GEORGIAN BIOMEDICAL NEWS

ISSN (Online): 2720-8796 ISSN (Print): 2720-7994

VOLUME 1. ISSUE 1. JANUARY-MARCH 2023

Peri-Implant Sulcular Fluid (PISF) Nitric Oxide (NO) as an Early Marker of Inflammation

Emir Bayandurov[1], Zurab Orjonikidze[1], Tamar Sanikidze[2]

DOI: 10.52340/GBMN.2023.01.01.11

ABSTRACT

BACKGROUND.

Nitric oxide (NO) plays an essential role in the regulation of peri-implant soft tissue inflammation, immunomodulation, antimicrobial defense, and anabolic and bone resorption processes. The alterations of NO play important role in the pathogenesis of periodontitis.

OBJECTIVES

In the present study, we aimed to evaluate the role of the peri-implant sulcular fluid (PISF) nitric oxide (NO) as a marker of early inflammation.

METHODS

Overall, 20 practically healthy persons (aged from 18 to 65 years) with a dental implant placed in the chewing group of teeth, good oral cavity hygiene (Board index <20%), and the need for rehabilitation were included in the study. The content of nitric oxide (NO) in PISF was measured before and 1, 2, and 3 months after implantation and compared with similar values of GSF of healthy teeth.

RESULTS

The Herniarin-treated mice showed approximately the same results as irradiated mice on post-irradiation days 2 and 7. Furthermore, on days 14 and 30 absorption spectrum of erythrocyte membrane proteins significantly increased (P<0.05) in the Herniarin-treated experimental group. In the CSF of healthy teeth of studied patients, NO content did not significantly change during the post-implantation period, while the NO concentration in PISF was statistically higher than the initial level in the first and second post-implantation months (25.09±0.77 μM and 19.47±0.84 μM, respectively), and returned to the nearly initial level 3 months after implantation (17.19±0.5 μM).

CONCLUSIONS

The results of the present study indicate the importance of NO metabolism to the inflammatory process around dental implants. PISF appears to have diagnostic potential for early prediction of inflammation after implantation. Further studies are needed to evaluate and compare PISF and GCF, especially concerning the inflammatory process and bone remodeling.

KEYWORDS

Gingival crevicular fluid (GCF); nitric oxide (NO); peri-implant inflammation; peri-implant sulcular fluid (PISF).

BACKGROUND

Implant-based dental rehabilitation becomes one of the alternatives to the therapeutic options for totally or partially edentulous patients. However, the incidence of peri-implant disease increased with the growth of dental implant users.[1]

Several methods are currently used to assess the survival and prognosis of surrounding dental implant (peri-implant) tissues.[2] Periodontal gingival inflammation, plaque accumulation, probing depth, and bleeding on probing are traditional methods for the evaluation of peri-implant clinical status.[3] However, they can evaluate the progressive inflammatory process in peri-implant tissues rather than detect the early inflammatory response.[4]

Based on this, there is a growing interest in the development of new site-specific tests with higher specificity and sensitivity which may overcome the well-known limitations.[5]

The peri-implant sulcus is quite similar to periodontal crevices anatomically, functionally, and environmentally.[6] The gingival crevicular fluid (GCF) is the osmotically mediated physiological exudate originating from serum and tissue fluid that seeps through the crevicular and junctional epithelium. GCF plays an essential role in maintaining the structure of junctional epithelium and the antimicrobial defense of periodontium; its flow reflects the cellular response in the periodontium by the constituents from the gingival crevice and is an important determinant of the status of periodontal tissues.[7]

The presence of a similar fluid was demonstrated in the peri-implant sulcus. This peri-implant sulcular fluid (PISF), like GSF, is composed of serum and local tissue breakdown products, inflammatory mediators (cytokines, prostaglandins), tissue degradation signal molecules (matrix metalloproteinases, acute phase proteins), minerals, bone

metabolism markers, and antibodies against dental plaque bacteria.[8,9] Thus, the study of GCF and PISF can be useful in terms of detecting early markers of inflammation in both gum and peri-implant tissues.[10,11]

Nitric oxide (NO), as a small-sized, highly reactive secondary messenger molecule, plays an essential role in the regulation of peri-implant soft tissue inflammation, immunomodulation, antimicrobial defense, and anabolic and bone resorption processes.

