Original Article – Prospective Study

Evaluation of Serum Metal Ion Levels in Dental Implant Patients: A Prospective Study

Gayathri Gopi, S. Shanmugasundaram[1], V. B. Krishnakumar Raja[1], K. Mohamed Afradh

Department of Oral and Maxillofacial Surgery, Thai Moogambigai Dental College and Hospital, [1]Department of Oral and Maxillofacial Surgery, SRM Dental College and Hospital, Chennai, Tamil Nadu, India

Abstract

Introduction: Titanium is the most commonly used bio-inert implant material. Nevertheless, there is a possibility of systemic release of metal ions, which could have clinical implications like implant failure and toxicity. This prospective study focuses on the evaluation of serum metal ion levels in patients receiving dental implants. The aim of the study is to evaluate the release of titanium, aluminium, and vanadium from dental implants by comparing the preoperative and postoperative serum levels of these ions. **Methodology:** Serum samples were collected from 30 patients undergoing dental implant placement preoperatively and postoperatively at intervals of 6 weeks, 3, 6, and 12 months. These samples were analyzed for titanium, aluminium, and vanadium levels using Inductively Coupled Plasma Optical Emission Spectrometry. The difference in preoperative and postoperative serum levels was measured and statistically analyzed using the paired *t*-test. **Results:** There was a slight difference in the postoperative levels of titanium and aluminium (2.30 and 4.07 mg/dl) as compared to the preoperative levels (2.28 and 2.30 mg/dl), which was statistically insignificant ($P > 0.5$). The serum levels of vanadium were too insignificant to be detected by the instrument (<0.0088 mg/dl). **Discussion:** Mild increase in the titanium and aluminium levels in blood serum was noted. These metallic ion levels might increase significantly due to which further clinical research with larger sample sizes and a long-term follow-up period is required to evaluate the clinical effects of metallic ion release from dental implants. There is no significant difference in the serum metal ion levels before and after the implant placement, although a little increase is observed in the aluminium ion levels after the implant placement.

Keywords: Aluminium, dental implant, spectrometry, titanium, vanadium

Introduction

The use of dental implants for prosthetic teeth replacement has gained importance in the last two decades and implants are now the primary mode of treatment for edentulism.[1] Most implants used today are made from titanium or titanium alloys, which is the material of choice due to its low density, good mechanical properties, and ability to osseointegrate.[2] However, questions have always been raised regarding metal ion release from implants and its clinical effects.

Several authors have studied the release of titanium from various orthopaedic and oral implants. Levine *et al*. did a 10-year follow-up on patients who had undergone total hip arthroplasty and stated that these patients had significantly higher levels of cobalt, chromium, and titanium as compared to controls.[3] On the other hand, Bianco *et al*. studied the difference in serum and urine titanium before and after implant placement in rabbits and concluded that there was no significant increase.[4]

Most dental implants nowadays are alloyed with aluminium and vanadium to improve the mechanical properties.[5] The release of these metals from dental implants into the bloodstream, and their clinical effects have not been studied adequately.

The purpose of this study was to evaluate the release of titanium, aluminium, and vanadium from dental implants by

Access this article online

Quick Response Code:

Website: www.amsjournal.com

DOI: 10.4103/ams.ams_70_21

Address for correspondence: Dr. K. Mohamed Afradh, 136/13, Ajanta Flats, Jawaharlal Nehru Road, Thirumangalam, Anna Nagar West, Chennai - 600 040, Tamil Nadu, India.
E-mail: dr.afradh@yahoo.com

Received: 09-03-2021 **Last Revised:** 03-08-2021
Accepted: 01-09-2021 **Published:** 01-02-2022

How to cite this article: Gopi G, Shanmugasundaram S, Krishnakumar Raja VB, Afradh KM. Evaluation of serum metal ion levels in dental implant patients: A prospective study. Ann Maxillofac Surg 2021;11:261-5.

comparing the preoperative and postoperative serum levels of these ions.

Methodology

The study was conducted in the department of oral and maxillofacial surgery of our institute over a period of 2 years extending from 2011 to 2013. This study was a prospective, quasi-experimental uncontrolled study where each patient served as his/her own control. The study protocol was approved by the Institutional Review Board (IRB number–SRMDC/IRB/2011/MDS/No. 405).

$P < 0.05$ is considered to be statistically significant.

Sample selection

The subjects for the study were patients who had come to our institution for replacement of missing teeth.

