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Comparison of implant-supported rehabilitation in smokers and non-smokers with conventional and short tuberosity implants: an evaluation of prosthetic, peri-implant, and cytokine profiles

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Abstract. – OBJECTIVE: This study aimed to assess periodontal parameters, radiographic (CBL), and prosthetic parameters along with levels of matrix metalloproteinase-9 (MMP-9) and interleukin-1β (IL-1β) in smokers undergoing rehabilitation using conventional implants and short tuberosity implants (STIs).

SUBJECTS AND METHODS: The duration of the study was six months. A structured questionnaire was made to be filled out by all participants. The participants were included in the study based on predefined inclusion and exclusion criteria for smokers and non-smokers with STIs. Peri-implant parameters were assessed based on peri-implant plaque index (PIPI), bleeding on probing (BoP), and peri-implant periodontal depth (PIPD) ≥4 mm. Collection of peri-implant crevicular fluid (PICF) and measurement of MMP-9 and IL-1β was performed using ELISA. Data related to peri-implant clinical and radiographic parameters were reported in mean and percentages. Pearson Chi-square test was employed for categorical data sets, whereas the Kruskal-Wallis test was used for the comparison of means between groups. Bonferroni post hoc adjustment test was applied for multiple comparisons. Differences were found to be significant $p<0.01$

RESULTS: Among the four groups, one hundred participants were included. The mean age of participants in groups 1 (44±4.5 yrs) and 3 (44±2.1 yrs) showed no significant difference from participants in groups 2 (42±3.8 yrs) and 4 (43±3.5 yrs). The duration of the smoking habit in cigarette smokers with STIs was 22.7±1.4 yrs, and cigarette smokers with conventional implants were 23.8±1.9 yrs with a daily frequency of 11.2±2.5 in group 1 and 11.33±2.1 in group 3. The means for PIPI and PIPD were found to be significantly worse in cigarette smokers with STIs (PIPI 62.4±5.9; PIPD 5.3±2.1) and conventional implants (PIPI 63.3±6.1; PIPD 5.5±1.9) compared to non-smokers with STIs (PIPI 29.2±3.6; PIPD 3.1±0.1) and conventional implants (PIPI 28.1±3.4; PIPD 3.2±0.3). BoP was significantly higher in non-smokers compared to smokers with STIs (smokers 24.2±8.3; non-smokers 36.5±21.2) and conventional implants (smokers 21.6±7.4; non-smokers 38.4±24.1) ($p<0.01$). The level of IL-1β (pg/ml) and the level of MMP-9 (ng/ml) were found to be significantly higher in cigarette smokers with STIs and conventional implants in comparison to non-smokers ($p<0.01$).

CONCLUSIONS: Periodontal (PIPI, PIPD, and BoP) along with radiographic (CBL) and prosthetic parameters were compromised in smokers compared to non-smokers. Patients with conventional implants and STI showed comparable clinical, radiographic, and prosthetic parameters among smokers. Utilization of dental services along with cessation programs should be encouraged for smokers.

Key Words:
Short tuberosity implant, Periodontal parameters, Smokers, Radiographic parameters, prosthetic parameters, Conventional implant.

Introduction

One of the leading risk factors for bone loss around natural teeth and dental implants is the habitual smoking of tobacco[1]. Current evidence highlights that smoking increases the production of advanced glycation end products (AGEs) in the gingival tissues and fibroblasts in the periodontium. AGEs interact with their receptors RAGE, along with the expression of reactive oxygen spe-

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cies (ROS), resulting in oxidative bursts within the periodontium[2,3]. This indirectly alters the function of leukocytes and a hike in pro-inflammatory cytokines in the gingival crevicular fluid (GCF) of smokers[4]. Implant failure in smokers is 9 times higher than in non-smokers as smokers are associated with poor quality of bone, delayed healing, and reduced bone height with a higher incidence of peri-implantitis. All factors compromising implant osseointegration and survival[5,6].

Apart from the cellular changes in the periodontium, the quality and quantity of bone in habitual smokers are compromised posteriorly in the maxilla[7,8]. This is due to the structure of cortical plates with low-density trabeculae bone along with bone height due to maxillary sinus[7]. Therefore, the success rate of the implant in the maxilla is halved compared to the mandible, with the principal cause being primary instability[9,10]. For success and better prognosis of implant, treatment age is an important indicator. The quantity of bone is related to the width and length of the implant, whereas osseointegration is related to bone quality[11]. The factor of age is compromised in elderly patients with poor healing, increased cortical porosity, and compromised alveolar bone conditions[11,12]. Similarly, surgical approaches in the maxillary arch, including sinus lifting, have extended healing time and escalated the risk of complications and cost[13]. A recent study by Moy et al[14] claimed that advancing age compromises implant prognosis.

