Myeloperoxidase as a Measure of Polymorphonuclear Leukocyte Response in Inflammatory Status Around Immediately and Delayed Loaded Dental Implants: A Randomized Controlled Clinical Trial

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ABSTRACT

Background: As well as gingival crevicular fluid (GCF), peri-implant sulcus fluid (PISF) may have a potential diagnostic value for the early identification of metabolic and destructive processes.

Purpose: The aim of this study was to analyze the potential impact of inflammation and loading on PISF myeloperoxidase (MPO) levels, in comparison with GCF.

Materials and Methods: A total of 220 sites, dental implant (immediately [IL] or delayed loaded [DL]), and natural tooth, either healthy/noninflamed or gingivitis/inflamed, were classified. Clinical parameters were recorded, and GCF/PISF samples were obtained. GCF/PISF MPO levels were spectrophotometrically determined.

Results: Clinical parameters demonstrated increases with the presence of gingival/peri-implant inflammation. Total MPO levels were higher at inflamed tooth and implant sites compared to noninflamed/healthy sites ($p < .05$). Although they did not reach a significance level, inflamed IL sites had higher total MPO levels than inflamed DL sites ($p = .401$). Gingival index and total MPO levels exhibited significant correlations ($p < .05$).

Conclusion: Using implants and natural teeth in the same study design, the findings of the present study support the close relationship between MPO production and inflammation, and may speculate a potential for loading of dental implants, contributing to the MPO content of PISF.

KEY WORDS: dental implants, inflammation, loading, myeloperoxidase, natural tooth

The traditional criteria for evaluating the disease status around dental implants are frequently based on radiographic and clinical changes, such as probing depth (PD) and mobility assessment.[1] Although these measures can provide information about the extent of the past peri-implant tissue destruction, they cannot actually reflect current tissue status nor can they predict the risk of peri-implant disease progression.[2,3] Thus, development of simple and reliable diagnostic tool(s) for early detection of initial peri-implant inflammatory process and for the prevention of any irreversible host reactions, such as destructive peri-implant disease, is an important goal.[3–6]

When such attempts are concerned, it can be seen that considerable interest is devoted to peri-implant

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sulcus fluid (PISF) and the ingredients of this biologic fluid.[6–9] PISF is an osmotically mediated transudate/exudate, which consists of a large array of ingredients.[3] The composition and volumetric features of both PISF and gingival crevice fluid (GCF) clearly depend on the condition of surrounding tissues. [6,9–12] Studies are available that particularly concentrate on the potential diagnostic value of the ingredients of PISF for the early identification of metabolic and destructive processes that could precede the clinical course of peri-implant inflammatory process.[3,4,7,9] A close relationship between the status and degree of clinical peri-implant tissue inflammation and various PISF components such as interleukin-1β,[8] PGE_2,[13] matrix metalloproteinases,[7] aspartate aminotransferase,[14] α-glucuronidase,[7] products of nitric oxide metabolism,[6] and myeloperoxidase (MPO)[7,9] were demonstrated.

MPO, an enzyme located at the azurophilic granules of polymorphonuclear leukocytes (PMNs),[9,15,16] contributes to protease activity and connective tissue breakdown through inhibiting antiproteases and activating proteases, and thus, changing the protease/antiprotease balance.[15,17] Increased activity of the MPO at periodontitis sites and decreased activity following treatment are suggested to support the role for MPO in destructive periodontal diseases.[15,16,18] Because of the higher PISF MPO levels at inflamed sites, MPO is also considered as a promising marker of inflammation around dental implants.[9]

Besides maintaining the clinically healthy status of peri-implant tissues, force application and the timing of loading (eg, immediate [IL], early, delayed [DL]) may influence bone remodeling around dental implants.[6,19,20] Force application in general has the capacity to affect the regulation of bone remodeling.[19,21,22] Thus, type of force application and the timing of loading may affect implant survival.

