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Review Article

Toxicity of titanium in dental implants- Implications on patient health and clinical practice

Sankar Madhavan[1,*], Vineetha Venugopal[2], Joseph Johny[3]

[1]*Dept. of Prosthodontics, Sree Anjaneya Institute of Dental Sciences, Calicut, Kerala, India*
[2]*Dept. of Dentofacial Orthodontics, Sree Anjaneya Institute of Dental Sciences, Calicut, Kerala, India*
[3]*Dept. of Oral Medicine and Radiology, Sree Anjaneya Institute of Dental Sciences, Calicut, Kerala, India*

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ABSTRACT

The use of titanium implants in dentistry has become increasingly popular due to their biocompatibility and excellent mechanical properties. However, the release of titanium ions from the implants has the potential to lead to local and systemic toxicity, which may cause implant failure or have negative consequences on the body. In this article, the causes of titanium toxicity are discussed, including implant design, surgical methods, and patient specific elements. It also looks at the possible health hazards of titanium poisoning, such as inflammation, allergic reaction and neurological issues.

1. Introduction

Titanium is a widely used metal for dental implants because of its biocompatibility, mechanical strength, and resistance to corrosion. There have been worries about the possible toxicity of titanium and its alloys in dental implantology, despite the material's many advantages. While titanium toxicity is rare, it can occur and may result in various adverse effects.

Titanium toxicity from dental implants can occur due to the release of titanium ions from the implant surface into surrounding tissues. These ions can trigger an inflammatory response, leading to the accumulation of immune cells and the release of reactive oxygen species (ROS).[1] In some cases, the release of titanium ions may also lead to bone resorption around the implant, which compromises implant stability and leading implant failure.[2]

Studies have shown that under certain conditions, titanium ions can be released from the implant surface and enter the surrounding tissues, leading to cellular and tissue damage. This process is known as corrosion, and it can be accelerated by factors such as high acidity, high temperature, and mechanical stress.[3]

While the evidence for titanium toxicity is limited, it is essential for clinicians to be aware of the potential risks associated with the use of titanium implants. Patients with a history of metal allergies or autoimmune diseases may be particularly susceptible to titanium toxicity and should be evaluated carefully before undergoing implant surgery.[4]

2. Causes of Titanium Toxicity in Dental Implants

There have been some reports of titanium toxicity in dental implant patients. The exact causes of titanium toxicity are still not fully understood, but some possible factors include:

1. *Allergic reaction:* Some patients may be allergic to titanium or other components of the implant, such as nickel, chromium, or molybdenum. Allergic reactions can cause inflammation, pain, and other symptoms, and may require implant removal.[5]

* *Corresponding author*.
E-mail address: drsankarmadhavan@gmail.com (S. Madhavan).

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2. *Corrosion:* Although titanium is highly resistant to corrosion, it can still corrode over time, especially if exposed to acidic environments or other corrosive substances. Corrosion can release metal ions into the surrounding tissues, which can lead to inflammation and other adverse effects.[6]
3. *Overloading:* Dental implants that are overloaded or subjected to excessive force can cause bone loss and implant failure. This can also result in the release of metal ions and other particles into the surrounding tissues, leading to inflammation and toxicity.[7]
4. *Poor implant design or placement:* If the implant is poorly designed or placed, it can cause mechanical stress or pressure on the surrounding tissues, leading to inflammation and toxicity.[8]
5. *Impurities in the titanium:* Impurities in the titanium used for the implant, such as iron or qaluminum, can also cause toxicity.[9]

3. Mechanism of Titanium Toxicity

The mechanisms underlying titanium toxicity in dental implants are not yet fully understood, but several potential mechanisms have been proposed based on studies in vitro and in vivo. These mechanisms include.