Inclusion criteria

1. Participants requiring replacement of single missing tooth in upper central incisor region
2. Participants between the age group of 18–71 years
3. Healthy patients with no underlying medical conditions
4. Participans with adequate bone volume to accommodate an implant of appropriate dimension
5. Co-operative patients, willing for the surgery and proper follow-up.

Exclusion criteria

1. Patients who had underlying medical conditions
2. Patients with deleterious habits such as smoking and tobacco chewing.
3. Patients with parafunctional habits
4. Patients who required multiple implants or had a history of dental or orthopaedic implant placement.

An informed consent was obtained in writing from all the patients before the procedure. Preoperative computed tomography (CT) scans were taken for all patients to assess bone quality. The implant recipient bone site was classified based on Misch's grading for bone density[5] and only cases that had Grade D2 were taken up for the study to ensure uniformity in bone quality.

Sample size

Our study included 30 participants, of which 18 were male and 12 were female.

Sample collection and analysis

Prior to placement of the implant, serum samples were collected from each patient to establish the baseline levels of the titanium, aluminium, and vanadium ions. 10 ml of blood was withdrawn from each patient into sterile vacutainers, without the use of any anti-coagulant. The blood was allowed to clot strictly for 20 min at room temperature, and then centrifuged to extract serum; if allowed to remain for longer periods, there would be risk of external contamination.

All serum samples were transported to the Sophisticated Instrument and Analytical Facility (SIAF) at Indian Institute of Technology, Chennai. The samples were analyzed for titanium, aluminium, and vanadium using Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES) on a Perkin Elmer optimal 5300 DV ICP-OES instrument (ICP-OES, ELAN DRC II, Perkin Elmer, SCIEX, Inc.).

Implants were then placed using a flapless technique. In all patients, the implant used was Micro-Textured surface (MTX) tapered, screw-vent type, which was coated with hydroxyapatite in the mid-section. (Zimmer Inc.). Loading of the implant was done after 6 months.

Follow-up

All patients were recalled at intervals of 6 weeks, 3 months, 6 months, and 12 months after implant placement. At each visit, blood samples were collected, serum extracted, and sent for analysis of metal ions as mentioned above.

Normality of data collected was assessed using the Kolmogorov–Smirnov test. Mean, median, and standard deviations were calculated for all patient groups. Since the datasets were interdependent, statistical analysis of parameters was done using the paired *t*-test for small samples. If the data were nonnormal, the Mann–Whitney *U* test would have been applied. All statistical analyses were carried out using the SPSS software version 16 (IBM Corp., Armonk, N.Y., USA in 2009).

Results

Thirty patients requiring replacement of the maxillary central incisor were taken up for the study. Of this, one patient was excluded because of improper follow-up. Of the remaining 29 patients, 18 were male and 11 were female. The age of the patients ranged from 18 to 71 years (mean 38.2 years).

In all patients, primary stability was achieved. Wound healing was satisfactory in all patients. One patient developed mild soft-tissue inflammation 2 weeks after placement. He was treated with curettage and local antimicrobial mouth rinses, after which healing was uneventful. Postoperative CT scans taken before loading, 6 months after implant placement showed good union between the bone and implant.

The difference in serum titanium levels before and after placement of implants is summarized in Table 1. Although there was a mild increase in the mean serum titanium levels, the difference was not statistically significant. Similarly, the serum aluminium levels also showed a minimal increase after placement of implants, but the results were not statistically significant. These levels are summarized in Table 2.

The serum concentration of vanadium fell below the detectable limit of the ICP-OES, which was 0.0088 mg/dl.

Discussion

Although titanium is classified as a bio-inert material, studies have proven that titanium from orthopaedic implants does get released into the bloodstream.[6] However, the release of metal ions specifically from dental implants has rarely been touched

Table 1: Difference in serum titanium levels before and after implant placement

Titanium levels (mg/dl)	Before placement	After placement			
		6 weeks	3 months	6 months	12 months
Mean	2.28	2.27	2.29	2.29	2.30
Std deviation	0.69	0.70	0.69	0.68	0.69
Range	1.11-3.77	1.13-3.77	1.13-3.78	1.13-3.78	1.14-3.78
SEM	0.1260	0.1278	0.1260	0.1242	0.1260
P		0.9558	0.9554	0.9551	0.9110

