagnosis and Dental Radiology at Future university
2- Lecturer of Oral Medicine, Periodontology, Oral Diagnosis and Dental Radiology department Faculty of Dental Medicine for Girls Al-Azhar University
3- Head of department of Oral Medicine, Periodontology, Oral Diagnosis and Dental Radiology Faculty of Dental Medicine Future University in Egypt.
4- Professor of Oral Medicine, Periodontology, Oral Diagnosis and Dental Radiology Faculty of Dental Medicine for Girls Al-Azhar University

The term osseointegration described as a direct anatomical and functional contact between bone tissues as well as the implant surface[1]. Osseointegration is a process that creates a strong, hard bond between surrounding bone tissue and the surface of implant, which essentially for implant survival. Without osseointegration, biological failure would occur, resulting in implant failure[2].To improve osseointegration different methods of healing modulation after the placement of the implant are used. This modulation is achieved by using different synthetic and natural materials to enhance osteopromotion which lead to osseointegration without compromising the mechanical outcomes and tissue integration[3]. A novel notion of concentrated growth factors was introduced by Sacco. The preparation of concentrated growth factor (CGF) necessitated the use of venous blood with different rpm ranging from 2400-2700-3000. The membrane of CGF has a complex three dimensional architecture, making it a platelet, fibrin, leukocyte, and growth factor-rich biomaterial[4]. When compared to platelet rich fibrin and other platelet concentrates, CGF contains higher levels of growth factors, thus due to variable centrifuging speed strategy with mechanical ascent and descend which used to fully activate alpha granules in platelets and generate patient- derived blood product enriched with high levels of growth factors. This strategy enhance the ability of bone, soft tissue, and skin to regenerate [5]. The CGF can be conceived of as a modern trend of fibrin matrix blocks with a high growth factors concentration such as platelet derived growth factors (PDGF), insulin-like growth factors (IGF), bone morphogenic protein (BMP), transforming growth factor-b (TGF-b) and other important factors. CGF deliver these specific growth factors at the application site [6]. Hyaluronic acid (HA, also known as hyaluronan; its conjugated base is hyaluronate) is non-sulfated, acidic glycosaminoglycan found throughout the body. The dermis' connective tissue, synovial fluid, the dental pulp matrix, and other regions of the body contain HA. Hyaluronic acid supports cellular structure and functions as a lubricant by preserving the viscoelasticity of the extracellular matrix (ECM). It maintains tissues hydrated and preserves the ECM's physical shape as an ECM component. HA is also known to be the ligand for cluster of differentiation 44 (CD44). It regulates cell motility and adhesion through its interaction with CD44 [7].

SUBJECTS AND METHODS

Study design:

This study included 12 implants for patients suffering from edentulous area in upper premolar area. Our participants were selected from the out-patient clinic of the department of oral medicine and periodontology, Oral diagnosis and radiology, Faculty of Dental Medicine, Al-Azhar University.

Sample size:

For evaluating the effect of adding hyaluronic acid and concentrated growth factor around delayed dental implant, independent t test was used to compare between two groups. A total sample size of 12 patients (6 in every group) was sufficient to determine an impact value ranging from 1.42 to 1.48 with a power (1-β error) of 0.8(80%) Using a two-sided hypothesis test with Significance level (α error) 0.05 for data. Patients were randomly divided into two groups [8].

Preoperative assessment

Clinical assessment: All the cases were evaluated thoroughly by clinic-radiological assessment including: Chief complaint, past medical history, personal and family history, extra oral and intra oral examination, Cone beam computed tomography (CBCT) was used to record bone height then width of area of interest to choose the suitable implant size (diameter and length) and to draw the implant future recipient site by using available data, and pre-operative intraoral photographs. Full mouth scaling and root debridement were obtained followed by proper oral hygiene instruction. Patients were free of any systemic disease.

