Titanium particles in tissues from peri-implant mucositis: An exfoliative cytology-based pilot study

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INTRODUCTION

Titanium is considered to be the metal of choice for oral and maxillofacial and orthopedic implants. It is mainly opted owing to its high strength and inertness. It is a highly reactive metal which develops a passivating layer of titanium dioxide (TiO₂) over its surface on exposure to air or fluids. This layer forms the interface between the biological milieu and the implant. It is responsible for biocompatibility by decreasing the material reactivity and partially preventing corrosion.[1] Commercially pure titanium and extra low interstitial Ti-6Al-4V alloy are the most common titanium-based implant biomaterials.[2] Loss of TiO₂ layer without reformation could lead to corrosion similar to the other base metals.[3] In the oral environment, titanium is subjected to conditions of varying pH, due to inflammatory or other processes that can turn the medium acidic, active dissolution of metal ions can occur upon exposure of the bulk metal.[4,5] The normal rate of corrosion of titanium is 0.13 mm/year, which is quite acceptable for a noble biomaterial.[5]

Limited literature is available demonstrating the corrosion of titanium in vivo. Previous studies have demonstrated the presence of titanium particles in patients with and without peri-implantitis using exfoliative cytology.[6,7]

To the best of our knowledge, no studies were conducted to demonstrate the presence of titanium particles in mucosa of peri-implant mucositis. Hence, the aim of this study was to determine the presence of titanium in the peri-implant mucosa of patients having single implants and compare its presence among the mild with moderate-to-severe groups of peri-implant mucositis patients.

MATERIALS AND METHODS

The study protocol was presented in the Institutional Review Board, and permission was obtained for conducting the same (vide Ref. No. BDC/Exam/84/2014–2015). The selection criteria included forty nonsmoking male and female participants with good general health and oral hygiene within the age group of 35–45 years. Participants with single healthy titanium implants wherein the gingival former was placed 4–6 months after the implant insertion were included in the study.[8] The implants selected for this present study belonged to Nobel Biocare® system Replace CC type, Switzerland. The dimensions of the implants selected were dependent on the residual ridge quality, which varied from patient to patient.

Abstract:

Background: To evaluate the presence of titanium particles in the peri-implant mucosa of unloaded single implants. Materials and Methods: Forty participants with single unloaded implants were selected. They were divided equally into two groups: Group 1 with mild and Group 2 with moderate-to-severe peri-implant mucositis. Cytologic smears of peri-implant mucosa were obtained using cytobrush during second-stage surgery. Results: Study states that 60% of participants of Group 2 were positive for titanium particles in peri-implant cytology. Conclusion: This study concludes that the titanium particles might be the initiators of the inflammation around implant.

Key words:
Corrosion, cytology, dental implant, mucosa, titanium
to patient. However, participants with oral piercings, metallic prosthesis, or metal restorations on neighboring teeth and those undergoing orthodontic therapy were excluded from this study.

Informed consent was obtained from the participants before the commencement of the study. The screening and diagnosis of participants with single implant was made based on a modified gingival index (MGI) given by Lobene et al., 1986. All the selected participants were divided into two groups: Group 1 mild gingivitis (n = 20) - MGI of each single implant in the range of 0.1–1 and Group 2 moderate-to-severe gingivitis (n = 20) - MGI of each single implant in the range of 1.1–3. Before the final impression, the gingival former was removed and using a cytobrush, exfoliate cytological samples of the peri-implant mucosa were collected at the level of union of the sulcular epithelium and the oral epithelium. The cytological smears obtained were spray fixed and stained using the Papanicolaou method. The smears were then mounted on the microscope slides and analyzed under transmitted light microscopy in six fields per slide by a single experienced oral pathologist. The presence of metal-like opaque particulate aggregates was identified, as the corrosion products of the titanium implants.

RESULTS

Table 1 presents the prevalence of titanium particles in peri-implant soft tissues in both the groups. Comparison of the presence of titanium particles in the two groups was made using Fisher’s exact test. In the present study, titanium particles were found in the peri-implant soft tissues of 12 out of 40 patients, and all of them were in moderate-to-severe gingivitis group. The rest of the smears appeared to be normal in nature [Figure 1a, 1b].

**Table 1: Group-wise distribution of presence/absence of titanium particles in peri-implant mucosa**

| Group   | Diagnosis                  | Titanium particles detected | Titanium particles not detected | Total number of patients (n) |
|---------|----------------------------|----------------------------|--------------------------------|------------------------------|
| Group I | Mild gingivitis            | 0                          | 20                             | 20                           |
| Group II| Moderate to severe gingivitis | 12                         | 8                              | 20                           |

DISCUSSION

Titanium has proven to be a revolutionary material of choice in implant dentistry since the last 50 years. This could be attributed to its excellent biocompatibility and inert behavior. However, in the recent years, studies have demonstrated the presence of titanium particles in peri-implant mucosa. The pH of saliva is also known to influence the corrosion rate of these titanium particles. The exact nature of these particles whether inert or not remains to be established. Furthermore, the presence of these particles in different severities of inflammation has not been studied. To the best of our knowledge, this study is the first of its kind in evaluating the titanium particulate corrosion in stages of peri-implant mucositis.

In the present study, titanium particles in peri-implant tissue were demonstrated in 60% of participants categorized under Group 2 while none were identified in Group 1. This could be attributed to the inflammatory cell infiltrate-like macrophages. Cytotoxicity has been demonstrated in osteoblast cell cultures exposed to metallic wear debris, although the metal ion concentrate, the ions within bone in vivo have not been established. It has been hypothesized that these titanium particles in systemic implants act like foreign bodies and may provoke the inflammatory responses leading to bone resorption. In the presence of metal ions, osteoblasts are able to release pro-inflammatory cytokines such as transforming growth factor beta 1, tumor necrosis factor alpha, interleukin 1 beta (IL-1 β), and most commonly, IL-6 into the microenvironment. These cytokines can, in turn, activate the differentiation of preosteoclasts into mature bone resorbing cells. A review on the loosening of peri-prosthetic total joint replacements stated that the preosteoclasts, secreted as a result of wear particles in joint replacement implants, would lead to osteolysis, namely “aseptic osteolysis.” This leads to loosening of the implant and poses a severe challenge and impact on peri-implant mucosal health. Similarly, titanium corrosion from dental implants in the oral cavity might also lead to loosening of dental implants by “aseptic osteolysis.” Extensive literature search has been done, and no study has been done regarding this phenomenon in introraal implants. Although the present study does neither quantify the amount of titanium leached in response to corrosion nor its ability in igniting inflammation but invites further prospective studies in this aspect for proving the same.

Studies demonstrating the presence of titanium particles in vivo are present in literature. However, whether they remain inert or initiate any inflammatory responses is still yet to be proven. These particles may also bind to the proteins and could get disseminated to distant organs systemically through vascular and lymphatic channels. However, the interactions of these particles at distant organs are not established.

Within the limitations of our study, it can be concluded that the incidence of titanium particles in the peri-implant soft tissue
increases with an increase in clinical inflammation. Further studies should be designed to probe the rate of particle release in response to several factors, with their role in the progression of peri-implant disease. Long-term studies with larger sample size are required to establish the role of peri-implant titanium particles.

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**Conflicts of interest**
There are no conflicts of interest.

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