EFFECT OF CONCENTRATED GROWTH FACTORS ON IMPLANT STABILITY, OSSEOINTEGRATION AND BONE DENSITY AROUND IMPLANT SURFACE: A RANDOMIZED CONTROL STUDY

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Abstract:
Aim: To study the Effect of Concentrated growth factors on Implant stability, osseointegration and bone density around implant surface
Settings and Design: Total of 60 sample specimens were made of 35mm X 2mm X 2mm dimensions. Two groups were made- Group 1 _without glass fibres' and Group 2 _with glass fibres'. Each group included three subgroups- Subgroup A _PMMA', Subgroup B _Protemp'Subgroup C _Cooltemp'. All subgroups included ten specimens each.
Methods and Material: Total two groups: Control group (Group 1) and study group (Group 2), with a sample size of total 19 implants were taken. In Group 2, implants were placed with CGF. For Group 1, implants were placed without CGF.
Statistical analysis used:. The statistical Analysis was done on SPSS version 21.0.The paired t-test and unpaired t test were done accordingly.
Results: CGF is significantly better in the regeneration of bone around the implants when compared with non CGF groups.
Conclusions CGF also aided in increasing the density of the bone around the implant from baseline to a much higher level.

Key-words: CGF, Implant, Bone Density

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INTRODUCTION

The third generation of concentrated platelet, CGF (Concentrated growth factors) was first proposed by Sacco in 2006. CGF is made from autologous venous blood with no addition of any biological agents, non-toxic, no immunogenicity, and separated by special centrifugation. CGF has strong tissue regeneration ability and biodiversity, stable fibrin matrix, high tensile strength, and a large quantity of osteoblasts. Collectively, CGF is a powerful biological scaffold and growth factor library [1]. CGF has been extensively used in various situations, ranging from the flling of extraction sockets [2] to the filling of a cavity after cystectomy [3], implant surgery [4], sinus augmentation procedures [5], simple GBR procedures or as a membrane support in recession coverage [6]. Further, CGF is considered to relieve postoperative pain and swelling, and reduce the occurrence of alveoar osteitis [7].

That the implant has sufficient stability, after placement it is important for providing the necessary bone formation around the implant, and for the optimal distribution of functional forces at the implant-bone interface during healing [8–10]. It can be said that resonance frequency analysis (RFA) is a very important tool for tracking the osseointegration process [11, 12]. RFA is a technique that allows tracking the changes in stability not only during implant placement but also during healing and later periods [13].

MATERIAL AND METHOD:

A prospective study was conducted in the Department of Prosthodontics, Sardar patel post graduate institute of Dental science and Hospital, Lucknow. Ethical clearance obtained from Ethical Committee of, Sardar patel post graduate institute of Dental science and Hospital, Lucknow Uttar Pradesh, India, reference no: FR/01/030722/IEC/ SPPGIDMS, dated: 03/07/22

- Sampling procedure: Random selection of population (Sealed envelope method)
- Number of groups: Control group (Group 1) and study group (Group 2)
- Sample size: 19

For Group 2, implants were placed with CGF. For Group 1, implants were placed without CGF.

Cylindrical implants were used in each patient in the maxillary posterior region. The diameter of the implant was 3.5 or 4.0 mm, and the length was 10 mm. Patients were rehabilitated with a fixed prosthesis, such as a single crown or bridge. Patients included in the study were randomly included in to two groups of study and control groups.

The implanted regions were evaluated preoperatively with panoramic radiography and computed tomography (CT) images. In the study group, the socket walls were laid with CGF membrane while the implant surfaces were washed with the thrombocyte-deprived part of the tube. No different procedure was done to the implants and socket in the control group.

CGF preparation

A standard, disposable, 10-ml non-anticoagulant tube and a centrifuge device (MEDIFUGE MF 200) were used. Intravenous blood samples from the patients were placed in centrifuge tubes without anticoagulants and accelerated for 30 s, centrifuged at 2700 rpm for 4 min, 2400 rpm for 4 min, 2700 rpm for 4 min, and 3000 rpm for 3 min, and decelerated for 36 s to stop.

Three layers were observed in the tube as: red blood cell layer at the bottom, platelet-deprived plasma layer (without cell) at the top, and fibrin gel with concentrated growth factor and platelet aggregation in the middle. The uppermost platelet-deprived fraction was removed with a sterile syringe. The layer in the form of a membrane containing the concentrated growth membrane was held with the aid of a hemostatic clamp, separated from the red blood cell layer by cutting with a pair of scissors and was then pressed to form a membrane.