Surgical procedure[9, 10]:

All surgical steps were carried out under strict aseptic conditions. Following local anesthesia of surgical area, (Articaine 4% with noradrenalin 1:100,000), After testing anesthesia Paracrestal incision was performed on edentulous space and full thickness mucoperiosteal flap was reflected. The implant site was prepped according to the implant company's surgical protocol., till the desired dimensions under copious irrigation with normal saline. The final osteotomy diameters matched the implant sizes. During implant site preparation care was taken not to interfere with neighboring teeth and the angulation of placement was identical to the pre-existing tooth. Group A: The concentrated growth factor (CGF) was taken from venous blood of patient. Intravenous blood samples from patients' blood were placed in centrifuge tubes without

anticoagulants and centrifuged as follow acceleration for 30 seconds, then increase speed to 2700 rpm for 4 minutes, decrease speed to 2400 rpm for 4 minutes, increase speed to 2700 rpm for 4 minutes, more increase in speed up to 3000 rpm for 3 minutes, and decelerated for 36 seconds until stop. In the tube, there were three layers: in the bottom a red blood cell layer, on the top a platelet-depleted plasma layer (no cells), in the middle a layer platelet aggregate with fibrin gel contained concentrated growth factor. To separate middle layer which contained concentrated growth factor from the layer in the bottom a surgical scissor was used. Group B: CGF was inserted then hyaluronic acid was injected inside the osteotomy and applied on the implant fixture. The implants were submerged under the crest of alveolar ridge by 1mm. The primary stability was assessed using Osstell for all implant by the situation of a smart peg into the fixture of implant, which is secured into the implantation and the usage of a transducer, which is held adjacent to and upright to the Smart Peg without really creating touching as shown in (Fig.1). The implant fixture was covered by cover screw. The flap was sutured using interrupted suture.

Six months after surgery, the cover screw was removed then assessed the secondary stability using Osstell, then placement A restorative cap (gingival former) for two weeks then the abutment supplied by the implant system company. After that proper adjustment of the abutment and direct impression was made for fixed appliance construction by heavy and light rubber base impression material. The final crown made of porcelain fused to metal cemented on abutment.

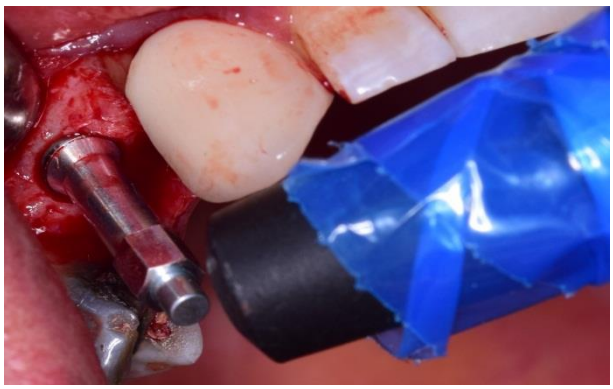

Figure (1): A photograph showing measuring implant stability using Osstell.

Postoperative instructions:

After surgery, all patients were instructed to apply extra oral ice bags (10-20 minutes) over implant site to prevent hematoma formation. and to prescribe antibiotic (Augmentin 1g twice/day for 7 days), analgesic (Ibuprofen 600mg 3 times/day for 3 days) and to wash with 0.12% chlorhexidine gluconate oral wash two times daily after surgery.

Statistical analysis:

To compare between normal distributed data one-way anova test was used followed by Post Hoc test for multiple comparisons between different groups. For non-normal distributed data Kruskal-Wallis was used followed by Mann-Whitney Test for pairwise comparisons between groups. $P \geq 0.05$ was considered statistically significant (95% significance level) and Shapiro Wilk test was used for assessing data normality. SPSS statistical package was used for statistical evaluation (version 25, IBM Co. USA).

RESULTS

-Implant stability

Changes in implant stability within the groups:

Within group A the mean of implant stability was (52.43±1.77) after insertion immediately and increased to (66.58±5.36) After 6 Months. The mean of Implant Stability differed statistically significantly between the two- time intervals. ($P \leq 0.003$). On the other hand, the mean of implant stability within group B was (51.53±2.36) after insertion immediately, this number decreased to (40.7±5.87) After 6 Months. In the mean of implant stability there was a statistical significance difference between two-time interval at ($P \leq 0.004$).

Table (1): Mean ±SD of Implant Stability within the two groups at different time intervals.

	Group A	Group B
At base line	52.43±1.77	51.53±2.36
After 6 Months	66.58±5.36	40.7±5.87
P-value	0.003^{S}	0.004^{S}

- NS= Nonsignificant - S= statistically significant at $P \leq 0.05$

Changes in implant stability between two groups:

At base line there was no statistical significance difference in the mean of implant stability between the two groups (group A (52.43±1.77), group B (51.53±2.36)) at (P-value=0.818). However, the mean of implant stability decreased after six months at group B (40.7±5.87) and there was statistically significant difference between the two groups in the mean of implant stability at (P-value=0.004).

