

Determination Of Salivary Cytokines Level In Patients With Peri Implant Mucositis And Peri- Implantitis With Peri-Implant Maintenance Therapy

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ABSTRACT: Background: The present study was conducted to determine the level of salivary cytokines in the absence or presence of periodontal and peri-implant maintenance therapy (TMPP). **Materials & Methods:** 48 patients with signs of peri implant mucositis and peri- implantitis were divided into 2 groups. Group I that performed TMPP regularly (GTP=24) and group II did not perform TMPP regularly, (GNTP=24). Cytokines such as IL-1 β , IL-10, MMP-2, RANK, TGF- β and TNF- α were determined using diagnostic kit.

Results: There was non- significant difference in salivary biomarkers level between T1 and T2 in patients with peri implant mucositis and peri- implantitis ($P > 0.05$). There was non-significant difference ($P > 0.05$) in concentration of IL- I β , IL- 10, TGF- β , MMP- 2 and RANK between MP and PI patients in both GNTP and GTP group whereas TNF- α showed significant difference between MP and PI patients in GNTP group ($P < 0.05$).

Conclusion: The level of tumor necrotic factor alpha was higher in patients with peri-implantitis in patients with GNTP as compared to other cytokines.

Key words: Cytokines, Peri-implantitis, IL- 10

1. INTRODUCTION

Peri implant mucositis and peri- implantitis are two commonly encountered conditions around dental implants. Peri implant mucositis is the inflammation of mucosa around dental implant and peri- implantitis is the inflammation of tissues such as soft and hard around dental implant. There is excessive bone loss in this condition.¹

Cytokines are low molecular protein, also considered as markers of inflammation. The concentration of cytokines increases in peri- implantitis. Peri-implantitis is a result of an unregulated inflammatory response of the host to antigene bacterial determinants from dental plaque.² In peri-implantitis there is an interactions complex between bacterial products, host cells and locally produced biological active. It is evident that cytokines, chemokines,

enzymes of cellular destruction are generated as an outcome of tissue destruction in periodontitis and peri- implant diseases and are released in saliva.³

It is found that immunological markers may be useful in detection of peri- implant diseases. Saliva, blood and gingival crevicular fluid (GCF) are three medium in which these makers can be measured.⁴ However, saliva being pain free, non- invasive and easy to collected and thus is frequently used. Numerous research have been conducted assessing the concentration of salivary biomarkers in Peri implant mucositis and peri- implantitis.⁵ The present study was conducted to determine the level of salivary cytokines in the absence or presence of periodontal and peri-implant maintenance therapy (TMPP).

2. METHODOLOGY

48 patients with signs of peri implant mucositis and peri- implantitis were enrolled for the study. The diagnosis of the condition was based on the presence of > 6 mm probing depth and >3 mm bone loss. The enrollment of the patients was done after they agreed to participate in the study. The research protocol was presented to the ethical review committee of the institute for their approval.

Patients information such as name, age, gender etc. was recorded. They were divided into 2 groups. Group I that performed TMPP regularly, one visit/year (GTP=24) and group II did not perform TMPP regularly, < one visit/year (GNTP=24). Parameters such as clinical attachment level (CAL), periodontal probing depth (PPD) and peri-implant probing depth (PIPD), periodontal and peri-implant plaque index, bleeding on probing (BOP) and bleeding on peri-implant probing (BOPi) were recorded at baseline and after 4 years. Digital intraoral radiographs were obtained to assess bony changes such as bone loss.

Patients were made to refrain from breakfast, eating and drinking on the day of study. 5 ml of the unstimulated saliva was collected in a pipette. Cytokines such as IL-1 β , IL-10, MMP-2 complex, RANK, TGF- β and TNF- α were determined using diagnostic kit. Results were expressed as mean which were statistically analyzed. P value <0.05 was considered significant.

3. RESULTS

Table I Characteristics

| Variants | Baseline (T1) | | P value | Final (T2) | | P value |
|-----------------------------|---------------|-----|---------|------------|-----|---------|
| | GNTP | GTP | | GNTP | GTP | |
| Periodontal diagnosis | | | | | | |
| Healthy | 18 | 15 | 0.15 | 14 | 17 | 0.08 |
| Periodontitis | 6 | 9 | | 10 | 7 | |
| Peri- implant diagnosis | | | | | | |
| Healthy | 0 | 0 | | 0 | 8 | 0 |
| Peri-implant mucositis (MP) | 24 | 24 | | 13 | 12 | |
| Peri-implantitis (PI) | 0 | 0 | | 11 | 4 | |

Table I shows that the number of periodontitis patients increased from 6 to 10 from baseline to final examination in GNTP group. The number of peri-implant mucositis patients increased from 24 to 13 in GNTP group from baseline to final examination whereas number of Peri-implantitis patients increased to 11. The difference was non- significant (P> 0.05).