1. Generation of Reactive Oxygen Species (ROS): Titanium ions and particles can induce the production of ROS, which can cause cellular damage and inflammation in surrounding tissues.[10]
2. Activation of the Immune System: Titanium particles and ions can activate the immune system by stimulating the release of cytokines and other inflammatory mediators. This can lead to the recruitment of immune cells and the production of pro-inflammatory factors, which can damage surrounding tissues.[11]
3. Disruption of Cellular Signaling Pathways: Titanium particles and ions can interfere with cellular signaling pathways, which can affect cell growth and differentiation. This can lead to changes in cellular behavior and contribute to the development of toxicity.[12]
4. Direct Cytotoxicity: High concentrations of titanium particles and ions can directly damage cells by inducing necrosis or apoptosis. This can lead to tissue damage and the release of pro-inflammatory mediators, contributing to inflammation and toxicity.[13]

4. Symptoms of Titanium Toxicity

The symptoms of titanium toxicity depend on the route of exposure and the duration and extent of exposure. There is limited information on the toxicity of titanium in humans. However, several animal studies have reported the effects of titanium exposure, which may include:

1. *Respiratory system:* Inhalation of titanium dust or fumes may cause respiratory irritation, cough, shortness of breath, and wheezing. In rats, inhalation of high concentrations of titanium dioxide (TiO2) nanoparticles caused inflammation, lung damage, and fibrosis in the lungs.[14,15]
2. *Nervous system:* Exposure to high levels of titanium in the workplace may cause neurological symptoms such as headaches, dizziness, and tremors. In rats, injection of titanium nanoparticles into the brain caused neuroinflammation and damage to the blood-brain barrier.[16,17]
3. *Skin:* Exposure to titanium dust or fumes may cause skin irritation, rash, and itching. In rabbits, topical application of titanium dioxide nanoparticles caused skin irritation and damage.[18]
4. *Gastrointestinal system:* Ingestion of titanium-containing substances may cause gastrointestinal symptoms such as nausea, vomiting, and diarrhea. In rats, ingestion of high doses of titanium dioxide nanoparticles caused inflammation and damage to the stomach and intestines.[9]

It is important to note that these effects have been observed in animals at high doses or after exposure to nanoparticles, which are much smaller in size than conventional titanium particles. The toxicity of titanium in humans is still being studied, and more research is needed to determine the safe levels of exposure to titanium.

5. Diagnosis of Titanium Toxicity

Currently, there is no consensus on the safe levels of titanium in the body, as different studies have used different exposure scenarios and biomarkers to measure titanium levels. However, several studies have suggested that high levels of titanium in the body may be associated with adverse health effects, such as immunological reactions and genotoxicity.

One of the most commonly used methods to diagnose titanium toxicity is by measuring the levels of titanium in the blood, urine, or tissues. Blood and urine titanium levels can be measured using various analytical techniques, such as inductively coupled plasma mass spectrometry (ICP-MS) or atomic absorption spectrometry (AAS). Tissue titanium levels can be measured using biopsy or post-mortem analysis.[19]

Another diagnostic tool for titanium toxicity is the lymphocyte transformation test (LTT), which is a functional assay that measures the proliferation of lymphocytes in response to titanium ions. The LTT has been used to diagnose titanium hypersensitivity and implant-related disease.[20]

In addition, imaging techniques such as X-ray and magnetic resonance imaging (MRI) can be used to detect

the presence of titanium in the body, particularly in cases where implant-related disease is suspected.[21]

It is important to note that the diagnosis of titanium toxicity should be based on a combination of clinical symptoms, laboratory tests, and imaging studies, and should be made by a qualified medical professional.

6. Treatment of Titanium Toxicity

In cases where titanium toxicity is suspected, the treatment will depend on the severity of the symptoms and the location of the titanium implant.

The treatment of titanium toxicity caused by dental implants typically involves removal of the implant and supportive care. If the toxicity is local, such as in the form of inflammation or infection at the implant site, the implant may need to be removed and antibiotics may be prescribed. If the toxicity is systemic, such as in the form of skin rashes, joint pain, or other symptoms, the implant may need to be removed and the patient may require supportive care such as pain management and monitoring of organ function.