Table 2: Difference in serum aluminium levels before and after implant placement

Titanium levels (mg/dl)	Before placement	After placement			
		6 weeks	3 months	6 months	12 months
Mean	4.05	4.05	4.06	4.08	4.07
Std deviation	0.80	0.80	0.80	0.81	0.81
Range	2.49-5.54	2.49-5.53	2.49-5.56	2.50-5.54	2.50-5.54
SEM	0.1461	0.1461	0.1461	0.1479	0.1479
P		1.000	0.9616	0.8857	0.9237

upon, in both animal and human studies. The alloys that are commercially available in titanium are pure titanium (cpTi) and Ti-6Al-4V and both are found to give good clinical success rates of up to 99% at a time span of 10 years. Both the alloys are biocompatible with the native tissues when they are in contact with bone and the gingival tissues and also helps in osseointegration for stability of the implants.[7]

Various mechanisms may contribute to metallic ion release from implants. These include mechanical wear, electrochemical corrosion, and a combination of the two, called fretting corrosion.[8] Mechanical factors such as, the micro-gap and fluorides can also influence the proportion of metal particles and ions released from implants and restorations. The implant surfaces and restorations are exposed to the saliva, bacteria and chemicals that can potentially dissolve the titanium oxide layer and, therefore, corrosion cycles can be initiated.[9] Therapeutical substances such as fluorides and hydrogen peroxide can promote the degradation of titanium-based dental implant and abutments leading to the release of toxic ions.[10] The galvanic corrosion of implant/superstructure systems is important in the following two aspects: (1) the possibility of biological effects that may result from the dissolution of alloy components and (2) the current flow that results from galvanic corrosion may lead to bone destruction.[11] The corrosion resistance of Ti alloys depends on an oxide film (TiO2), called "passive layer," the disruption of which causes release of ions.[12,13]

Titanium is most commonly used in the form of titanium dioxide. Rapid expansion of products containing titanium increases percutaneous and permucosal exposure of titanium. Titanium allergy is lesser compared to other metal materials. It is advisable to ask the patients about hypersensitivity reactions before implant placement and patch testing can also be performed in patients who have a previous history of allergic reactions.[14,15]

The material used for implants can determine the amount of corrosion, and it has been shown that less titanium is released from titanium alloys as compared to commercially pure titanium.[16] Serum Ti levels were not related to total implant-bone surface area, number of the implants, and gender.[17] Studies have shown that diameter and total area of the implant were of less importance for the Ti released to the bone.[18] The fate of metal ions thus released also depends on the size of the particles. While larger particles may remain in the area of the implant, smaller particles can either be ingested by macrophages or can disseminate through lymphatics to areas such as the bone marrow, liver, and spleen.[4,19] If the corrosion increases, metallic ions released from the implants would eventually find their way into the bloodstream and get concentrated in the erythrocytes. Therefore, measurement of these ion levels in the blood would be an accurate predictor of chemical and mechanical implant wear. There is no correlation in blood titanium levels as the surface area is small between dental implants and total-implant bone. Bloodstream carries the corrosion products to spleen, hair, and lungs and lead to increase in serum levels.[20]

The release of metallic ions from implants may have both local and systemic effects. It is common to find Ti ions at the level of peri-implant tissues, that are relatively higher in peri-implantitis sites compared to healthy implants.[21,22] Titanium dental implants are the most commonly used material in dentistry and is associated with antenna activity and the electromagnetic waves may produce harmful effects.[23]

The level of corrosion in titanium and its association with peri-implantitis creates awareness in association between peri-implantitis and periodontitis.[24] The presence of the corrosion in the long term may lead to release of ions into the tissues around the implant surface and can cause disintegration of the implant and material fatigue leading to failure of implant and abutment fracture.[25]

Although titanium has not shown any adverse effects in humans, studies in rats have shown titanium as being responsible for toxic reactions in the lungs.[26] On the other hand, aluminium has been proven to be toxic to humans. Increased levels of aluminium in the blood have been linked to Alzheimer's disease, Parkinson's disease, and diabetic encephalopathy.[27] Chronic exposure to aluminium has been shown to increase the risk of osteomalacia and pathological fractures.[28] Increased levels of vanadium have been linked with kidney damage and gastrointestinal irritation.[29]

Mercuri *et al*. had compared metal ion levels in various surgical techniques and has stated that in the dental implant group, one of the patients had elevated levels of serum titanium and another patient showed elevated levels of both serum levels of titanium and chromium.[30]

To date, there is only one study that has assessed levels of all the three metal ions – titanium, aluminium, and vanadium in the blood of patients who have undergone implant placement.[31] This study used absorption spectrometry (AS) to assess ion levels in blood, and no significant difference was found in these levels in patients before and after the procedure. The method used in the current study was ICP-OES, which is believed to be a superior method to AS.[32] Despite this, we did not find any significant difference in metal ion levels before and after implant placement. There was a mild, nonsignificant increase in metal ion levels.

