Comparison of superoxide dismutase levels among patients with diverse surface treated dental implants: a prospective clinical study

Abstract

Background
Implants have evolved in terms of shape, size, and surface in order to optimize the success rate. Exploring the antioxidant levels around different surface treated dental implants is essential to improve the performance of implants. The present study was to detect and measure the level of superoxide dismutase (SOD), which is an antioxidant enzyme among patients with sandblasted acid-etched and anodized surface dental implants.

Materials and Methods
In this prospective clinical study, 78 patients who had undergone implant placement for missing single posterior tooth in mandible using sandblasted acid-etched and anodized surface dental implants during August 2019 - December 2019 were enrolled and were categorized into Group 1: SLA (n=27), Group 2: SLActive (n=26), Group 3: TiUnite (n=25) based on the surface modification of the implants. Peri-implant crevicular fluid (PICF) was collected and SOD was quantified using ELISA kit at 3 months and 1 year. One-way ANOVA followed by Tukey's HSD post hoc was done for statistical analysis. For intragroup comparison, paired t test was used.

Results
SOD level in group 3 implants was significantly lower than group 1 and group 2 ($p \leq 0.05$). On pairwise comparison between the groups, there was a statistically significant difference both at baseline ($p \leq 0.05$) and 1-year follow up ($p \leq 0.05$). Intragroup comparison revealed a statistically significant difference from baseline in all the three groups ($p \leq 0.05$).

Conclusion
Superoxide dismutase level in peri-implant crevicular fluid was low around TiUnite dental implant as compared to SLA and SLActive implants.

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Keywords

Acid-etched, Anodization, Dental implant, Oxidative stress, Sandblasting, Superoxide dismutase.

INTRODUCTION

Dental implants have gained paramount importance for replacement of missing teeth. In spite of its success rate, few individuals experience implant failure due to failure in osseointegration causing peri-implant disease(1). Peri-implant disease comprises of peri-implant mucositis and peri-implantitis. Peri-implant mucositis affects the soft tissues around the implant without involving the bone. Whereas, involvement of bone is noted in peri-implantitis(2). To minimize the occurrence of peri-implant disease, implants have evolved in terms of shape, size, and surface in order to optimize implant success and longevity.

Numerous surface modifications of implants are carried out to enhance the success of dental implants. Acid treatments, sandblasting, or various oxidization mechanisms are used as the principal methods of surface modification for implants. Sandblasted-acid etched (SLA) implant surfaces are produced by sandblasting with coarse grit particles to change the implant's macrostructure and then etching the surface with an acid to induce micro-irregularities (3). The implants are also hydroxylated, cleansed under nitrogen protection, and kept in an isotonic saline solution until they are used. This process creates a surface termed SLActive, an upgrade over SLA surface that has higher wettability(4). Another surface modification technique is anodization, which thickens the titanium dioxide layer by electrochemically altering the titanium implant surface(5).

The surface treatment of dental implants increases the roughness, which in turn help with osseointegration. However, such changes in surface topography also have a small but indirect impact on microbial adhesion. Research evidence suggests that bacterial plaque is the etiology of peri-implantitis similar to periodontitis. Although the bacterial plaque causes initiation of peri-implantis, the host-bacterial interaction contribute to the progression of the disease around implants(6). Following this, various pro-inflammatory mediators are generated which attracts the neutrophils to the infection site. Neutrophils and other inflammatory cells produce reactive oxygen species as a result of a respiratory burst in response to this bacterial insult. Reactive oxygen species are highly toxic to the microbes; however, they can also initiate tissue damage. This tips the oxidant-antioxidant balance, resulting in oxidative stress(7).

Antioxidants are compounds that will considerably slow down or prevent oxidation of a substrate when present in low quantities compared to that of the substrate. They protect the host either by preventing the formation of reactive oxygen species or by scavenging the reactive metabolites and converting the reactive molecules into less reactive(8).

Superoxide dismutase (SOD) is an enzyme that combat the oxygen radical superoxide that is generated during inflammation. It defends the cell against reactive oxygen species' harmful effects(9). There are studies about the relation between SOD and inflammation in the oral cavity. Chapple IL et al., reported that low total antioxidant status was observed among patients with periodontal diseases (10). Sculley DV et al., examined the salivary and gingival tissue antioxidant status in periodontal diseases and found a decrease in antioxidant profile and increase in oxidative stress(11). Similarly, low total antioxidant status was observed in peri-implant disease conditions(12). And the SOD level was markedly low during inflammatory in oral cavity(13).

