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Efficacy of application of i-PRF to the surface of implants to improve osseointegration during the healing period: A split-mouth pilot study

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ABSTRACT

Aim Osseointegration time influences the overall time between Implant placement and delivery of the prosthesis. It is a complex process that is controlled by a number of inflammatory mediators and growth factors. i-PRF has the capability of providing a fibrin scaffold and also releasing essential growth factors such as PDGF and TGF which are responsible for bone remodeling. This study aimed to check whether the application of i-PRF (injectable-platelet rich fibrin) as a surface coating over the implant just before placement can aid in faster osseointegration.

Materials and methods This study was conducted at the Department of Oral Implantology at the Saveetha Dental College and Hospital in Chennai. The patient inclusion criteria were: age between 18-60 years, bilaterally missing posterior mandibular teeth and adequate bone for the placement of conventional implants. The total sample included 10 patients. This split-mouth trial included two groups: Group A (test), including sites in which Straumann SLA (Sandblasted Large grit Acid-etched) implants coated with i-PRF were placed, and Group B (controls), which included sites in which Straumann SLActive implants were placed. ISQ values were recorded using RFA smart pegs on the day of placement and follow-up at 1 week and 6 weeks. Statistical analysis was performed using the Wilcoxon Sign Rank Test to check for any significant difference between the two groups.

Results The results of this pilot study showed that the ISQ values that were recorded during the specific time periods were similar between the two groups and had no significant difference. At 6 weeks both groups achieved ideal stability for loading of implants. This is an indication that the coated implants were able to match the faster osseointegration time of the active implants.

Conclusion The results of this study show the scope of using i-PRF on the surface of implants to improve its stability and faster osseointegration. Further prospective clinical trials with a larger sample size should be done to confirm the role of i-PRF in the process of osseointegration.

INTRODUCTION

Successful osseointegration is the first step in long-term survival and stability of a dental implant (1). Advances in the field of oral implantology has been accompanied by the ever-growing demand for faster treatment times. Osseointegration time is a key factor that influences the overall time between implant placement and delivery of the prosthesis. Surface modifications by implant manufacturers are aimed at improving the bone-implant contact (BIC) and also decreasing the time required for complete osseointegration before the implant can be loaded (2). The entire osseointegration cascade is a complex process controlled by a number for inflammatory mediators and growth factors (3). Therefore, another technique for improving the BIC and reducing osseointegration time could be represented by the use of autologous blood derivatives that contain a rich supply of growth factors and bone-specific proteins. Platelet concentrations have been utilized in dentistry for over three decades. They are capable of releasing high doses of growth factors responsible for inducing tissue regeneration. Older generations of these autologous concentrates included PRP which lost its popularity due to concerns over the use of anticoagulants to prepare it (4). PRF is the second generation that is prepared without the use of anticoagulants (5). Autologous blood derivatives demonstrated the ability to release higher concentrations of various growth factors and induce higher fibroblast migration and expression of PDGF, TGF-β, and collagen 1 (6). A key feature is the formation of a fibrin clot that serves as a three-dimensional scaffold for tissue regeneration. Since PRF does not contain anticoagulants, it forms a fibrin clot within minutes after blood collection (7,8). An injectable formulation of PRF (i-PRF) was developed without the use of anticoagulants. It is obtained by centrifugation at lower speeds (700 rpm) for only 3 min and thus must be utilized within 15 min

prior to fibrin clot formation. i-PRF significantly increases human gingival fibroblast cell migration, proliferation, and spreading (7). Other advantages include faster tissue angiogenesis, which leads to faster wound healing (9). Implant manufacturers offering surface modifications claim to induce better BIC and faster osseointegration time, however, these features also significantly increase the cost of each implant. Beside surface modifications provided by the manufacturer, the use of i-PRF as a surface coating performed as a chairside procedure to coat the surface of the implant just prior to placement can be implemented to improve osseointegration. It could possibly serve as a simple, economical, and effective way of ensuring better implants success and quicker treatment time. The fact that it is in a liquid formulation, it can be evenly applied all over the implant surface.

The aim of the study was to compare the stability of active implants vs normal implants coated with i-PRF during their healing period to determine whether i-PRF has any role to play in osseointegration time. It was hypothesized that there would be no significant difference in the ISQ values between the two groups recorded at the specific intervals. The null hypothesis was that osseointegration time claimed by implant manufacturers of active implants would be faster than that of normal surface treated implants coated with i-PRF just before placement.