This study did not take into account the other sources that could contribute to raised serum titanium and aluminium levels. Processed food is known to contain large quantities of titanium; trace amounts are also found in drinking water, soil and air.[33] Aluminium is more ubiquitous and can also be taken up from soil, water, and air.[34] The addition of preservatives to processed food and packaging of such foods also increases aluminium exposure.[35] To avoid confounding, each patient in this study served as their own control. However, no attempt was made to standardize ion levels in this cross-section of population before the study. Such standardization, if done for future studies, would enable the use of a separate control group and randomization, thereby lessening bias. In the recent years, various other implant materials are available in the form of tantalum and zirconium to avoid titanium toxicity; however, long-term success rate is good with titanium compared to the other materials and toxicity of titanium is minimal and is involved only with the peri-implant tissues.[36]

In the present study, patients were followed up for 12 months. However, dental implants are designed to last a lifetime, and the expected lifespan of an implant is around 40 years. Therefore, if these patients were followed up for greater periods, it is possible that the metallic ion levels might increase to levels that could eventually be clinically significant.

Conclusion

This study shows that there is no significant difference in the serum metal ion levels before and after the implant placement, although a little increase is observed in the aluminium ion levels after the implant placement. More studies with long-term follow-up and larger sample will be required to evaluate the serum titanium and aluminium levels.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Jorge JR, Barão VA, Delben JA, Faverani LP, Queiroz TP, Assunção WG. Titanium in dentistry: Historical development, state of the art and future perspectives. J Indian Prosthodont Soc 2013;13:71-7.
2. Carlsson L, Röstlund T, Albrektsson B, Albrektsson T, Brånemark PI. Osseointegration of titanium implants. Acta Orthop Scand 1986;57:285-9.
3. Levine BR, Hsu AR, Skipor AK, Hallab NJ, Paprosky WG, Galante JO, *et al*. Ten-year outcome of serum metal ion levels after primary total hip arthroplasty. J Bone Joint Surg Am 2013;95:512-8.
4. Bianco PD, Ducheyne P, Cuckler JM. Titanium serum and urine levels in rabbits with a titanium implant in the absence of wear. Biomaterials 1996;117:1937-42.
5. Misch CE. Contemporary Implant Dentistry. 3rd ed. St. Louis: Mosby; 2010. p. 40, 130-46, 245-50, 280.
6. Frisken KW, Dandie GW, Lugowski S, Jordan G. A study of titanium release into body organs following the insertion of single threaded screw implants into the mandibles of sheep. Aust Dent J 2002;47:214-7.
7. Nicholson JW. Titanium alloys for dental implants: A review. Prosthesis 2020;2:100-16.
8. Zaffe D, Bertoldi C, Consolo U. Element release from titanium devices used in oral and maxillofacial surgery. Biomaterials 2003;24:1093-9.
9. Delgado-Ruiz R, Romanos G. Potential causes of titanium particle and ion release in implant dentistry: A systematic review. Int J Mol Sci 2018;19:E3585.
10. Peñarrieta-Juanito G, Sordi MB, Henriques B, Dotto ME, Teughels W, Silva FS, *et al.* Surface damage of dental implant systems and ions release after exposure to fluoride and hydrogen peroxide. J Periodontal Res 2019;54:46-52.
11. Alrabeah GO, Knowles JC, Petridis H. The effect of platform switching on the levels of metal ion release from different implant-abutment couples. Int J Oral Sci 2016;8:117-25.
12. Barbieri M, Mencio F, Papi P, Rosella D, Di Carlo S, Valente T, *et al.* Corrosion behavior of dental implants immersed into human saliva: Preliminary results of an *in vitro* study. Eur Rev Med Pharmacol Sci 2017;21:3543-8.
13. Markowska-Szczupak A, Endo-Kimura M, Paszkiewicz O, Kowalska E. Are titania photocatalysts and titanium implants safe? Review on the toxicity of titanium compounds. Nanomaterials (Basel) 2020;10:E2065.
14. Hosoki M, Nishigawa K, Miyamoto Y, Ohe G, Matsuka Y. Allergic contact dermatitis caused by titanium screws and dental implants. J Prosthodont Res 2016;60:213-9.
15. Mombelli A, Hashim D, Cionca N. What is the impact of titanium particles and biocorrosion on implant survival and complications? A critical review. Clin Oral Implants Res 2018;29 Suppl 18:37-53.