After the implantation, inflammatory processes may increase NO production in peri-implant tissues due to the intensification of inducible NO-synthase (iNOS) expression by proinflammatory cytokines or a decrease in NO content as a result of its transformation into peroxynitrite under oxidative stress conditions.[12] It was shown that the alterations of NO play important role in the pathogenesis of periodontitis.[13,14]

In the present study, we aimed to evaluate the role of PISF nitric oxide (NO) as a marker of early inflammation.

METHODS

Study design

Overall, 20 practically healthy persons (aged from 18 to 65 years) with a dental implant placed in the chewing group of teeth, good oral cavity hygiene (Board index <20%),[15] and the need for rehabilitation were included in the study after receiving informed consent.

The comorbidities (allergy, cancer, hepatitis, diabetes of various severity, endocrine system disorders, stomach ulcer diseases, chronic gastritis, colitis, respiratory diseases), pregnancy, and use of osseointegration-modulating medications (including anti-inflammatory drugs) 6 months before the implantation were exclusion criteria.

The content of nitric oxide (NO) in PISF was measured before and 1, 2, and 3 months after implantation and compared with similar values of GSF of healthy teeth.

The study design was approved by the Ethics Committee of Tbilisi State Medical University (TSMU).

Collection of gingival crevicular fluid (GCF) and peri-implant sulcus fluid (PISF)

PISF and GCF were obtained by the method proposed by Rudin and co-authors (Rudin HJ, 1970) with minimal mechanical irritation.

The identified areas sampled were treated with sterile cotton swabs to remove dental plaque and then air-dried to prevent plaque and saliva contamination. Strips of standardized paper (Periopaper, no.593525) was placed at the entrance of the grooves of the implant and healthy teeth and inserted to a standardized depth of 1 mm to avoid further mechanical irritation. The sampling time was standardized and equal to 30 seconds. Samples contaminated with blood were not used.

For safe storage of PISF and GCF samples, the paper strips were placed in a sterile Eppendorf tube and stored at 20^0C until laboratory analysis before and 1, 2, and 3 months after implantation.

Determination of NO content in saliva

The samples of GSF of PISF in an amount of 100 microliters placed on microplates were incubated at room temperature for 10 minutes after adding 0.5 ml of freshly prepared Greiss reagent. The absorbance intensity of each sample was measured at a wavelength of 540 nm.[16] The nitric oxide (NO) concentration was measured via a standard curve prepared using sodium nitrite.

Statistical analysis

Statistical significance was tested using one-way ANOVA and a two-sample t-test. Relationships yielding p-values less than 0.05 were considered significant. All values were expressed as the mean ± SE.

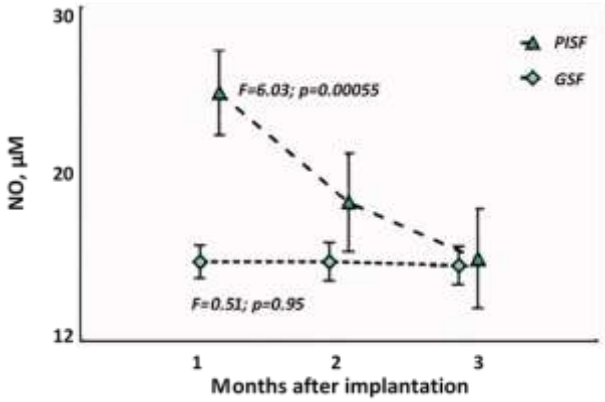
RESULTS

Table 1 and Figure 1 represent the dynamics of the NO concentration measured in GSF and PISF 1, 2, and 3 months after implantation. In the CSF of healthy teeth of studied patients, NO content did not significantly change during the post-implantation period, while the NO concentration in PISF was statistically higher than the initial level in the first and second post-implantation months (25.09±0.77 μM and 19.47±0.84 μM, respectively), and returned to the nearly initial level 3 months after implantation (17.19±0.5 μM).