To overcome this problem short tuberosity implants (STIs) are considered over traditional implants in the posterior maxilla of patients who have compromised bone quantity[15]. STI is a contemporary approach that is less likely to damage vital structures and has clinical advantages over conventional implants, including an increased number of locations for implant treatment, reduced risk of surgical paraesthesia, less chance of alveolar bone overheating, easier removal in case of failure, and less risk of morbidity due to avoidance of lateral sinus augmentation[16-18]. From the patient's perspective, it has a low cost, less discomfort, and time reduction[19].

Recent work by Akram et al[20] showed that radiographic parameters i.e., crestal bone loss (CBL), and periodontal parameters i.e., bleeding on probing (BoP), peri-implant pocket depth (PIPD), and peri-implant plaque index (PIPI) are worse in smokers with conventional implants. Similarly, Daood et al[21], in their recent work, proclaimed high collagen breakdown in habitual smokers. To our knowledge from indexed literature, there are no studies to assess periodontal and radiographic parameters along with pro-inflammatory cytokines levels interleukin 1β, matrix metalloproteinase-9 (MMP-9) in peri-implant sulcular fluid (PICF) among participants with conventional and STI among smokers. It is hypothesized that the use of STIs will show better outcomes than conventional implants in smokers, in addition, a compromise in clinical and radiographic peri-implant parameters will be observed in STIs and regular implants. Therefore, the present study aimed to assess periodontal (PIPI, BoP, and PIPD) radiographic (CBL), and prosthetic parameters along with levels of MMP-9 and IL-1β in smokers undergoing rehabilitation using conventional implants and short tuberosity implants (STIs).

Subjects and Methods

Ethical Guidelines and Study Design

The present cross-sectional study was performed in line with the guiding principle of the Declaration of Helsinki involving human participants and adhered to STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines. The research ethics review committee of the specialist dental practice and research center (SDRC-019-21) in Riyadh, approved the study. The duration of the study was six months. The participants were asked to sign the consent form with the aims and objectives of the study. All participating subjects were allowed to leave the study for any reason.

Study Questionnaire

The subjects were enrolled at a private setup Center for specialist dental practice and clinical research in Riyadh, Saudi Arabia. All enrolled participants had no contributory medical conditions. A structured questionnaire evaluating, demographics (age, gender), duration of an implant in service, smoking and brushing habits and cause of missing teeth, family history of cigarette smoking, and frequency of cigarette smoking was completed by all participants under the supervision of a clinician.

Inclusion and Exclusion Criteria

The participants were included in the study based on the following inclusion criteria. Physical and systemically healthy cigarette smokers >10

cigarettes per day, for the last 5 years. Non-smokers did not smoke cigarettes in the last 5 years. Smokers and non-smokers have at least one STI (≤8 mm) in posterior maxillary tuberosity or one conventional implant in the premolar region. Patients were excluded from the study due to the following exclusion criteria: habitual consumers of alcohol and smokeless tobacco, having systemic conditions of HIV, hepatitis, heart failure, kidney disease, and diabetes. Edentulous patients who took non-steroidal anti-inflammatory drugs (NSAIDs) and antibiotics in the last six months. Patients with periodontal therapy in the 3 months, lactating females, and patients suffering from bruxism[22,23].

Peri-implant Assessment of Clinical and Radiographic Parameters

A trained examiner (H.T.), who was blinded to different study groups, did all the clinical examinations. The kappa score for intra-examiner reliability in the assessment of peri-implant probing depth (PIPD) was calculated to be 0.91. Measurements (PIPI, PIPD, and BoP) were taken from six sites. Implants were assessed (mesiobuccal, mid and distobuccal, mid palatal, mesio-palatal, and distal palatal) and were displayed as mean percentages per participant. PIPD ≥4 mm was measured to the nearest whole millimeter (mm) from the gingival margin to the most apical gingival tissue penetration of the periodontal probe tip (UNC-15, Hu-Friedy, Chicago, IL, USA), according to the consensus report of the seventh European workshop on periodontology-2011[24,25]. Periodontal and peri-implant scoring for plaque index PIPI and BoP were based upon dichotomous recording as present=1 and absent=0 and were displayed as mean percentages per participant.