All these studies, either directly or indirectly, support the diagnostic potential for PISF and also highlight the need for a better understanding of the biological mechanisms and interactions at dental implant sites.[6,7,8,13,14] They also divert our interests toward the potential similarities between PISF and GCF. Thus, studies focusing on different measures of peri-implant inflammation, the impact of force, and the similarities of PISF and GCF in response to inflammation within the same study design may be considered to be beneficial for further clarification of the peri-implant biological events. The present study was conducted to analyze PISF and GCF MPO levels in response to the presence/absence of clinical inflammation and IL or DL of dental implants via implant-supported fixed prosthesis.

MATERIALS AND METHODS

Patient Selection

Thirteen patients, who had first molar loss bilaterally in the mandibular area, referred to the Department of Prosthodontics, seeking prosthodontic rehabilitation were included. The average age of the patients (nine women and four men) was 39.8 ± 7.73 years (age range: 27 to 55 years). The study protocol was explained in detail to all patients, and they were asked to sign informed consent forms. Ethical approval for this study was obtained from the Ethics Committee of Hacettepe University. Their general healths were good, they had no known allergies, and all were nonsmokers. After consent was obtained, they were introduced to the surgical procedure. Presurgical radiographic evaluation was carried out with dental computerized tomography (CT). All patients received two mandibular endosseous dental implants, 11.5 mm in length and 4 mm in diameter (Brånemark System®, Nobel Biocare AB, Göteborg, Sweden) to the first mandibular molar regions bilaterally.

Surgical Procedure and Prosthodontic Rehabilitation

The surgeries in the present study were performed by the same oral surgeon. Local anesthesia was obtained by Ultracain D-S (Hoechst Marion Russel, Frankfurt/Main, Germany). A mid-crestal incision with sulcular releasing incisions at the adjacent teeth was performed. Full thickness flaps were reflected, and osteotomies were prepared at the mandibular molar sites as determined on dental CT prior to the surgical procedure. Following the placement of dental implants, resonance frequency values of both implants were measured by Osstell™ (Integration Diagnostics AB, Göteborg, Sweden). The transducer was mounted on the implants orthoradially, with the upright part on the oral side. The frequency response of the system was measured immediately after implant placement to determine the stability of implants.[23] Implant stability quotient values more than 65, which indicated high primary stability, were included in the study to provide a standardized methodology.[24] After performing initial resonance frequency measurements, one site of

the patient determined as IL and the other side was DL.[25] Randomization for IL and DL selection was performed by coin toss.

In the IL group, prosthetic procedures were performed prior to suturing the soft tissues. Abutment connection was performed immediately after surgery, provisional crowns were cemented within the same day, and definitive fully occluding metal–ceramic crowns were introduced within 7 days.[25]

While in the DL group, healing abutments (3 mm) (Nobel Biocare AB) were screwed to the implants, and then mucoperiosteal flaps were approximated and sutured according to one-stage surgery. In this group, the definitive fully occluding metal–ceramic crowns were fabricated and cemented onto the abutments after 3 months of healing.[25] The same prosthodontist provided all prosthodontic rehabilitation.

Clinical Examination

The clinical evaluations were performed by the same periodontist. The following clinical parameters were recorded for evaluating clinical status of the dental implants and natural teeth including plaque index (PI),[26] gingival index (GI),[27] PD, and gingival bleeding time index.[28] All measurements were performed at four sites around each dental implant and natural tooth, and were carried out the nearest millimeter using a Michigan "O" probe.

Determination of Experimental Groups

A total of 220 sites, dental implant ($n = 109$) and natural tooth ($n = 111$) sites, were classified as either clinically healthy sites or sites with clinical inflammation based on the GI score of a given dental implant or natural tooth site. A GI score of 0 was considered to represent the state of health (noninflamed); a GI score of >0 represented inflammation. Radiographic analysis of the noninflamed and inflamed dental implants, and noninflamed/healthy and inflamed/gingivitis sites did not demonstrate any alveolar bone loss.