TABLE 1. NO concentrations in gingival crevicular fluid (GCF) of healthy teeth and peri-implant sulcus fluid (PISF) before and 1, 2 and 3 months after implantation

	Number of samples	*Before implantation*	*After implantation*		
			1 month	*2 months*	*3 months*
GSF	20	16.17±0.23	16.30±0.6	16.26±0.4	16.1±0.3
PISF	20	16.22±0.16	25.09±0.8	19.47±0.8	17.19±0.5

FIGURE 1. NO concentrations in gingival crevicular fluid (GCF) of healthy teeth and peri-implant sulcus fluid (PISF) 1, 2 and 3 months after implantation



Georgian Biomedical News
ISSN (Online): 2720-8796 ISSN (Print): 2720-7994

DISCUSSION

Nitric oxide (NO) plays an essential role in peri-implant tissue inflammation and bone remodeling. As a secondary messenger, NO represents a mediator of the nonspecific immune response with beneficial and harmful effects.[17-19] During and after implantation, the alteration of NO production occurs in response to inflammatory reactions and oxidative stress of peri-implant tissues. The inflammatory process leads to the release of polymorphonuclear neutrophils or leukocytes (PMN), macrophages, lymphocytes, and mast cells. The lysosomes of these inflammatory cells contain enzymes that degrade the bacterial and metabolic by-products during the process of phagocytosis. However, these enzymes are capable of degrading gingival tissue components as well. According to the existing evidence, a small amount of NO constitutively produced by osteoblasts can act as a stimulator of osteoblast growth and differentiation.

A high concentration of NO in PISF can have an inhibitory effect on osteoblastic growth and differentiation and/or stimulate bone resorption may be partly due to its pro-apoptotic effects.[20] NO is also affected by the loading of dental implants. Mechanical stimulus is one of the factors involved in bone remodeling.[21] Therefore, the diagnostic potential of PISF should be interpreted with caution due to the limited number of analyzed samples.

According to the results of our study, the level of NO in CSF of healthy teeth of studied patients did not significantly change during three months of the post-implantation period, while the content of NO in PISF one month after implantation increased by 55% compared to the initial level and gradually decreased during next two months to the before implantation level. The increased NO concentration in PISF of dental implants indicates the inflammation of the peri-implant tissues. The finding of an increase in PISF NO metabolism at inflamed sites is in line with the previously reported results of a comparative analysis of existing studies.[22,23]

CONCLUSION

The results of the present study indicate the importance of NO metabolism to the inflammatory process around dental implants. PISF appears to have diagnostic potential for early prediction of inflammation after implantation. Further studies are needed to evaluate and compare PISF and GCF, especially concerning the inflammatory process and bone remodeling.

AUTHOR AFILIATION

[1] Department of Oral Surgery and Implantology, Tbilisi State Medical University, Tbilisi, Georgia;

[2] Department of Physics, Biophysics, Biomechanics and Informative Technologies, Tbilisi State Medical University, Tbilisi, Georgia.