Radiographic parameters i.e., CBL, were measured by an experienced clinician (T.A.), with a reliability score of kappa 0.80. A software program was used to assess the supra crestal part of the alveolar bone crest. Digital periapical radiographs (Ektaspeed plus; Kodak, Rochester, NY, USA) were assessed using a computer display to measure the peri-implant CBL, standardized using long cone parallel techniques.

Collection of PICFand Measurement of MMP-9 and IL-1β

Sites of peri-implant were isolated and dried using cotton pellets and air syringes. Paper strips (Periopaper, Oraflow Inc, UK) 1-2 mm were inserted for the collection of PICF samples in the sulcus or pocket for 30 sec. Strips that were contaminated with blood and saliva were discarded. A calibrated gingival fluid measuring device (Periotron 8000, New York, NY, USA) was used for the measurement of PICF. The PICF samples were eluted and pooled in a buffered solution of phosphate (1 ml) for 60 mins before the PICF solution was made to freeze at -80°C. A trained technician analyzed the biomarkers blinded to the experimental groups. PICF samples were centrifuged at 4°C for 15 mins. ELISA Kit was used for the quantification of MMP-9 and IL-1β according to the recommendation of the manufacturer. The levels of IL-1β and MMP-9 were determined in picograms/milliliter (pg/ml) and nanogram/milliliter (ng/ml). Standard curves in each assay were taken as results.

Statistical Analysis

Statistical software SPSS [Statistics 28.0.1.1 Windows (IBM Corp., Armonk, NY, USA)] was used for statistical analysis. Data related to peri-implant clinical and radiographic parameters were reported in mean and percentages. Kolmogorov-Smirnov test was used for the assessment of the normal distribution of data. Pearson Chi-square test was applied for categorical data sets, whereas the Kruskal-Wallis test was employed for the comparison of means between groups. For multiple comparisons, the Bonferroni test was applied. Significance level $p<0.05$.

Results

General Characteristics of Study Participants

Among all four groups, a hundred participants were included. Fifty smokers had STIs and conventional implants, and fifty non-smokers had STIs and conventional implants (controls). The total number of implants assessed in group 1 was 30, with a duration of the implant function of 82.4±10.5 months. Similarly, in group 2, 29 implants with a duration of 76.8±13.9 months. 32 dental implants with a functional duration of 74.25±11.22 months, were included in group 3, and group 4 included 31 dental implants with a functional duration of 71.54±10.66 months. The mean age of participants was comparable (p=0.16) in the control (group 2, 52±3.8 yrs, and group 4, 53±3.5 yrs) and experimental groups (group 1, 54±4.5 yrs, and group 3, 54±2.1 yrs). The duration of the smoking habit in years was 22.7±1.4 years, with a daily frequency of 11.2±2.5 in group

1 and 23.8±1.9 years, with a daily regularity of 11.33±2.1 in group 3. Family history of tobacco use was more dominant in the smoker's group (i.e., group 1 and group 3) compared to non-smokers. Among all participants, the major reason for missing teeth was caries (79%), followed by periodontal disease (21%). When questioning brushing habits, the incidence of brushing teeth was more prevalent in the smokers' group with STIs (26%) and conventional implants (25%). However, the frequency of dental visits in the smoker group was less compared to the non-smoker group (Table I).

Peri-Implant Parameters Clinical and Radiographic

The mean findings of PIPI and PIPD ≥4 mm were found to be significantly worse in cigarette smokers with STIs (62.4±5.9) (5.3±2.1) (p<0.01) and conventional implants (63.3±6.1) (5.5±1.9) (p<0.01) compared to non-smokers with STIs (29.2±3.6) (3.1±0.1) and conventional implants (28.1±3.4) (3.2±0.3). BoP was significantly higher in non-smokers (36.5±21.2) compared to smokers with STIs (24.2±8.3) and conventional implants (21.6±7.4) (p<0.01). PIPI, PIPD ≥4 mm, and BoP were found to be comparable among group 2 and group 4 controls (p>0.01). CBL was found to be higher in group 1 and group 3 cigarette smokers with STIs and conventional implants compared to non-smokers (p<0.01) (Table II). Smokers with STI, when compared to cigarette smokers with a conventional implant for parameters i.e., PIPD, PIPI, and BoP, demonstrated comparable outcomes with similar radiographic and peri-implant parameters (p>0.01) (Table II).