PISF/GCF Sampling

To avoid blood contamination and possible stimulation of PISF/GCF flow during clinical measurements, PISF/GCF samples were collected prior to clinical recordings, except PI.[5] At 1, 3, 6, 9, and 12 months postimplantation, PISF was collected from bilateral mandibular molar regions, and GCF was collected from maxillary molar regions, bilaterally. PISF/GCF samples were obtained according to the method described by Rüdin and colleagues[29] using standardized paper strips (Periopaper®, no. 593525, Ora Flow, Inc., Amityville, NY, USA). Briefly, following the isolation of the sampling area with sterile cotton roles, supragingival plaque was removed and the site was gently air dried to reduce any contamination with plaque and saliva. Extreme care was taken to minimize the level of mechanical irritation during PISF/GCF sampling as this is known to affect the actual fluid volume in a given site.[5] Therefore, paper strips were placed at the entrance of peri-implant sulcus and natural tooth crevice, and were inserted to a standardized depth of 1 mm at each site regardless of the PD. Sampling time was also standardized as 30 seconds. Papers with visible blood contaminations were discarded. To eliminate the risk of evaporation, paper strips with PISF/GCF were immediately transported to previously calibrated Periotron 8000® (Ora Flow, Inc., Plainview, NY, USA) for volume determination. Prior to sampling, the Periotron 8000 was switched on and allowed to warm up before a blank paper strip was placed in the device and the reading dial was set to zero.[30] The calibration of the device was checked with periodic intervals and performed by triplicate readings as previously described.[13,31] Following sampling, the PISF/GCF collected was measured in Periotron units, which were converted to microliters by MLCONVRT.EXE software (Ora Flow).[31] To eliminate the risk of evaporation, strips with PISF/GCF were placed in sterile, firmly wrapped Eppendorf tubes immediately and stored at –20°C until the day of laboratory analysis. PISF and GCF samplings were performed by the same periodontist.

Determination of MPO Level of PISF/GCF

MPO activity of PISF/GCF was measured using the spectrophotometric MPO assay that is a modification of the method reported by Suzuki and colleagues.[32] Briefly, the assay mixture consisted of 50 mM phosphate buffer (pH 5.4), 1.6 mM synthetic substrate tetramethyl benzidine (TMB), 0.5% hexadecyltrimethyl ammonium bromide, 1 mM H_2O_2, and 50 µL GCF extract. The reaction was initiated by the addition of H_2O_2, and the rate of TMB oxidation was followed at 655 nm using a recording spectrophotometer. Considering the initial and linear phase of the reaction, the absorbance change per minute was determined. One unit of MPO activity was expressed as the amount of enzyme producing one absorbance change

under assay conditions. MPO activity in PISF/GCF samples was calculated and expressed both as enzyme concentration and the total enzyme activity.

Statistical Analysis

SPSS 11.5.0 software for Windows (SPSS, Chicago, IL, USA) was used for all statistical analyses. For clinical parameters and PISF/GCF nitrite and MPO levels in noninflamed/healthy and inflamed/gingivitis sites, the Shapiro–Wilk test was used to test the normality of the distribution. Because data were not normally distributed, the Kruskal–Wallis analysis followed by Mann–Whitney test with Bonferroni correction was performed for comparison of healthy/noninflamed and inflamed/gingivitis sites. The correlation between MPO levels and clinical inflammatory status was analyzed with Spearman's correlation coefficient. The p value less than 0.05 was considered statistically significant. Further, for clinical parameters and PISF MPO levels according to the implant loading protocol, the Shapiro–Wilk test was used to test the normality of the distribution. Because data were not normally distributed, the Kruskal–Wallis analysis followed by Mann–Whitney test with Bonferroni correction was performed for comparison of healthy/noninflamed and inflamed/gingivitis sites for IL and/or DL implants.

RESULTS

A total of 26 dental implants were loaded. During the study period, only one implant was lost in the IL group after 4 weeks in the healing period. The reason for the failure in the IL group in the present study may be attributed to the patient's collaboration which was far from optimal, and caused significant stress to the crown during the healing period.

Follow-up ranged from 1 to 12 months, with a mean of 9.23 months. Eight patients were followed up 1 to 12 months, while other subjects with a number of three and two patients were followed up 1 to 6 months and 1 to 3 months, respectively.