Although the role of antioxidants in peri-implant disease conditions has been studied (12, 14), there is a lacunae about the influence of different surface treatments of dental implants on antioxidants in peri-implant sulcus. In this context, this study was done to detect and measure the level of SOD among patients with sandblasted acid-etched (SLA, SLActive) and anodized (TiUnite) dental implants.

MATERIALS AND METHODS

Study population

In this prospective clinical study, all patients of 25-60 years who had undergone implant placement for missing single posterior tooth in mandible using sandblasted acid-etched and anodized surface dental implants during August 2019 - December 2019 in Department of Periodontics and Implantology, Saveetha Dental College and Hospitals Chennai, India were enrolled according to strict inclusion and exclusion criteria and were categorized based on the surface modification of the dental implants.

The study followed STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines and was conducted based on Helsinki Declaration of 1975, as revised in 2013. Each participant signed a consent form acknowledging their voluntary participation in the study and the protocol was reviewed and approved by the Institutional Ethical Committee. Sample size was calculated using mean and standard deviation values from a previous study (15) using G*Power Software, Version 3.0. An α of 0.05 and a power of 80% were selected. The target sample size was 70 implants.

Inclusion criteria

1. Subjects with implant placement for missing single posterior tooth (first or second molar) in mandible
2. Subjects of age between 25 and 60 years
3. Subjects with opposing natural tooth
4. Subjects with good systemic health

5. Periodontally healthy subjects
6. Subjects with implant placement done in minimum 6 months healed extraction sockets
7. Subjects with implant placement done with sufficient bone volume observed in cone-beam computed tomography
8. Subjects with implant placement done with the insertion torque of between 35 and 45 Ncm
9. Implants placed subcrestally, verified by digital periapical radiograph
10. Presence of keratinized mucosa width of ⩾2 mm around the implant
11. Subjects with plaque index (PI) score of 0.1-0.9 (Silness and Loe 1964) and gingival index (GI) score of 0.1-1 (Loe and Silness 1963)

Exclusion criteria

1. Subjects with immunocompromised conditions
2. Subjects who had undergone chemotherapy or radiotherapy
3. Subjects with underlying systemic illness
4. Pregnant or lactating women
5. Smokers
6. Poor oral hygiene and motivation
7. Periodontitis patients
8. Subjects with parafunctional habits
9. Subjects with bone metabolic diseases and under treatment with intravenous amino-bisphosphonates
10. Subjects under long term medications
11. Subjects with major bone grafting procedures at implant placement
12. Active inflammation or pathologies adjacent to implant
13. History of extraction due to any cysts, granulomas or tumors

Seventy-eight subjects with 78 implants fulfilled the study criteria and were divided into three groups, Group 1: SLA (SLA®, Straumann, Basel, Switzerland; n=27), Group 2: SLActive (SLActive®, Straumann, Basel, Switzerland; n=26), Group 3: TiUnite (TiUnite®, Nobel Biocare, Gothenburg, Sweden; n=25) based on the surface modification of the dental implants. All were internal-hex varying platform root analog bone level implants.

Surgical procedure

Surgical and restorative procedures in three groups were performed by experienced surgeons of the same institution. After raising mucoperiosteal flaps through a crestal incision, sequential bone drills were used to prepare the osteotomy. The osteotomy was then assessed using 2 mm diameter paralleling pin and digital periapical radiograph. All were bone level implants placed 0.5 mm subcrestally, verified by digital periapical radiograph. Titanium-healing abutments were installed. Table 1 depicts the implants used in each group. The flap was sutured with 4-0 non-absorbable polypropylene monofilament (Orilene®; Orion Sutures Pvt Ltd., Bangalore, India). Patients were prescribed with antibiotics (Amoxicillin 500 mg thrice daily for three days) and analgesics (Zerodol-SP twice daily for two days).

Patients were reinforced with plaque control measures which includes brushing using soft toothbrush and also chlorhexidine gel (Hexigel®, ICPA Health Products Ltd., GIDC, Ankleshwar, India) was prescribed to be used for 1 week after the surgery. After 1 week, sutures were removed and routine oral hygiene instructions were given. All the implants were allowed to heal for 3 months without loading. During stage 2 uncovery procedure, the peri-implant health and osseointegration were evaluated. During this time (3 months), peri-implant crevicular fluid (PICF) (baseline) was collected to assess the SOD levels. All the patients were given final cement retained implant-supported porcelain-fused-to-metal prosthetic restoration. Patients were on maintenance visits every 3 months and oral hygiene instructions were reinforced. After the completion of the restorative phase (1 year from implant placement), all patients were re-examined and PICF was collected.