Levels of IL-1β and MMP-9 in PICF

The level of IL-1β (pg/ml) and the level of MMP-9 (ng/ml) were found to be significantly higher in cigarette smokers with STIs and conventional implants in comparison to non-smokers (p<0.01) (Table III).

Table I. General characteristics of the cohort of smokers and non-smokers with STIs and conventional implant.

Characteristics	Group 1: Cigarette smokers with STIs	Group 2: Non-smokers with STIs (controls)	Group 3: Cigarette smokers with conventional implant	Group 4: Non-smokers with conventional implant (controls)	p-value
Male Patients (n)	n=25	n=25	n=25	n=25	
Age years (mean ± SD)	54±4.5	52±3.8	54±2.1	53±3.5	0.16
Duration of smoking in years (mean ± SD)	22.7±1.4	N/A	23.8±1.9	N/A	0.12
Daily frequency of smoking (mean ± SD)	11.2±2.5	N/A	11.33±2.1	N/A	0.87
Number of dental implants	30	29	32	31	0.97
Type of Restoration					
Screw retained	24	23	27	25	0.65
Cemented	6	6	5	6	
Family history of tobacco use (n)	21	11	19	14	0.11
Reason for missing tooth %					
Caries	79	85	77	89	0.44
Periodontal	21	15	22	11	
Trauma	0	0	1	0	
Implant function duration in months	82.4±10.5	76.8±13.9	74.25±11.22	71.54±10.66	
Brushing %					
Once daily	22	18	21	17	0.30
Twice daily	4	6	4	8	
Number of dental visits	3	6	2	8	0.11

Short tuberosity Implant (STI). p<0.05 was considered statistically significant.

Table II. Peri-implant parameters and crestal bone loss in a cohort of smokers and non-smokers with STIs and conventional implant.

Peri-implant parameters	Group 1: Cigarette smokers with STIs	Group 2: Non-smokers with STIs (controls)	Group 3: Cigarette smokers with conventional implant	Group 4: Non-smokers with conventional implant (controls)	*p*-value
PIPI %	62.4±5.9[a]	29.2±3.6[b]	63.3±6.1[a]	28.1±3.4[b]	<0.01*
BoP %	24.2±8.3[a]	36.5±21.2[b]	21.6±7.4[a]	38.4±24.1[b]	<0.01*
PIPD % ≥4 mm	5.3±2.1[a]	3.1±0.1[b]	5.5±1.9[a]	3.2±0.3[a]	<0.01*
CBL mm	4.3±0.3[a]	2.1±0.1[b]	4.4±0.2[a]	2.3±0.2[b]	<0.01*

*$p<0.05$ was considered statistically significant. Data with different lower-case alphabets denote significant differences within each row ($p<0.05$).

Table III. MMP-9 and IL-1β in GCF of smokers and non-smokers with STI and conventional implant.

Parameters	Group 1: Cigarette smokers with STIs	Group 2: Non-smokers with STIs (controls)	Group 3: Cigarette smokers with conventional implant	Group 4: Non-smokers with conventional implant (controls)	*p*-value
PICF volume in µl	3.1±0.5[a]	1.8±0.1[b]	3.3±0.6[a]	1.6±0.2[b]	<0.01*
Level of IL-1β pg/ml	285.12±19.6[a]	125.87±18.6[b]	289.44±21.5[a]	123.98±17.2[b]	<0.01*
Level of MMP-9 (ng/ml)	109.25±13.6[a]	37.6±16.2[b]	110.6±12.5[a]	39.5±18.4[b]	<0.01*

*$p<0.05$ was considered statistically significant. Data with different lower-case alphabets denote significant differences within each row ($p<0.05$)

Prosthetic Parameters

A total of 8 STIs failed i.e., 2 in the non-smokers and 6 in the smokers group. The failure was reported due to the following reasons: smokers lack osseointegration and implant loosening (n=4). Among smoker patients, chipping of ceramic and fracture of the framework were also noted (n=2). In non-smokers, the loosening of the abutment screw failed (n=2).

Discussion

The present study was based on the hypothesis that the use of STIs will show better outcomes than conventional implants in smokers and non-smokers. The hypothesis was rejected as there was no difference in periodontal, radiographic, and level of biomarkers IL-1β and MMP-9 in smokers rehabilitated with conventional implants or STIs. Through literature and available evidence, it is already established that smokers with conventional implants have significant bone loss with poor periodontal disease (PIPI, PIPD, and BoP) around implants in comparison to non-smokers[24-26]. However, to our knowledge, the present study was the first to compare periodontal and radiographic parameters along with biomarkers in smokers with STIs and conventional implants.