Analysis of Clinical Parameters of Natural Teeth and Dental Implants Grouped by State of Inflammation

Descriptive statistical analysis and actual p values are provided in Table 1. When natural teeth sites and dental implant sites were concerned, clinical parameters, including PI, PD, and PISF/GCF volume, were higher in inflamed/gingivitis sites than clinically noninflamed/healthy sites ($p < .05$). Comparison of clinically healthy natural tooth and noninflamed dental implant sites revealed no significant difference ($p > .05$). When inflamed implants and natural tooth sites with gingivitis were compared, the natural tooth group had higher PI ($p = .05$) scores and PISF/GCF volume ($p = .004$).

Analysis of MPO Levels of Natural Teeth and Dental Implants Grouped by State of Inflammation

Descriptive statistical analysis and actual p values are provided in Table 1. Total and concentration modes of data presentation did not match and presented different trends. Total MPO levels were higher at inflamed tooth ($p = .04$) and implant ($p = .027$) sites compared to noninflamed/healthy sites. Total MPO levels did not present any significant difference between healthy natural tooth and noninflamed dental implant sites ($p = .734$). In a similar manner, inflamed natural tooth and dental implant sites did not present any significant difference ($p = .282$). Despite these differences for total MPO levels, differences between MPO concentration were not significant in any such analysis ($p > .05$).

Analysis of Dental Implants Grouped by Loading Protocol

Table 2 shows data for the recorded clinical parameters, PISF volume, MPO levels, and MPO concentration of the sites of DL and IL dental implants. Mean PI was significantly higher for inflamed IL ($p = .0001$) and DL ($p = .001$) sites compared to noninflamed IL and DL sites. Inflamed DL sites had higher PD than noninflamed DL sites ($p = .006$). Noninflamed IL and DL sites presented similar PISF values ($p = .875$). Inflamed IL sites ($p = .001$) and DL sites ($p = .003$) presented higher PISF volume than noninflamed sites. Similarly, PISF volume at inflamed IL sites presented a trend of increase than PISF volume at inflamed DL sites, but was not significant ($p > .05$). Although it did not reach a significance level, total MPO levels both at inflamed DL and IL sites were higher than noninflamed DL and IL sites ($p > .05$). When noninflamed IL and DL sites were compared, total MPO levels did not present any difference ($p = .489$). Concentration mode of data presentation was also nonsignificant ($p > .05$).

TABLE 1 Statistical Analysis of Clinical Parameters and Myeloperoxidase (MPO) Levels of Periodontal Healthy/Noninflamed (Gingival Index [GI] = 0), Gingivitis/Inflamed (GI > 0) Natural Tooth and Dental Implant Sites