16. Okazaki Y, Gotoh E. Comparison of metal release from various metallic biomaterials *in vitro*. Biomaterials 2005;26:11-21.
17. Sridhar S, Wang F, Wilson TG, Palmer K, Valderrama P, Rodrigues DC. The role of bacterial biofilm and mechanical forces in modulating dental implant failures. J Mech Behav Biomed Mater 2019;92:118-27.
18. Pettersson M, Pettersson J, Molin Thorén M, Johansson A. Release of titanium after insertion of dental implants with different surface characteristics – An *ex vivo* animal study. Acta Biomater Odontol Scand 2017;3:63-73.
19. Urban RM, Jacobs JJ, Tomlinson MJ, Gavrilovic J, Black J, Peoc'h M. Dissemination of wear particles to the liver, spleen, and abdominal lymph nodes of patients with hip or knee replacement. J Bone Joint Surg Am 2000;82:457-76.
20. Temiz M, Dayi E, Saruhan N. Evaluation of blood titanium levels and total bone contact area of dental implants. Biomed Res Int 2018;2018:4121639.
21. del Amo FS, Garaicoa-Pazmiño C, Fretwurst T, Castilho RM, Squarize CH. Dental implants-associated release of titanium particles: A systematic review. Clin Oral Implants Res 2018;29:1085-100.
22. Zabala A, Blunt L, Aginagalde A, Llavori I, Tato W. Development of a novel method to characterize mean surface peak curvature as a signature of tribological performance of dental implant surfaces. Surf Topogr: Metrol Prop ;8:024001.
23. Tibau AV, Grube BD, Velez BJ, Vega VM, Mutter J. Titanium exposure and human health. Oral Sci Int 2019;16:15-24.
24. Safioti LM, Kotsakis GA, Pozhitkov AE, Chung WO, Daubert DM. Increased levels of dissolved titanium are associated with peri-implantitis – A cross-sectional study. J Periodontol 2017;88:436-42.
25. Noumbissi S, Scarano A, Gupta S. A literature review study on atomic ions dissolution of titanium and its alloys in implant dentistry. Materials (Basel) 2019;12:E368.
26. Wang JX, Fan YB, Gao Y, Hu QH, Wang TC. TiO2 nanoparticles translocation and potential toxicological effect in rats after intraarticular injection. Biomaterials 2009;30:4590-600.
27. Savory J, Ghribi O. Can studies of aluminium toxicity *in vivo* and *in vitro* provide relevant information on the pathogenesis and aetiology of Alzheimer's disease? J Alzheimer's Dis 2007;11:429-30.
28. Jeffery EH, Abreo K, Burgess E, Cannata J, Greger JL. Systemic aluminum toxicity: Effects on bone, hematopoietic tissue, and kidney. J Toxicol Environ Health 1996;48:649-65.
29. Goldfine AB, Patti ME, Zuberi L, Goldstein BJ, LeBlanc R, Landaker EJ, *et al.* Metabolic effects of vanadyl sulfate in humans with non-insulin-dependent diabetes mellitus: *In vivo* and *in vitro* studies. Metabolism 2000;49:400-10.
30. Mercuri LG, Miloro M, Skipor A, Sukatjo C, Mathew MT. Serum metal levels in maxillofacial reconstructive surgery patients. J Oral Maxillofac Surg 2019;77:e59.
31. Smith DC, Lugowski S, McHugh A, Deporter D, Watson PA, Chipman M. Systemic metal ion levels in dental implant patients. Int J Oral Maxillofac Implants 1997;12:828-34.
32. Lee S, Goh BT, Lai SH, Tideman H, Stoelinga PJ, Jansen JA. Peri-implant and systemic release of metallic elements following insertion of a mandibular modular endoprosthesis in Macaca fascicularis. Acta Biomater 2009;5:3640-6.
33. Pettersson M, Pettersson J, Johansson A, Molin Thorén M. Titanium release in peri-implantitis. J Oral Rehabil 2019;46:179-88.
34. Day JP. Biochemistry of aluminium in relation to the assessment of aluminium exposure in humans. Environ Geochem Health 1990;12:75-6.
35. Lopez FE, Cabrera C, Lorenzo ML, Lopez MC. Aluminum levels in convenience and fast foods: *In vitro* study of the absorbable fraction. Sci Total Environ 2002;300:69-79.
36. Bruschi M, Steinmüller-Nethl D, Goriwoda W, Rasse M. Composition and modifications of dental implant surfaces. J Oral Implants 2015;2015:527426. [doi: org/10.1155/2015/527426].