Abundant PIPI is the pathological cause of periodontal disease related to peri-implant. Cumulative PIPI results in the formation of deep pocketing and increasing BoP. If left untreated, this may result in poor radiographic levels. BoP is the classic indicator of periodontal and peri-implant inflammation[27,28]. BoP in the present study was found to be significantly less in smokers compared to non-smokers. This decline in BoP is caused by nicotine in tobacco linked to a descent in the cellular healing response and a decrease in the tendency to bleed. Nicotine has a vasoconstrictive effect on gingival blood vessels[29-31], which indirectly results in a decrease in BoP. Similarly, other periodontal parameters i.e., PIPI and PIPD, were found to be significantly higher in smokers rehabilitated with conventional dental implants and STIs compared to non-smokers. Upsurge in PIPD and PIPI are linked with periodontal-patho-

genic microbes in the oral biofilm[32]. Evidence advocates that a PD less than 3.5 mm, which was observed in non-smokers, is a non-pathological sulcus deepening[33]. Therefore, a PIPD of less than 3.5 defines the success of a dental implant. Regular dental visits and maintaining proper and regular oral hygiene care demarcate the success of the dental implant[34,35]. It can be observed from the present study that utilization of dental services was more profound in non-smokers participants compared to non-smokers. On the assessment of radiographic parameters, CBL was found to be higher in smokers compared to non-smokers. Several aspects are related to this result. It is recognized that nicotine in tobacco reduces cellular response and delays healing[28,36]. Moreover, tobacco impairs new bone formation and jeopardizes bone-to-implant contact i.e., osseointegration[37,38]. Evidence suggests habitual cigarette smoking is an established risk factor for CBL. Hence, with increased age, CBL is found to decrease, but in cigarette smokers, this bone loss is aggravated twofold[39]. Also, it is estimated that surgical interventions may also influence CBL[40,41]. Therefore, it is recommended to understand these conclusions with caution.

Detrimental pro-inflammatory biomarkers IL-β and MMP-9 were found to be significantly high in smokers in comparison to non-smokers. Smoking on a habitual basis increases the levels of AGEs in the soft tissues of the oral cavity gingiva and periodontal tissues[42,43]. ROS is produced when there is an augmented interface between AGEs and their receptors RAGE alters the function of polymorphonuclear cells, declining the production of antibodies, improving bacterial adhesion, and increasing the load of the inflammatory burden by cumulating the levels of cytokines in GCF, and crevicular fluid[42,44]. This mechanism of action of ROS is responsible for the inflammation of connective tissues and bone deterioration in cigarette smokers. It is hypothesized the same mechanism is responsible for predisposition in levels of IL-β and MMP-9 in smokers. However, further studies are pre-requisite involving different biomarkers in patients with habitual smokers[36,42,43].

The findings of the present study showed that family history was the contributing factor in habitual cigarette smokers. The author of the current study suggests that an anti-tobacco campaign and awareness programs should be conducted regularly to inform the community about the harmful effects of smoking on general well-being[45,46].

Limitations

It is important to recognize the limitations of the study. Patients with systemic diseases were not made part of the present study, as diabetes mellitus (DM) is a predisposing factor for peri-implant diseases. Other proinflammatory cytokines, tissue necrosis factor-alpha (TNF-α), and different types of interleukin (IL-2, IL-6, IL-8) need to be assessed. Individuals using other tobacco forms i.e., electronic cigarettes, and water pipes, were not included. Since female participants have different bone densities, and cortical porosity in the mandible and maxilla, this may predispose the outcome of the present study.

Conclusions

Periodontal (PIPI, PIPD, and BoP) along with radiographic (CBL) and prosthetic parameters were compromised in smokers compared to non-smokers. Patients with conventional implants and STI showed comparable clinical, radiographic, and prosthetic parameters among smokers. Utilization of dental services along with cessation programs should be encouraged for smokers.

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Authors' Contributions

Conceptualization, Methodology, Software Validation; Formal analysis; Investigation, Resources; data curation, writing–original draft preparation, writing–review and editing; visualization was performed by AA, EMA, SA, AR, FV, and TA.

Conflict of Interest

The authors declare that there was no conflict of interest.

Informed Consent

Written consent was signed by the participating individuals after being informed about the purpose of the study and the possibility to withdraw at any point.

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Ethics Approval

The research ethics review committee of the specialist dental practice and research center (SDRC-019-21) in Riyadh, approved the study.

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