Sample collection

Each selected implant site was isolated with sterile cotton, after the supragingival plaque was removed using sterile curettes. Using a 1-5 µL calibrated microcapillary pipette (Sigma-Aldrich®, Missouri, USA), peri-implant crevicular fluid (PICF) was collected. The obtained samples were kept in storage at -20°C for subsequent SOD analysis using ELISA kit. Sample collection was done by a single examiner (AR).

Analysis of Superoxide Dismutase

Human Superoxide Dismutase (SOD) ELISA kit (Elabscience®, USA) was used based on manufacturer's instructions to determine the levels of superoxide dismutase (SOD). The results of were represented as pg/mL. The threshold for SOD detection with this kit was set to be 37.5 pg/mL.

Statistical Analysis

Statistical Package for Social Sciences (SPSS Software, Version 23.0; IBM Corp., Armonk, NY, USA) was utilized to analyse the data. The Kolmogorov-Smirnov test and the Shapiro-Wilk test results followed a parametric distribution. One way ANOVA (analysis of variance) was used to compare mean age, PI, GI and SOD level between the three groups. Gender distribution was assessed using Chi-square test. For pairwise comparison, Tukey's HSD post hoc test was performed. For intragroup comparison, paired t test

Implant Dimension	Group 1 (n)	Group 2 (n)	Group 3 (n)	Total (n)
4.1 * 10	18	17		35
4.1 * 12	6	5		11
4.8 * 10	3	4		7
4.3 * 10			12	12
4.3 * 11.5			9	9
5 * 10			4	4
Total (n)	27	26	25	78

Tab. 1 Implants included in the study.

	Group 1 (n=27)	Group 2 (n=26)	Group 3 (n=25)	p value
Age (years)	42.16±10.67	42.12±9.51	40.56±9.30	0.807
Gender (M/F)	14/13	12/14	12/13	0.808
PI	0.59±0.04	0.60±0.03	0.61±0.04	0.864
GI	0.58±0.03	0.56±0.04	0.58±0.02	0.943

Tab. 2 Demographic data of the study population.

Type of implants	Baseline (3 months)	1 year
Group 1	Mean±SD: 216.32±2.40	Mean±SD: 196.75±1.48
Group 2	Mean±SD: 240.67±7.09	Mean±SD: 214.49±3.86
Group 3	Mean±SD: 204.73±1.96	Mean±SD: 180.05±1.53
ANOVA Test	p = 0.000*	p = 0.000*
Tukey's HSD post hoc test	Group 1 vs Group 2 Mean Difference: -24.348 p = 0.000*	Group 1 vs Group 2 Mean Difference: -17.744 p = 0.000*
	Group 1 vs Group 3 Mean Difference: 11.591 p = 0.000*	Group 1 vs Group 3 Mean Difference: 16.692 p = 0.000*
	Group 2 vs Group 3 Mean Difference: 35.938 p = 0.000*	Group 2 vs Group 3 Mean Difference: 34.436 p = 0.000*

**Statistically significant*

Tab. 3 Comparison of SOD levels between three types of implants at different time periods.

Type of implants	Baseline SOD – 1 year SOD	
	t	p value
Group 1	31.101	0.000*
Group 2	15.588	0.000*
Group 3	54.677	0.000*

**Statistically significant*

Tab. 4 Intragroup comparison of SOD levels (Paired t test).

was used. A statistically significant result was defined as p value less than 0.05.

RESULTS

Table 2 summarizes the demographic characteristics of the study groups. There was a statistical insignificance between the three study groups in relation to age (p = 0.807), gender (p = 0.808), PI (p = 0.864) and GI (p = 0.943). At baseline, the SOD levels in group 3 implants was significantly lower than groups 1 and 2 (204.73±1.96 pg/mL vs. 216.32±2.40 pg/mL and 240.67±7.09 pg/mL, respectively; p = 0.000). Also at 1 year, it was group 3 implants those with significantly lower SOD when compared with groups 1 and 2 (180.05±1.53 pg/mL vs. 196.75±1.48 pg/mL and 214.49±3.86 pg/mL, respectively; p = 0.000).

Additionally, on pairwise comparison, there was a statistically significant difference between group 1 and group 2 (p=0.000), group 1 and group 3 (p=0.000), group 2 and group 3 (p=0.000) at baseline and 1-year follow up (Table 3). Table 4 depicts the intragroup comparison of SOD. There was a statistically significant difference from baseline in all the three groups (p=0.000).