		PI		PD		GCF/PISF Volume		Total MPO Level (U)		MPO Concentration (U/μL)	
Tooth											
Periodontal health ($n = 11$)	Mean ± standard deviation	0.27 ± 0.34		1.93 ± 0.37		0.18 ± 0.09		0.19 ± 0.17		1.21 ± 1.44	
	Median	0.25		2.00		0.14		0.14		1.12	
	(Minimum–maximum)	(0.00–1.00)		(1.25–2.50)		(0.10–0.37)		(0.00–0.58)		(0.00–5.24)	
Gingivitis ($n = 100$)	Mean ± standard deviation	0.91 ± 0.48		2.22 ± 0.43		0.39 ± 0.22		0.46 ± 0.49		1.36 ± 1.34	
	Median	1.00		2.25		0.33		0.29		0.97	
	(Minimum–maximum)	(0.00–3.00)		(1.25–3.50)		(0.09–1.27)		(0.00–2.30)		(0.00–7.39)	
Implant											
Noninflamed ($n = 35$)	Mean ± standard deviation	0.26 ± 0.35		1.85 ± 0.60		0.16 ± 0.09		0.27 ± 0.39		1.84 ± 2.87	
	Median	0.00		2.00		0.13		0.11		0.86	
	(Minimum–maximum)	(0.00–1.00)		(1.00–3.00)		(0.04–0.40)		(0.00–1.76)		(0.00–15.00)	
Inflamed ($n = 74$)	Mean ± standard deviation	0.81 ± 0.63		2.43 ± 0.78		0.32 ± 0.22		0.49 ± 0.71		1.91 ± 2.52	
	Median	0.50		2.25		0.26		0.25		0.91	
	(Minimum–maximum)	(0.00–4.00)		(1.00–5.25)		(0.06–1.19)		(0.00–4.46)		(0.00–11.88)	
Tooth		*z*	*p*	*z*	*p*	*z*	*p*	*z*	*P*	*z*	*p*
Healthy versus gingivitis		−4.071	0.0001*	−2.019	0.044*	−3.816	0.0001*	−2.058	0.040*	NS	NS
Implant		*z*	*p*	*z*	*p*	*z*	*p*	*z*	*p*	*z*	*p*
Noninflamed versus inflamed		−5.193	0.0001*	−3.441	0.001*	−4.582	0.0001*	−2.212	0.027*	NS	NS
Healthy/Noninflamed		*z*	*p*	*z*	*p*	*z*	*p*	*z*	*p*	*z*	*p*
Tooth versus implant		−0.210	0.834	−0.313	0.754	−0.956	0.339	−0.340	0.734	NS	NS
Gingivitis/Inflamed		*z*	*p*	*z*	*p*	*z*	*p*	*z*	*p*	*z*	*p*
Tooth versus implant		−1.963	0.05*	−1.528	0.127	−2.885	0.004*	−1.075	0.282	NS	NS

*$p < .05$.

GCF = gingival crevicular fluid; NS = not significant; PD = probing depth; PI = plaque index; PISF = peri-implant sulcus fluid.

TABLE 2 Statistical Analysis of Clinical Parameters and Myeloperoxidase (MPO) Levels of Delayed Loaded (DL) and Immediately Loaded (IL) Dental Implants

		PI		PD		GCF/PISF Volume		Total MPO Level (U)		MPO Concentration (U/μL)	
DL											
Healthy ($n = 23$)	Mean ± standard deviation	0.30 ± 0.38		1.74 ± 0.62		0.16 ± 0.09		0.26 ± 0.44		1.95 ± 3.39	
	Median	0.00		1.5		0.13		0.09		0.69	
	(Minimum–maximum)	(0.00–1.00)		(1.00–3.00)		(0.04–0.40)		(0.00–1.76)		(0.00–15.00)	
Inflamed ($n = 36$)	Mean ± standard deviation	0.66 ± 0.41		2.29 ± 0.67		0.29 ± 0.21		0.47 ± 0.83		1.88 ± 2.88	
	Median	0.50		2.25		0.24		0.22		0.73	
	(Minimum–maximum)	(0.00–2.00)		(1.00–3.75)		(0.06–1.19)		(0.00–4.46)		(0.00–11.88)	
IL											
Healthy ($n = 12$)	Mean ± standard deviation	0.19 ± 0.26		2.06 ± 0.53		0.16 ± 0.09		0.27 ± 0.32		1.61 ± 1.49	
	Median	0.00		2.12		0.14		0.18		1.50	
	(Minimum–maximum)	(0.00–1.00)		(1.00–2.75)		(0.06–0.34)		(0.00–1.08)		(0.00–3.86)	
Inflamed ($n = 38$)	Mean ± standard deviation	0.95 ± 0.76		2.56 ± 0.86		0.33 ± 0.22		0.51 ± 0.57		1.92 ± 2.15	
	Median	0.75		2.25		0.27		0.26		1.13	
	(Minimum–maximum)	(0.00–4.00)		(1.25–5.25)		(0.09–1.15)		(0.00–1.94)		(0.00–8.4)	
Delayed		z	p	z	p	z	p	z	p	z	p
Noninflamed versus inflamed		−3.214	0.001*	−2.771	0.006*	−3.352	0.001*	−1.706	0.088	NS	NS
Immediate		z	p	z	p	z	p	z	p	z	p
Noninflamed versus inflamed		−4.027	0.0001*	−1.683	0.092	−3.001	0.003*	−1.129	0.259	NS	NS
Inflamed/Inflamed		z	p	z	p	z	p	z	p	z	p
Delayed versus immediate		−1.412	0.158	−1.299	0.194	−0.730	0.465	−0.840	0.401	NS	NS
Noninflamed/Noninflamed		z	p	z	p	z	p	z	p	z	p
Delayed versus immediate		−0.690	0.490	−1.459	0.145	−0.157	0.875	−0.692	0.489	NS	NS