SURGICAL PROCEDURE:

All routine surgical procedures, with and without placement of CGF, were performed under local anaesthesia, for the placement of implant in the patients, by the same surgeon. The implant surgery was completed in one session. The patients were recommended to apply cold compresses after the surgery. Patients were prescribed antibiotic, analgesic, and antiseptic mouthwash for 1 week.

Clinical evaluation of osseointegration by Resonance frequency analysis measurements (RFA)

Osstell ISQ system (Osstell®, integration Diagnostic AB, Goteborg, Sweden) consist of osstell ISQ instrument, probe, charger, USB cable and test peg. Osstell ISQ was used for measurement of implant stability. The system includes the use of a SmartPeg™ attached to the dental implant or abutment by means of an integrated screw. The SmartPeg is excited by a magnetic pulse from the measurement probe on the handheld instrument. The resonance frequency, which is the measure of implant stability, is calculated from the response signal. Results are displayed on the instrument as the Implant Stability

Quotient (ISQ), which is scaled from 1 to 100. The higher the value, the more stable the implant.

Radiographic evaluation:
All implants involved in this study were followed up radiographically by Cone beam computed tomography (CBCT) and OPG to evaluate horizontal and vertical dimensional changes of bone along with the assessment of the bone density. Bone Density Evaluation: Radiographic Evaluation Orthopantomogram (OPG) and cone beam computed tomography (CBCT) were performed immediately postoperative and at intervals of 1, 3 and 6 months to assess
Densitometric analysis was performed around dental implants on CBCT image by using Densitometric software BioRad. This analysis gives the bone density around the immersed dental implants by grayscale. Final prosthesis (porcelain fused to metal crown) was placed after 6 months.

Implant Survival Rate: soft tissue inflammation and healing, were assessed for the survival rate of implants...1. Peri-implantitis. 2 .Lack of osseointegration.3.Psychological factor.
The patients were observed at: Immediate Postoperative, 1month, 3 month and 6 month.

Inclusion Criteria:
- Good Oral Hygiene
- patients with implants in the maxillary anterior and premolar region.

Exclusion criteria:
- Presence of systemic diseases preventing implantation
- Having blood disease so as to prevent centrifugation
- Previous implantation or augmentation of the same region
- The need for any other additional bone augmentation procedures (such as maxillary sinus
- augmentation, distraction osteogenesis)
- Allergy to one of the materials to be used during operation
- Pregnancy
- Smoking

Statistical analysis
The statistical Analysis was done on SPSS version 21.0.The values were represented in Mn ±SD and N (%). The paired 't' test was used to test the significance of variable from baseline (here day 1) and change was compared by unpaired 't' test at different time intervals. $p<0.005$ was taken and was statistically significant.

Results
Table No. 1 Age wise Distribution of Patients in the Study

Age Interval	N	%
22 - 40	07	36.84
41 - 60	09	47.37
< 60	03	15.79
Total	**19**	**100.00**

Mean±SD of Age = 46.39±14.98
Range = 22 – 65 years

Table no.2 The distribution of patients and Implant in control and study groups

	Control Group			Study Group		
S. No.	*No. Of Implant per patient*	*No.Of patient*	*Total No.Of Implant*	*No. Of Implant per patient*	*No.Of patient*	*Total No. Of Implant*
1	1	2	2	1	5	5
2	2	-	-	2	1	2
3	3	3	9	3	3	9
4	4	1	4	4	1	4
5	5	2	10	5	1	5
Total	-	8	25	-	11	25
	Male Patient=3 Female Patient=5			**Male Patient=4 Female Patient=7**		

Table No. 3 Comparison of ISQ at different follow ups in Control Group

Follow up (N=25)	Immediate Post operative	Month 1	Month 3	Month 6
Mn±SD of ISQ	76.84±6.15	75.45±5.22	75.06+4.91	74.82±4.30
Change of ISQ from Immediate Post Operative (Mn±SD)	-	-1.35±11.63	-1.74±1.14	-1.98+1.57
't'	-	4.14	7.63	6.31
'p'	-	p<0.001(Sig)	p<0.001(Sig)	p<0.001(Sig)
% change in ISQ	-	-1.76%	-2.26%	-2.58%