Table II Assessment of salivary biomarkers

| Biomarkers | GNTP | | P value | GTP | | P value |
|---------------|---------|--------|---------|---------|---------|---------|
| | MP | PI | | MP | PI | |
| IL- I β | 22314.5 | 1964.2 | 0.18 | 20124.1 | 10136.7 | 0.09 |
| IL- 10 | 4.8 | 8.4 | 0.14 | 4.4 | 4.9 | 0.97 |
| TGF- β | 1.5 | 5.6 | 0.09 | 10.7 | 23.6 | 0.08 |
| TNF- a | 2.3 | 14.3 | 0.05 | - | 2.1 | - |
| MMP- 2 | 27.5 | 54.3 | 0.07 | 7.8 | 7.2 | 0.94 |
| RANK | 38.4 | 33.8 | 0.91 | 2.1 | - | - |

Table II shows that there was non- significant difference ($P > 0.05$) in concentration of IL- I β , IL- 10, TGF- β , MMP- 2 and RANK between MP and PI patients in both GNTP and GTP group whereas TNF- a showed significant difference between MP and PI patients in GNTP group ($P < 0.05$).

Table III Comparison of salivary biomarkers at T1 and T2 in both groups

| Biomarkers | MP | | P value | PI | | P value |
|---------------|---------|---------|---------|---------|---------|---------|
| | T1 | T2 | | T1 | T2 | |
| IL- I β | 17124.6 | 21316.2 | 0.21 | 21315.2 | 42132.5 | 0.54 |
| IL- 10 | 4.3 | 4.4 | 0.32 | 8.1 | 7.5 | 0.81 |
| TGF- β | 9.8 | 5.7 | 0.15 | 5.6 | 10.3 | 0.42 |
| TNF- a | - | 1.3 | - | 12.1 | 10.8 | 0.35 |
| MMP- 2 | 14.6 | 18.3 | 0.71 | 25.4 | 40.2 | 0.09 |
| RANK | 22.3 | 21.2 | 0.91 | 26.3 | 24.5 | 0.97 |

Table III shows that there was non- significant difference in salivary biomarkers level between T1 and T2 in patients with peri implant mucositis and peri- implantitis ($P > 0.05$).

Discussion

It is evident that local response to peri-implant bacterial infection is in immunological and biochemical way very alike to the response in periodontal diseases. The occurrence of pathogenic bacteria, presence of cytokines, MMP, prostaglandin, interleukin, interleukin- 10, MMP- 2 and tumour necrotic factor alpha modify the progression of periodontal diseases.⁶ Peri-implant fluid (PICF) is widely used for the assessment of cytokines in the peri- implant tissue. This fluid fills the peri-implant sulcus and cytokines present in it, reflecting physiological interaction of gingival epithelium and local leukocytes on the micro-organisms of dental plaque and oral flora. Microorganisms are competent of synthesizing harmful products that injure epithelium and connecting tissue cells and extracellular content.⁷ The present study was conducted to determine the level of salivary cytokines in the absence or presence of periodontal and peri-implant maintenance therapy (TMPP).

In present study, 48 patients were divided into 2 groups. Group I underwent TMPP regularly, (GTP=24) and group II did not perform TMPP regularly (GNTP=24). Gomes et al⁸ determined the levels of salivary biomarkers in patients with diagnosis of peri-implant mucositis in the absence or presence of periodontal and peri-implant maintenance therapy (TMPP) in 80 patients. It was observed that there was 43.9% prevalence of peri-implantitis

in the GNTP group as compared to 18% in GTP group. Patients who presented peri-implant mucositis and had resolution at T2 were in the GTP group. After 5 years, there was an increase in the incidence of periodontitis in the GNTP group compared to the GTP group. The results of the study revealed an increase in the salivary concentration of TNF- α in the GNTP group compared to the GTP group.