*$p < .05$.
GCF = gingival crevicular fluid; NS = not significant; PD = probing depth; PI = plaque index; PISF = peri-implant sulcus fluid.

When 220 sites, including 109 dental implant and 111 natural tooth sites, were evaluated, significant correlations were determined between GI and total MPO levels ($p = .008$; $r = .177$). Moreover, there was a significant correlation between total MPO level and PD ($p = .017$; $r = .161$), and also a significant correlation between total MPO level and PISF/GCF volume ($p = .00001$; $r = .234$).

Further, a significant correlation ($p < .05$) was achieved between total MPO level and MPO concentration at both IL and DL implant sites in cases of both inflamed and noninflamed status. In natural tooth sites, a significant correlation ($p < .05$) was also determined between total MPO level and MPO concentration at both healthy and gingivitis sites.

DISCUSSION

It is well known that a considerable amount of MPO is produced during periodontal diseases,[12,18] and the primary source of this enzyme is the PMNs that accumulate at such sites as a part of the host–bacteria interaction.[33,34] However, MPO production is not confined to periodontally diseased sites, and it also extends to sites that are designated as clinically healthy. Although they were lower than the periodontally diseased sites, detectable levels of GCF MPO were found at all of the clinically healthy sites in the present study. This finding is in line with previous studies demonstrating the presence of GCF MPO at clinically healthy sites.[9,12,15,16,18] As healthy gingival tissue is shown to exhibit low numbers of PMNs, and clinically healthy sites are shown to present with a certain level of subclinical inflammation and the subgingival bacteria, 100% presence of GCF MPO in the present may be attributed to such histological and microbiological features of clinical periodontal health.[15,17,33,35]

Likewise, GCF similar results were also observed for PISF samples and their MPO content. All PISF samples from peri-implant sites that were designated as clinically healthy contained detectable levels of MPO, which confirm the previous studies demonstrating MPO at clinically healthy peri-implant sites.[7,9] When taken together, the 100% availability of MPO in both GCF and PISF samples from clinically healthy sites may also highlight the similarity of PMN response of clinically healthy periodontal and peri-implant tissues.

It is well-demonstrated that PMNs accumulate at inflamed periodontal sites as a result of host–bacteria interaction,[33,34] and more GCF MPO may reflect the increase in gingival inflammation as a result of additional migrating leukocytes[15,17] and the hyperactive state of these cells.[17] Most of the studies demonstrated elevated levels of MPO at periodontitis and gingivitis sites,[12,18] a decrease in GCF MPO levels following periodontal treatment,[12] and the close relationship between GCF MPO activity with the clinical and microbial signs of periodontal disease.[3,12,16,18] Because sites with periodontal disease contained higher levels of GCF MPO than clinically healthy sites, findings of the present study support the previous studies suggesting a role for MPO in the pathogenesis of periodontal diseases.[7,9,12,16]