Table (2): Mean ±SD of Implant Stability between two groups at different time intervals.

	Group A	Group B	P-value
At base line	52.43±1.77	51.53±2.36	0.818^{NS}
After 6 Months	66.58±5.36	40.7±5.87	0.004^{S}

-NS= Nonsignificant - S= statistically significant at $P \leq 0.05$

DISCUSSION

Dental implants have established themselves as a reliable method for the rehabilitation of edentulous areas. Before implant there were two options available for replacing missing teeth either fixed or removable prosthesis. Dental implants have several advantages over conventional methods of replacing missing teeth; as it has a high success rate, improve maintenance of bone in edentulous site and decrease sensitivity of adjacent teeth[11, 12].

Immediate implant surgery has clearly gained popularity over the last decade due to less surgical interventions and increase rates of patient contentment. Although, the challenges in achieving primary stability and the risk of no bone development around implant due to micro-movements may be issues in implant longevity and aesthetic results. Dos Santos Canellas et al, showed a significant statistical difference in favor of delayed protocol. Implant failure was observed when the immediate implant technique was used, increasing the probability of implant loss by 3%[13].

Therefore, the goal of this study to test the influence of concentrated growth factor alone and mixed with hyaluronic acid on the osseointegration of delayed implant placement. A randomized study was applied on 12 patients. Smokers were excluded from this study as it decreased bone mineral density and reduced blood supply. Due to smoking and its releasing

substances as nicotine which has been shown to restrict osteoblast proliferation and secretion of osteogenic mediators such as bone-morphogenic protein 2 (BMP-2). Nicotine has been shown to promote the development of osteoclast-like cells when combined with LPS[14]. Also patients should be free from any systemic conditions that affect osseointegration[15].

Osseointegration is the foundation of dental implant success, which refers to the actual and prolonged contact between living bone tissue and pure titanium implant surface [16]. It is crucial to provide firm attachment of the dental implant within the alveolar bone, especially when the alveolar bone is reduced qualitatively and quantitatively. Enhancing osseointegration is the way to ensure predictability of implant in such cases. Modulation of healing with natural or synthetic materials is one approach of accelerating osseointegration[9].

CGF (concentrated growth factor) is a centrifuged plasma extract of autologous blood. CGF scaffolds have a different and unique three-dimensional (3D) fibrin network, this could create a favorable milieu for freshly generated tissue to grow inwards. Particularly, CGF has a high level of growth factors, platelets, and cytokines due to the improved manufacturing method[17]. Other methods to improve osseointegration is using synthetic materials such as Hyaluronic acid (HA) which found in the human body, it occurs naturally as a critical and important part of the extracellular matrix (ECM). In recent decades, HA has become increasingly popular in the specialty of bone regeneration[18].

As implant stability is one of the most important clinical aspects at clinical implant installation and one of the most important crucial elements in the osseointegration process so we measured implant stability using Osstell[19]. The resonance frequency analysis (RFA) is a direct method for evaluating osteointegration that provides valuable clinical objective data on implant stability. RFA is non-destructive and non-invasive technique to measure stability of dental implant. It is comparable in terms of the direction and type of fixed lateral force application to the implant, as well implant displacement measurement. At any stage of treatment, this method has the potential to provide clinically significant data on the condition of the implant-bone interface [20].

In current study we measured implant stability immediately after implant insertion and after 6 months and results showed that in group A there was a statistically significant difference in the mean of Implant Stability between the two-time intervals. CGF improves implant stability,

accelerate osseointegration by increasing osteoblast differentiation, and promotes bone healing around the implant. CGF contains more growth factors than other platelets preparations, which improves implant healing time. It has a positive effect on the implant osseointegration and stabilization values[17].

Pirpir et al., investigated the role of CGF in the stability of dental implants. They applied CGF with dental implants in test group and found increase in implant stability in compare to control group without CGF. [21].

Also, in current study we measured implant stability immediately after implant insertion and after 6 months and results showed that in group B there was a statistically significant decrease in the mean of Implant Stability between the two-time intervals and there was even a failure of one implant case.