MATERIALS AND METHODS

This study was conducted in the Department of Oral Implantology, Saveetha Dental College and Hospital, Chennai from September 2020 to February 2021. Ethical clearance for this study was obtained from the institutional review board. The patients included in the study were those who ere referred to the department for implant rehabilitation of mandibular posterior teeth. Patients were examined clinically, and the residual bone was evaluated using a CBCT. Blood examinations were also obtained to make sure the individuals were ideal candidates. Patients below the age of 18 years, with systemic conditions and/or active infections were excluded from the study. The patients selected had adequate bone available for conventional implant placement without the requirement for any grafting. A total of 10 patients fulfilling the inclusion criteria were recruited and the details of the study were clearly informed and their consent to participate in the study was obtained. There were no dropouts. Straumann Roxolid Implants were used. The allocation of the sites was randomized using a computer-generated list. In one site (Group A: Control) Straumann Roxolid BLT SLActive implants were placed and in the other site (Group B: Test) Straumann Roxolid BLT SLA implants were coated with i-PRF and placed.

The osteotomy sites were prepared using standard sequential drilling protocol for the full sequence. Just

FIG.1 i-PRF.

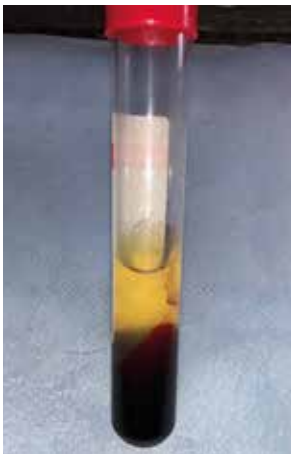
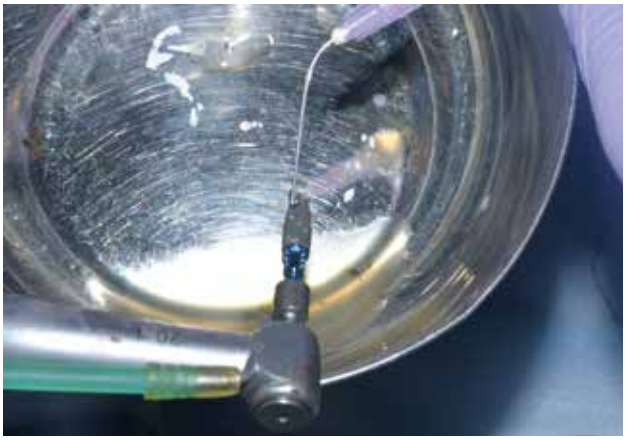


FIG.2 Coating of i-PRF on the implant surface.



before implant placement, the i-PRF was produced by obtaining 10 ml of the patient's blood in a plain glass test tube and immediately centrifuging it at 800RPM for 3 mins (Fig. 1). After 3 mins the straw-coloured liquid present at the top was extracted in a syringe and applied slowly over the implant surface taking care to make sure that it is evenly coated the entire surface of the implant (Fig. 2). The implants were placed equicrestally. The stability was measured using an Ostell device which measured the Resonance Frequency Analysis using smart pegs (Fig. 3). Stability was measured in the unit of ISQ (Implant Stability Quotient) values which range from 1 to 100 (Fig. 4). Readings were taken on day 0, 1 week, and 6 weeks. The follow-up readings at 1 week were done to observe the change in primary stability during the healing period. For the control group implants (SLActive) the manufacturer claims that the implants can be loaded at 6 weeks. Therefore the reading taken at 6 weeks was done to compare the ISQ values at the time of proposed loading of the implant. Healing abutments were placed on the implant before suturing. Standard post-operative instructions were given to all patients and they were medicated with analgesic (T. Zerodol SP BD for 5 days) and antibiotics (T. Augmentin 625 mg BD for 5 days).

Statistical analysis

Data were tabulated and results were analyzed using IBM SPSS Statistics Software Version .25. Wilcoxon Signed

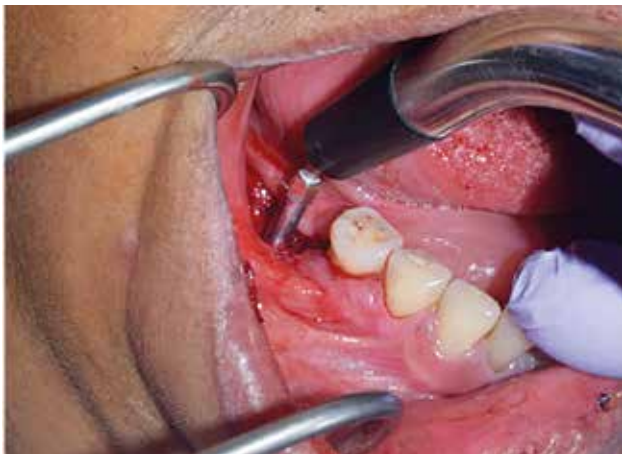


FIG. 3 ISQ readings recorded using RFA.