-ve Sign Showing decrease from Immediate Post operative

Table No. 4 Comparison of ISQ at different follow ups in study Group

Follow up (N=25)	Immediate Post operative	Month 1	Month 3	Month 6
Mn±SD of ISQ	77.94±4.26	79.45±4.32	79.10+5.12	78.94±4.32
Change of ISQ from Immediate Post Operative (Mn±SD)	-	+1.51±1.82	+1.16±1.12	+1.05+1.20
't'	-	4.15	5.18	4.38
'P'	-	p<0.001 (Sig)	p<0.001 (Sig)	p<0.001 (Sig)
% change in ISQ	-	1.94%	1.49%	1.35%

+ve Sign Showing increase from Immediate Post operative

Table No. 5 Comparison of Change in ISQ from Immediate Post Operative at different Follow ups in Control and Study Groups

	Control Group		Study Group				
Follow up	ISQ Change Mn±SD	% Change in ISQ	ISQ Change Mn±SD	% Change in ISQ	't'	'p'	Sig
Month 1	-1.35±1.63	-1.76	+1.51±1.82	+1.94	5.86	p<0.001	Sig
Month 3	-1.74±1.14	-2.26	+1.16±1.12	+1.49	6.90	p<.001	Sig
Month 6	-1.98±1.57	-2.58	+1.05±1.20	+1.35	6.76	p<.001	Sig

-ve Sign Showing reduction and + Sign showing increase

Table No. 6 Comparison of Bone density at different Follow ups in Control group

Follow up (N=25)	Immediate Post operative	Month 1	Month 3	Month 6
Mn±SD of Bone density	1509.2±24.6	1591.8±36.1	1704.9+42.3	1767.3±46.8
Change in bone density from Post Operative (Mn±SD)	-	82.6±15.6	195.7±28.10	258.1+32.9
't'	-	26.99	34.82	39.22
'P'	-	p<0.001 (Sig)	p<0.001 (Sig)	p<0.001 (Sig)
% change in bone density	-	5.47%	12.97%	17.01%

Table No. 7 Comparison of Bone density at different Follow ups in study group

Follow up (N=25)	Immediate Post operative	Month 1	Month 3	Month 6
Mn±SD of Bone density	1512.0±137.14	1639.5±102.93	1822.92+92.41	1924.25±82.73
Change in bone density from Post Operative (Mn±SD)	-	127.5±21.4	310.95±36.9	412.25+46.7
't'	-	29.8	42.13	43.92
'P'	-	p<0.001 (Sig)	p<0.001 (Sig)	p<0.001 (Sig)
% change in bone density	-	8.43%	20.57%	27.26%

Table No. 8 Comparison of Change in Bone density from Immediate Post Operative at different follow ups in Control and study Groups

	Control Group		Study Group				
Follow up	Bone density Change Mn±SD	% Change in Bone density	Bone density Change Mn±SD	% Change in Bone density	't'	'p'	Sig
Month 1	82.6±15.6	5.47%	127.5±21.4	8.43	8.21	p<0.001	Sig
Month 3	195.7±28.10	12.97%	310.95±36.9	20.57	12.44	p<.001	Sig
Month 6	258.1±32.9	17.01%	412.25±46.7	27.26	13.49	p<.001	Sig

Table No. 9 Comparison of Complication in Control and Study groups

S.No.	Complication	Control group (N=25)		Study group (N=25)		'p'	Sig.
		N	%	N	%		
1	Pain	3	12	1	4	0.61	NS
2	Swelling	4	16	1	4	0.35	NS
3.	Tenderness	2	8	-	-	0.49	NS
4.	Infection	1	4	-	-	P=1	NS
5.	Discomfort	2	8	1	4	P=1	NS
6.	Failure of Implant	-	-	-	-	-	-

In control group ISQ Mn±Sd was 76.84±6.15, 75.45±5.22, 75.06±4.91 and 74.84±4.30 at immediate post operative,1 month,3 month and 6 month which was significantly less from immediate post operative and % reduction was 1.76%, 2.26% and 2.58% at 1 month,3 month and 6 month.

In study group ISQ Mn±Sd of ISQ was 77.96±4.26, 79.45±4.32, 79.10±5.12 and 78.99±4.32 at immediate post operative,1 month,3 month and 6 month. Here % increase was1.94%, 1.49% and 1.35% at1 month,3 month and 6 month respectively.

In control group the bone density was 1509.2±24.6, 1591.8±36.1, 1704.9±42.3 and 1767.3±46.8 (Mn±SD) at immediate post operative, 1 month,3 month and 6 month respectively. % increase was 5.47%, 12.97%, 17.01% at 1 month,3 month and 6 month respectively.