Although several comparative studies on the platelet preparations in general and HA have been published [22], the effect of mixing both is not fully understood. In contrast with results of this study, Lio and Yasuyuki et al. (2016) studied the influence of HA on platelets in PRP by measuring releasing growth factors and found that the levels of growth factors released by PRP were increased by addition of HA. They recommended that the mixture of PRP and HA would be a more effective therapy than PRP or HA alone for osteoarthritis and tendinopathy.

CONCLUSION

In current study we found that Concentrated growth factor could be used with titanium implants without impairing bone formation and have positive effect in increasing implant stability.

ACKNOWLEDGEMENT

Many thanks to oral medicine and periodontology department, the Faculty of Dental Medicine, Al-Azhar University Girls' branch for their support in my work.

RECOMMENDATION

Further studies with longer period are needed.

CONFLICT OF INTEREST

There was no conflict of interest.

FUND

No funding had been received for this study.

REFERENCES

1. Ramakrishna, M., et al., *A brief history of osseointegration: A review.* 2021. **7**(1): p. 29-36.
2. Lemos, C., et al., *Survival of dental implants placed in HIV-positive patients: a systematic review.* 2018. **47**(10): p. 1336-1342.
3. Öncü, E., et al., *Posıtıve effect of platelet rich fibrin on osseointegration.* 2016. **21**(5): p. e601.
4. Saini, K., et al., *Journey of platelet concentrates: a review.* 2020. **13**(1): p. 185-191.
5. Hu, Y., et al., *Concentrated growth factor enhanced fat graft survival: a comparative study.* 2018. **44**(7): p. 976-984.
6. Bernardi, S., et al., *Histological characterization of Sacco's concentrated growth factors membrane.* 2017. **35**(1): p. 114-119.
7. Hemshekhar, M., et al., *Emerging roles of hyaluronic acid bioscaffolds in tissue engineering and regenerative medicine.* 2016. **86**: p. 917-928.
8. Faul, F., et al., *G* Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences.* 2007. **39**(2): p. 175-191.
9. Lokwani, B.V., et al., *The use of concentrated growth factor in dental implantology: A systematic review.* 2020. **20**(1): p. 3.
10. Yazan, M., et al., *Effect of hyaluronic acid on the osseointegration of dental implants.* 2019. **57**(1): p. 53-57.
11. Silva, K.C., et al., *Assessment of dental implant stability in areas previously submitted to maxillary sinus elevation.* 2018. **44**(2): p. 109-113.
12. Gupta, R., N. Gupta, and K.J.S.T.I.S.P. Weber, *Dental Implants. 2020 Aug 11*. 2020.
13. dos Santos Canellas, J.V., et al., *Which is the best choice after tooth extraction, immediate implant placement or delayed placement with alveolar ridge preservation? A systematic review and meta-analysis.* 2019. **47**(11): p. 1793-1802.
14. Shroff, Y., et al., *Smoking & Implant Failure: An Evidence Based Review.* 2018.

15. Schimmel, M., et al., *Effect of advanced age and/or systemic medical conditions on dental implant survival: A systematic review and meta-analysis.* 2018. **29**: p. 311-330.
16. Sahin, I., et al., *Effect of concentrated growth factor on osteoblast cell response.* 2018. **119**(6): p. 477-481.
17. Jin, R., et al., *Effects of concentrated growth factor on proliferation, migration, and differentiation of human dental pulp stem cells in vitro.* 2018. **9**: p. 2041731418817505.
18. Zhai, P., et al., *The application of hyaluronic acid in bone regeneration.* 2020. **151**: p. 1224-1239.
19. Tanaka, K., et al., *Relationship between cortical bone thickness and implant stability at the time of surgery and secondary stability after osseointegration measured using resonance frequency analysis.* 2018. **48**(6): p. 360-372.
20. Bafijari, D., et al., *Influence of resonance frequency analysis (RFA) measurements for successful osseointegration of dental implants during the healing period and its impact on implant assessed by Osstell mentor device.* 2019. **7**(23): p. 4110.
21. Pirpir, C., et al., *Evaluation of effectiveness of concentrated growth factor on osseointegration.* 2017. **3**(1): p. 1-6.
22. Afat, İ.M., et al., *Effects of leukocyte-and platelet-rich fibrin alone and combined with hyaluronic acid on pain, edema, and trismus after surgical extraction of impacted mandibular third molars.* 2018. **76**(5): p. 926-932.