FIG. 4 ISQ values shown on the physio dispenser.

Rank test was used to assess the statistical difference between the values of the two groups at different time intervals (day 0, 1 week and 6 weeks). P-value less than 0.05 was considered to be statistically significant.

RESULTS

The values of the RFA test were recorded, tabulated, and compared between the groups on the day of surgery and at the respective follow-up intervals. The ISQ values indicating the initial primary stability of the implants showed that none of them had poor/compromised primary stability. Similar primary stability values were recorded in both groups for each patient. All the implants placed in this study in both groups recorded ISQ values greater than 60 (Table 1).

As seen in Table 1, a characteristic drop in the primary

S.NO	AGE	GENDER	IMPLANT SITE	PRIMARY STABILITY	ISQ DAY0	ISQ 1 WEEK	ISQ 6 WEEK
1	34	Male	C-46	45Ncm	75	70	72
			T-36	45Ncm	74	73	76
2	42	Female	C-45	35Ncm	69	60	73
			T-36	35Ncm	71	62	74
3	28	Female	C-36	30Ncm	69	63	74
			T-47	35Ncm	71	62	72
4	51	Female	C-45	35Ncm	76	67	75
			T-36	35Ncm	71	66	74
5	61	Female	C -36	30Ncm	63	58	70
			T-46	30Ncm	65	61	71
6	23	Male	C-47	35Ncm	72	68	73
			T-46	30Ncm	69	67	74
7	37	Female	C-36	40Ncm	73	65	75
			T-46	35Ncm	74	63	73
8	41	Male	C-35	30Ncm	68	66	71
			T-47	45Ncm	70	65	72
9	52	Male	C-36	45Ncm	75	69	72
			T-46	45Ncm	76	69	73
10	28	Female	C-36	35Ncm	72	68	70
			T-46	35Ncm	71	66	70

TABLE 1 Stability quotient (ISQ) recorded at Day 0, 1 week and 6 weeks.

INTERVAL		MEAN +/- STANDARD DEVIATION
DAY-0	TEST	71.2 +/- 3.04
	CONTROL	71.3 +/- 4.02
DAY-7	TEST	65.4 +/- 3.68
	CONTROL	65.4 +/- 3.94
DAY-42	TEST	72.9 +/- 1.72
	CONTROL	72.5 +/- 1.84

TABLE 2 Shows the mean and standard deviation values of the samples in each group at specific time intervals.

STATISTICAL ANALYSIS-WILCOXON SIGNED-RANK TEST	
INTERVALS	P-VALUE
Median of differences between Control Day0 and Test Day0	0.718
Median of differences between Control Day7 and Test Day7	0.952
Median of differences between Control Day42 and Test Day42	0.624

TABLE 3 Shows the statistical values of the Wilcoxon signed-rank test which indicates no significant difference between any of the groups.

stability was seen in the values of both the groups recorded at 1 week. At 6 weeks the values of the control group showed ISQ values greater than 70. It was interesting to observe that the 6-week values of the test group were also above 70 and similar to those of the control group. In some patients, the values of the test group were a few points higher than that of the control group. Although not significantly higher to base any interpretation, it is still worthy of note. The healing of the soft tissue around the implant site also was good and uneventful in all sites.

The mean ISQ values for both groups at day 0, 1 week, and 6 weeks post-implant placement are shown in Table 2. When comparing the ISQ values between the two groups, the statistical test showed no significant difference amongst the ISQ values recorded at day 0 ($p=0.718$). The ISQ values recorded at the follow-up intervals between the two groups showed no significant difference, i.e. at 1 week ($p=0.952$) and at 6 weeks($p=0.624$).

DISCUSSION

In our study, the Ostell RFA setup was chosen to determine the stability of the implants during the healing period because it was felt that this was the most accurate and least invasive method. This system acts as a measure of implant-bone connection rigidity (10).

The results of our study showed that the values during the healing period and at 6 weeks were similar to those of the control group which indicates that the addition of i-PRF as a surface coating benefits in the quicker osseointegration of implants. The rationale of using Straumann SLActive implants as the control group was based on the fact that these active implants have the special surface treatment and are known to osseointegrate in 6 weeks, so they permit loading of the implants in 6 weeks instead of the conventional 3-month period. The goal in the development of SLActive implants was to achieve secondary stability at a faster rate by accelerating the osseointegration process (11). Its super hydrophilicity and its chemically improved surface have the potential to achieve secondary stability sooner than conventional implants.