We found that the number of peri-implant mucositis patients increased from 24 to 13 in GNTP group from baseline to final examination whereas number of Peri-implantitis patients increased to 11. The number of periodontitis patients increased from 6 to 10 from baseline to final examination in GNTP group. It is found that total salivary cytokines may represent only a fraction of the total content in saliva and that cytokines can be negatively affected by salivary components (mucin), which decreases the detection power of the ELISA assay.⁹

We observed that TNF- α showed significant difference between MP and PI patients in GNTP group ($P < 0.05$). We found that there was non-significant difference ($P > 0.05$) in concentration of IL-1 β , IL-10, TGF- β , MMP-2 and RANK between MP and PI patients in both GNTP and GTP group. Curtis et al¹⁰ revealed that the determination of IL-1 β in peri-implant crevicular fluid is helpful in the diagnosis of peri-implantitis. Authors found 3 times more cytokines in PICF in relation to the values in the initial stage.

Severino et al¹¹ conducted a study among 25 patients having 40 implants, 14 patients had peri-implantitis and 11 had healthy implants. Salivary cytokines such as IL-6, IL-10, IL-17 and IL-8 were evaluated in the peri-implant crevicular fluid (PCF). Authors showed that the level of IL-17 was significantly higher in peri-implantitis group in comparison to healthy patients ($p < 0.05$). There was no significant difference when comparing the levels of IL-6, IL-8 and IL-10 between both groups. There was a significant positive correlation between levels of IL-6 and IL-8 in the peri-implantitis group.

The research shows that specialist consultation is helpful in prevention in the development of periodontitis and subsequently peri-mucositis as well as peri-implantitis. It is further ascertained that TMPP minimizes the incident of peri-implantitis in subjects with a history of periodontitis, and the deficiency of TMPP is interconnected with a higher incidence of peri-implant bone loss in people with and without a history of periodontitis.¹²

The shortcoming of the study is small sample size.

4. CONCLUSION

Authors found that the level of tumor necrotic factor alpha was higher in patients with peri-implantitis in patients with GNTP as compared to other cytokines.

5. REFERENCES

- [1] Teles RP, Haffajee AD, Socransky SS. Peri-implant infections. *Clinical periodontology and implant dentistry*. 5th ed. Oxford: Blackwell Munksgaard; 2008; 268–77.
- [2] Berglundh T, Lindhe J, Lang NP. Peri-implant mucositis and Peri-implantitis. *Clinical periodontology and implant dentistry*. 5th ed. Oxford: Blackwell Munksgaard; 2008; 529–38.
- [3] Listgarten MA. Microorganisms and dental implants. *J Periodontol* 1999; 70(2): 220–2.
- [4] Mombelli A, Lang NP. Clinical parameters for the evaluation of dental implants. *Periodontol* 2000. 1994; 4: 81–6.
- [5] Prakasam S, Srinivasan M. Evaluation of salivary biomarker profiles following non-surgical management of chronic periodontitis. *Oral Dis*. 2014; 20(2): 171–7.

- [6] Lima CL, Acevedo AC, Grisi DC, Taba M Jr, Guerra E, De Luca Canto G. Host-derived salivary biomarkers in diagnosing periodontal disease: systematic review and meta-analysis. *J Clin Periodontol.* 2016;43(6):492-502.
- [7] Giannobile WV, Beikler T, Kinney JS, Ramseier CA, Morelli T, Wong DT. Saliva as a diagnostic tool for periodontal disease: current state and future directions. *Periodontology 2000.* 2009;50:52-64.
- [8] Gomes AM, Douglas-de-Oliveira DW, Ferreira SD, Silva TA, Cota LO, Costa FO. Periodontal disease, peri-implant disease and levels of salivary biomarkers IL-1 β , IL-10, RANK, OPG, MMP-2, TGF- β and TNF- α : follow-up over 5 years. *Journal of Applied Oral Science.* 2019;27.
- [9] Howe MS. Implant maintenance treatment and peri-implant health. *Evid Based Dent.* 2017;18(1):8-10.
- [10] Curtis DA, Kao RT, Plesh O, Finzen F, Franz L. Crevicular fluid analysis around two failing dental implants: a clinical report. *J. Prosthodont* 1997; 6(3): 210–4.
- [11] Severino VO, Napimoga MH, de Lima Pereira SA. Expression of IL-6, IL-10, IL-17 and IL-8 in the peri-implant crevicular fluid of patients with peri-implantitis. *Archives of oral biology.* 2011 Aug 1;56(8):823-8.
- [12] Rocuzzo M, De Angelis N, Bonino L, Aglietta M. Ten-year results of a three-arm prospective cohort study on implants in periodontally compromised patients. Part 1: implant loss and radiographic bone loss. *Clin Oral Implants Res.* 2010;21(5):490-6.