In study group the bone density (Mn±SD) was 1512.0±137.14, 1639.5±102.93, 1822.95±92.41 and 1924.25±82.73 (Mn±SD) at immediate post operative, 1 month,3 month and 6 month respectively. % increase was 8.43%, 20.57%, 27.26% at 1 month, 3 month and 6 month respectively.

On Comparison of Complication in Control and study groups**.**

Pain: The incidence of Pain was more in control group than study group but difference was non significant (P=0.61).

Swelling: The incidence of Swelling was more in control group than study group but difference was nonsignificant (P=0.35).

Tenderness: Incidence was more in control group than study group. But difference was non significant (P=0.49).

Infection: Incidence was more in control group than study group. But difference was non significant (P=1).

Discomfort : Incidence was more in control group than study group. But difference was non significant (P=1).

Failure of implant : No failure of implant in both groups.

DISCUSSION:

There are very few studies that determine the effects of CGF with their potential role in implant dentistry. However CGF is now developing as a practical treatment option due to various reasons. First, it can be used alone or in combination with synthetic graft materials and facilitate osseointegration.[14,15] Second, it is easy to prepare, and is inexpensive.[16] The various inferences discussed in the included studies show a positive trend towards the usage of CGF in implant dentistry.

The study was conducted on 19 patients with mean age of 46.39 years with SD 14.98 year. The minimum age was 22 years and maximum age was 65 years. Majority patients were from the age group 41-60 years, as shown in table 1.

50 implants were taken in study, with 25 implants in each control and study group, in the total of 19 patients, as shown in table 2.

The variable ISQ was observed in the control and study group at different time intervals of, immediate postoperative,1 month,3 month and in 6 month, after the placement of Implants.

As given in table no. 3 There was significant reduction in ISQ at different follow ups and it was maximum at six month in the the control group. Similar findings were found In the study done by Monov G, Fuerst G et al. And Barewal RM, Oates TW et al. there was a meaningful reduction in ISQ values measured sometime after the placement of implants.[17-18]

In table no.4 in the study group There was significant increase in ISQ at different follow ups from immediate postoperative in study group and it was maximum at 1 month. In the study done by Pirpir C, Yilmaz O et al. Similar results were found that an increase in the ISQ values was seen in the experimental group.[19]

In table no.5 in the Comparison of Change in ISQ from Immediate PostOperative at different Follow ups in Control and study Groups, there was Significant increase in ISQ in study group at different follow ups from immediate post operative and in control group, there was Significant reduction in ISQ from immediate post operative at different follow ups.

Hence the study group was found more effective for implant stability than control group at different follow ups.

In the study done by Cagasan Pirpir, Onur Yilmaz et al. they came to a similar conclusion that In the implants in the study group, an increase of stability was observed. [19]

Our result was also found to be alike with Fischer's study in which ISQ measurement values were found to increase with healing time when measured at 3, 6, and 12 months postoperatively.[20]

This suggested that CGF administration improved the implant primary stability by accelerating the osseointegration process.

However,in a study done by Özveri Koyuncu B, İçpınar Çelik K et al. they did not report any significant benefits of CGF on improving Implant stability.[21]

In table no. 6 and 7 There was significant increase in bone density at different follow ups in both control group and study group. This increase was maximum at 6 month both in control group and study group. This result is Similar to the findings by Manoj S, Punit J et al. [22] and Shetty M, Kalra R et al.[23] in their study.

In table 8 the study group was found more effective than control group according to bone density. The study group showed better statistically significant bone density as compared to the control group which was credited to the faster bone formation with CGF similar observations has also been reported by Kim et al. in his study.[24]

The success of implant restorations is decided by the implant stability and absence of complications during the follow-up period. In table 9 the incidence of swelling, tenderness, infection, discomfort, was more in the control group than study group and was nonsignificant, however the incidence of pain had a difference of ns(p=0.61), with 100% survival rate. This result is Similar to the findings by Manoj S, Punit J et al. and Shetty M, Kalra R et al. in their prospective study.[22,23] In the retrospective study done by Chen Y, Cai Z, Zheng D et al. is with a very similar findings that all the implants were stable and also pain free with 100% survival rate over a period of around 20 weeks.[25]

CONCLUSION:

In this study CGF is significantly better in the regeneration of bone around the implants when compared with non CGF groups. CGF did attribute to be a much simpler and a better platelet concentrate, in promoting osseous regeneration. In our present study CGF also aided in increasing the density of the bone around the implant from baseline to a much higher level. This trait can also be used in cases where bone mineralization is compromised. However, the exact action of CGF on bone mineralization needs to be studied further.

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Conflicts of interest
There are no conflicts of interest.

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