DISCUSSION

SLA, SLActive and TiUnite are the three dental implants that are frequently used in clinical settings. Each surface treatment, alters the physical and chemical make-up of implant. It's reasonable that the topographical disparities between different implant surfaces will affect the microbial profile (16,17). It is believed that the microorganisms causing peri-implantitis are comparable to periodontitis. It is well documented that gram negative organisms are more prevalent in periodontal and peri-implant diseases (18,19).

Bacterial endotoxins trigger a cascade of pro-inflammatory mediators (20). On titanium surfaces with various topographies, distinct immune environments made up of various inflammatory mediators can still be identified in such an inflammatory environment. By modifying the cell adhesion pattern, the different surface features of biomaterials such as texture, roughness and wettability, can affect the redox balance resulting in increase in reactive oxygen species and reduction in antioxidants (21). This might cause deleterious effect on osseointegration of the dental implants (22). Consequently, exploring the antioxidant profile around different surface treated dental implants is essential to improve the performance of implants. Eventhough each dental implant has unique surface property, it is unclear which implant surface maintains homeostatic balance with respect to oxidant-antioxidant system. This is the first study of its kind to assess the antioxidant enzyme, SOD by ELISA among SLA, SLActive and TiUnite dental implants.

In literature, the levels of SOD were assessed in periodontitis and peri-implantitis. Kim SC et al., compared the total antioxidant profile and superoxide dismutase level in periodontally diseased patients and periodontally healthy individuals and observed that both the total antioxidant and superoxide dismutase levels were markedly low among periodontally diseased patients (13). In addition, the systemic antioxidants were also found to be low among chronic periodontitis patients (23). Furthermore, total antioxidant profile and levels of superoxide dismutase in blood, gingival crevicular fluid and saliva were observed to be low in periodontitis patients (24). Similarly, when the total antioxidant profile, ascorbate and uric acid levels were studied in peri-implant health and disease, the results revealed that all the biochemical parameters were low in disease than in health (12).

The present study revealed that SOD level was significantly low around TiUnite dental implants followed by SLA and SLActive implants. This difference could be attributed due to the surface properties of the implants. Sand blasted and acid-etched surfaces presented with irregularities with more surface area, whereas, anodized surfaces presented with more pores with raised margins (25). In addition, the existence of grooves and pits in TiUnite's surface might prevent the bacteria from shear forces and facilitate strong adhesion (26). When TiUnite and SLA surfaces were compared in terms of disease progression, implants with TiUnite surface showed a greater disease progression and pronounced bone loss than implants with SLA surface. Also, TiUnite surface demonstrated a less favorable treatment outcome than implants with SLA surface (27). Furthermore, histological analysis on assessment of bone to implant contact has revealed that the contact percentage was higher around SLA than TiUnite surface, suggesting that the rate of osseointegration was higher around SLA (28). Therefore, TiUnite surface might be an conducive environment for bacterial adhesion, which might cause an alteration in redox potential, resulting in low SOD levels.

The present study data showed that the SLActive surface demonstrated higher SOD levels. Surface analysis have demonstrated that SLActive surface have increased hydrophilicity, which inhibits adhesion of hydrophobic bacteria on the implant surface. Furthermore, it was reported that the hydrophilic substrates displayed significant reductions in the extent of bacterial adhesion (29). This surface property helps in minimizing the adherence of pathogenic microorganisms onto the SLActive surface, thereby least likely alters the redox potential.

In this study, dissimilarities in the SOD levels were evident between the studied three implant surfaces, since lower level was observed in TiUnite implant surface. Our research also showed that SOD level around the SLActive surface appeared to be comparatively high. Based on the observations, it was evident that there was an alteration in redox balance around dental implants with different surface treatments.

Collectively, these findings support the notion that the redox balance is significantly influenced by the surface treatments applied to dental implants. The potential cause for the difference in SOD levels between various implant systems is surface characteristics that may affect bacterial adherence resulting in homeostatic imbalance. Eventhough the difference in antioxidant enzyme level is being negligible, it might affect the osseointegration thereby hamper the long-term success of the dental implants. Further studies are warranted to assess the influence of structural characteristics of dental implants on the microbiological and immunological pathways to substantiate these findings.

In summary, implants with different surface treatments might affect the redox balance, leading to reduction in antioxidant enzyme levels. Quantification of these markers periodically might help in predicting peri-implant risk, which in turn helps to initiate early

therapeutic intervention.

CONCLUSION

Superoxide dismutase level in peri-implant crevicular fluid was low around TiUnite dental implant as compared to SLA and SLActive implants.

Contribution statement

Both authors have made substantial contributions to conception and design of the study. AR has been involved in data collection, data analysis. AR and SSV have been involved in data interpretation, drafting the manuscript and revising it critically and have given final approval of the version to be published.

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