REFERENCES

1. Shama MM, Aboukhadr M, Madi M, Abdelhady S. COMPARISON BETWEEN LEVEL OF INTEREUKIN 10 IN THE GINGIVAL CREVICULAR FLUID AND PERI-IMPLANT SULCULAR FLUID AROUND HEALTHY DENTAL IMPLANTS (SPLIT MOUTH STUDY). Alexandria Dental Journal. (2016) Vol.41 Pages: 26:30
2. Albrektsson T, Zarb G, Worthington P, Eriksson AR. The long-term efficacy of currently used dental implants: a review and proposed critera for success. Int. J Oral Maxillofac Implants. 1986;1:11-25
3. Roos Leroy, Kenneth A Eaton, Amir Savage. Methodological issues in epidemiological studies of periodontitis - how can it be improved? BMC Oral Health volume 10, Article number: 8 (2010).
4. Löe H, Sillncss J, Periodontal disease in Pregnancy. 1. Pervalence and Severity.ActaOdontol Scand. 1963;21:533-51.
5. Greenstein G. Contemporary interpretation of probing depth assessments: Diagnostic and therapeutic indications. J Periodontol. 1996;68:1194-205
6. Berglundh T, Lindhe J, Erissson I, Mariello CP, Thamsen P.The soft tissue Barrier at implants and teeth.Clin Oral Implants Res. 1991;2:81-90
7. American Academy of Periodontology. Glossary of periodontal terms. Chicago: American Academy of Periodontology; 200. Abdullah C. Akman, D.D.S., Sezen Buyukozdemir Askin, D.D.S., Guliz N. Guncu, D.D.S., Rahime M. Nohutcu, D.D.S. Evaluation of Gingival Crevicular Fluid and Peri-Implant Sulcus Fluid Levels of Periostin: A Preliminary Report Journal of Periodontology; Copyright 2017 DOI: 10.1902/jop.2017.170315.
8. Subbarao KC, Nattuthurai GS, Sundararajan SK, Sujith I, Joseph J, Syedshah YP. Gingival Crevicular Fluid: An Overview. J Pharm Bioallied Sci. 2019 May;11(Suppl 2):S135-S139.
9. Abdullah C. Akman, D.D.S., Sezen Buyukozdemir Askin, D.D.S., Guliz N. Guncu, D.D.S., Rahime M. Nohutcu, D.D.S. Evaluation of Gingival Crevicular Fluid and Peri-Implant Sulcus Fluid Levels of Periostin: A Preliminary Report Journal of Periodontology; Copyright 2017 DOI: 10.1902/jop.2017.170315
10. Apse P, Ellen RP, Overall CM, Zarb GA. Microbiota and crevicular fluid collagenase activity in the Osseointigrated dental implant sulcus: a comparison of sites in edentulous and partially edentulous patients. J Periodontal Res. 1989;24:96-105.
11. Lang NP, Berglundh T. Woring Group 4 of seventh Euroup Workshop on Periodontology. Peri-implant diseases: Where are we now? Consensus of the seventh European workshop on periodontology.J ClinPeriodontol. 2011;38(suppl 11):178-81
12. Allaker RP, Silva Mendez LS, Hardie JM, Benjamin N. Antimicrobial effect of acidified nitrite on periodontal bacteria. Oral Microbiol Immunol. 2001 Aug;16(4):253-6. doi: 10.1034/j.1399-302x.2001.160410.x. PMID: 11442852
13. Menaka KB, Ramesh A, Thomas B, Kumari NS. Estimation of Nitric oxide as inflammatory marker in Periodontitis. J Indian Soc Periodontol 2009;13:75-8.
14. Akopov SE, Kankanian AP. Nitric oxide (NO) inactivation by polymorphonuclear leukocytes as a mechanism for the development of periodontal lesions. Stomatologiia (Mosk) 1996;75:12-4.
15. Ainamo, J. and Bay, I. (1975) Problems and Proposals for Recording Gingivitis and Plaque. International Dental Journal, 25, 229-235.
16. Grisham MB, Johnson GG, Lancaster JR Jr. Quantitation of nitrate and nitrite in extracellular fluids. Methods Enzymol. 1996;268:237-46. doi: 10.1016/s0076-6879(96)68026-4. PMID: 8782590
17. Kendall HK, Marshall RI, Bartold PM. Nitric oxide and tissue Destruction. Oral Dis 2001;7:2-10. Brennan PA, Thomas GJ, Langdon JD. The role of nitric oxide in Oral diseases. Arch Oral Biol 2003;48:93-100.

ISSN (Online): 2720-8796 ISSN (Print): 2720-7994

18. Van't Hof RJ, Ralston S. Nitric oxide and bone. Immunology2001;103:255-61 Kendall HK, Marshall RI, Bartold PM. Nitric oxide and tissue Destruction. Oral Dis 2001;7:2-10.
19. Brennan PA, Thomas GJ, Langdon JD. The role of nitric oxide in Oral diseases. Arch Oral Biol 2003;48:93-100. Van't Hof RJ, Ralston S. Nitric oxide and bone. Immunology2001;103:255-61.
20. Nachimento MH, Pelegrino MT, Pierettu JC, Seabra AB. How can nitric oxide help osteogenesis? AIMS Molecular Science, 7(1): 29–48. DOI: 10.3934/molsci.2020003.
21. Gokmenoglu C, Ozmeric N, Sungur C, Sahin Bildik R, Erguder I, Elgun S. Nitric oxide and arginase levels in peri-implant tissues after delayed loading. Arch Oral Biol. 2018 Jan;85:207-211. doi: 10.1016/j.archoralbio.2017.10.019. Epub 2017 Oct 23. PMID: 29127889
22. Farhan Durrani, Urvashi Ojha, VP Singh, Royana Singh1Nitric oxide level around dental implant: Indicator of an inflammatory process Journal of Dental Implants | Jan - Jun 2012 | Vol 2 | Issue 1, p. 9-14
23. Tözüm TF, Turkyilmaz I, Yamalik N, Tümer C, Kilinç A, Kilinç K, et al. Analysis of the possible Impact of inflammation severity and early and delayed loading on nitric oxide metabolism around dental implants. Int J Oral Maxillofac Implants 2005;20:547-56

Georgian Biomedical News
ISSN (Online): 2720-8796 ISSN (Print): 2720-7994