PISF samples from inflamed dental sites also presented with higher MPO levels than the noninflamed dental sites. Although PISF MPO content is not studied to the same level as GCF MPO content, there are studies demonstrating higher PISF MPO levels at inflamed peri-implant sites.[7,9] Further, Boutros and colleagues[7] demonstrated significantly higher MPO levels at failing implants compared to healthy sites and suggested MPO was a good candidate as a risk marker for dental implant failure.[7] In a similar manner, Liskmann and colleagues[9] demonstrated higher MPO levels in PISF from inflamed dental implant sites and suggested MPO as a promising marker of inflammation around endosseous dental implants. The higher MPO content of PISF from inflamed peri-implant sites and the positive correlations between GI and total MPO levels observed in the present study support the notion that MPO is involved in the peri-implant inflammatory process, and PISF MPO may serve as a diagnostic tool. As expressed by the MPO content of both biologic fluids (GCF and PISF), the PMN response of both the periodontal and peri-implant tissues is likely to be similar under inflammatory conditions. Based on this similarity of PISF and GCF MPO activity in response to inflammation, it may be suggested that a similar role for MPO in the pathogenesis of both periodontal diseases and peri-implant disorders is likely to be possible.

The association of an increased volume of GCF[29] and PISF[6,36] with an increase in the severity of inflammation is also well supported by evidence from the literature. In the present study, both PISF and GCF volumes were higher in inflamed/gingivitis sites than clinically noninflamed/healthy sites. Further, sites that are designated as clinically healthy yielded some GCF and PISF. Likewise, many previous GCF/PISF-related studies[6,16] demonstrating a discrepancy between

"concentration" and "total activity" modes of data presentation, it was not surprising to observe the significant contrast between total MPO levels and MPO concentration in GCF/PISF samples. Thus, it may be suggested that PISF shares similar volumetric features with GCF in terms of inflammatory response and the appropriate mode of data presentation, and it is in accordance with the description of PISF as an analogue for GCF from natural teeth.[9]

Different types of loading regimens for dental implants are available.[25] The IL of implants was suggested to achieve equal success rates as in delayed-loaded ones.[37–39] A high percentage of bone-implant contact in immediately loaded implants was also reported,[38,40,41] and in most of these studies, the success rate of immediately or early loaded implants was evaluated in terms of radiological and clinical parameters. In a recent study, PISF nitrite levels, an end product of nitric oxide metabolism, were analyzed in dental implants loaded either early or after a delay.[6] The results of this study demonstrated that loading of dental implants seemed to have the potential to influence the nitric oxide metabolism around dental implants in healthy and inflamed status.[6]

The total MPO levels did not present any difference when noninflamed IL and DL sites were compared in the present study. However, when peri-implant tissue was inflamed, higher total MPO levels were observed at the sites of IL implants compared to DL sites. The higher PISF total MPO levels at inflamed sites (both IL and DL) suggest inflammation as the primary determinant of the MPO content of PISF. Loading of dental implants does not seem to have a significant effect on PISF MPO levels on its own, because similar MPO levels are observed at healthy IL and DL implant sites. However, there is the potential of loading to contribute to PISF MPO content, as inflamed IL sites contained higher PISF MPO levels than inflamed DL sites. It can be speculated that force application to noninflamed tissues does not alter MPO production, while force application to inflamed tissues further increases MPO production. This situation is likely to have similarities with occlusal trauma which can cause changes in the alveolar bone and periodontal connective tissue in the presence of periodontal inflammation.[42,43]

Careful evaluation of both the "early" markers of inflammation and bone turnover in PISF may be of particular importance for the long-term success and maintenance of dental implants. MPO is clearly shown to be a marker of inflammatory process. However, its relation to force and loading needs further analysis. The potential similarities between periodontal and peri-implant tissues, and between GCF and PISF in response to inflammation and loading, may serve as a basis for a better understanding of the peri-implant pathologies and for the development of reliable tests in PISF for their early identification.

CONCLUSIONS

Using dental implants and natural teeth in the same study design, the findings of the present study support the close relationship between MPO production and inflammation and may suggest the similarity of periodontal and peri-implant tissues in reference to their PMN response and MPO production. Additionally, the potential for loading of dental implants to contribute to the MPO content of PISF may also be speculated. On the other hand, GCF and PISF are likely to share particular similarities when their volumetric features and MPO content are concerned. Analysis of PISF may serve for a better understanding of the molecular mechanisms around dental implants, which subsequently may aid to develop reliable diagnostic tool(s).

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