The osseointegration of an implant is dependent on two main factors: primary stability and, more importantly in our study, secondary stability. Time taken in achieving secondary stability is what dictates how soon a patient can get his implant rehabilitated. Unlike the primary stability which can be controlled, the clinician has no control over the secondary stability. It is entirely under the control of the body response of the individual that is receiving the implant. It is a complex biological healing process and includes a number of variables. Those variables include the systemic health of the individual as well as the surface design of the implant (12,13). In our study, in order to make sure there was no compromise in terms of systemic conditions or active infections, a blood test was obtained prior to surgery to make sure the patients were systemically healthy. In order to minimize bias, Straumann's Roxolid SLA surface was chosen because the company provides implants with both the normal SLA surface and the active SLActive surface.

SLActive surfaces are known for their super hydrophilicity (14). The surface has reduced atmospheric contamination and higher surface free energy which is a result of chemically activating the surface by rinsing under nitrogen and storing immersed in saline which produces a water contact angle of 0 degrees (15). Due to this increased hydrophilicity and surface free energy, its surface enhances osteoblast attraction and protein interactions. Also, there is higher adsorption of fibronectin compared to other surface types (16). In a study by Buser et al. bone apposition resulted to be significantly enhanced in the early stages of osseointegration of SLActive implants, that is 60% more bone after 2 weeks when compared to SLA implants, thereby showing the earlier formation of the more mature bone (17).

Comparative studies which examined the stability of SLA vs SLActive implants using RFA show significant improvement in the stability pattern with SLActive implants (18,19). In one such study the characteristic drop in primary stability was described and the subsequent increase that occurs during the osseointegration period as 'the break point'. This break point occurred after 2 weeks in SLActive implants, whereas for SLA implants

it occurred at 4 weeks (20). Therefore the fact that the results of this study showed similar ISQ values in both groups during the healing period is indicative that the addition of i-PRF as a surface coating does have some effect in producing faster osseointegration. There was no statistical significance in the ISQ values recorded at the specific intervals. This fact indicates that SLA implants coated with i-PRF osseointegrated at the same rate as the SLActive implants.

The development of i-PRF was based on the need for a liquid consistency of PRF which is known to have high concentrations of autologous growth factors (21). The old generation of blood derivative in a liquid consistency was PRP which had a high concentration of autologous growth factors but was not widely accepted because of concerns regarding the use of anticoagulants in its production (22). Recently i-PRF was introduced which was based on the principle that low-speed centrifugation of blood shows a higher number of cells including leukocytes. Higher centrifugation speeds cause a shift in the cells to the bottom of the tube. Reducing the centrifugation g-force would cause the concentration of leukocytes to remain in the top layer which is collected. (23) Leukocytes are immune cells that play a role during the wound healing process They mediate tissue regeneration by directing and recruiting various cell types required for wound healing (24). This low-speed centrifugation concept shows an increase in growth factor release from PRF clots. The release of growth factors has a direct influence on tissue regeneration by increasing the migration and proliferation of fibroblasts and collagen mRNA levels. Therefore if this mechanism can cause a faster wound healing process, then the addition of i-PRF on the implant surface should make osseointegration faster.

Previous studies have used PRF in adjunct to implant placement to improve osseointegration and have shown a positive effect (25,26). In our study the rationale behind the use of i-PRF was to make use of its liquid consistency which we believe is the only way to ensure that this autologous blood concentrate can be evenly distributed over the entire implant surface.

To the best of our knowledge, this is the first study that used i-PRF in this way and compared it to a commercially available implant that has the potential of faster osseointegration. The preparation of i-PRF can be done chairside by the clinician himself. It requires a very low cost of setup and it can be produced at any time with ease in a few minutes. Therefore the fact that it is extremely easy to produce and at the same time shows good results in making the process of osseointegration faster indicates that it can be used on a routine basis on any implant surface as a more economical alternative to the more expensive options that are commercially available.

As this is a pilot study with small sample size, further trials on human and animal models with larger sample sizes must be performed to confirm the present findings.

CONCLUSION

Within the limitations of this study, it can be concluded that the addition of i-PRF as a surface coating on the implant can improve osseointegration rate during the healing period. Therefore this can be used as a cost-effective alternative to active implants. Application of i-PRF on implants especially before placement in sites that are compromised or with poor quality bone can improve the success of the implant treatment.

Conflict of Interest notification

There is no conflict of interest

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