There is limited research on the specific treatment of titanium toxicity caused by dental implants, but studies have suggested that removal of the implant is necessary for resolution of symptoms. Additionally, some studies have suggested that chelating agents such as ethylenediaminetetraacetic acid (EDTA) may help remove excess titanium from the body and improve symptoms.[22]

There is currently no specific medication or therapy available to treat titanium toxicity. However, symptomatic treatment may be administered to manage the symptoms, such as anti-inflammatory medication, pain management, and physical therapy.

It is important to note that titanium toxicity is a relatively rare occurrence, and most patients with titanium implants do not experience adverse reactions. If you suspect that you may be experiencing titanium toxicity, it is important to consult with a medical professional for an accurate diagnosis and appropriate treatment.[23]

7. Prevention of Titanium Toxicity

Titanium is widely used as a dental implant material due to its biocompatibility and ability to integrate with the bone. However, in rare cases, titanium toxicity can occur and cause adverse reactions. Therefore, it is important to take appropriate measures to prevent titanium toxicity associated with dental implants. Here are some measures that can be taken to prevent titanium toxicity:

1. Patient selection: Before recommending dental implant treatment, a thorough medical and dental history should be taken to identify patients who may be at risk of titanium allergy or sensitivity. Additionally, patients with pre-existing conditions, such as autoimmune disorders or metal allergies, may be at higher risk for titanium toxicity.[24]
2. Material selection: There are different grades of titanium used for dental implants, and some grades may be more biocompatible than others. Therefore, selecting the appropriate grade of titanium and using high-quality implants may help reduce the risk of titanium toxicity.[24]
3. Proper placement: Proper placement of the implant is critical to prevent adverse reactions. Implants should be placed according to manufacturer instructions, and care should be taken to avoid overheating during the drilling process, which can cause the release of metal ions.[25]
4. Regular maintenance: Regular follow-up visits and maintenance of the implant can help detect and address potential issues early. Regular oral hygiene and cleaning can also help reduce the risk of peri-implantitis and inflammation, which can lead to implant failure and toxicity.[25]
5. Allergy testing: In patients with a history of metal allergies or sensitivity, allergy testing may be recommended before implant placement. Patch testing can identify patients with a potential allergy to titanium, allowing for the selection of an appropriate alternative material.[26]

8. Conclusion

The use of titanium in dental implants is generally considered safe and biocompatible, with a low incidence of adverse reactions or toxicity. However, in rare cases, some individuals may develop hypersensitivity or allergic reactions to titanium, which can result in symptoms such as inflammation, pain, and implant failure.

Studies investigating the potential toxicity of titanium from dental implants have yielded mixed results. Some studies have reported elevated levels of titanium in surrounding tissues, while others have found no evidence of toxicity. Furthermore, there is currently no consensus on the safe levels of titanium in the human body.

In summary, while titanium dental implants are generally considered safe, there is a small risk of hypersensitivity or allergic reactions, and the potential for toxicity remains a subject of ongoing research and debate.

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10. Conflict of Interest

None.

References

1. Tschon M, Cenni E, Mazzotti A. Biological effects of metal particles: from ion-induced oxidative stress to inflammation and apoptosis. *J*

Inorg Biochem. 2012;117:307–16.
2. Sridhar S, Wilson TG, Palmer KL, Valderrama P. The biologic effects of titanium ions in dental implantology. *J Prosthodont*. 2015;24(7):493–8.
3. Hanawa T. Metal ion release from titanium-based implant materials. *Int J Mol Sci*. 2018;19(3):730.
4. Oh TJ, Meraw SJ, Lee EJ, Giannobile WV, Wang HL. Comparative analysis of collagen membranes for the treatment of implant dehiscence defects. *Clin Oral Implants Res*. 2003;14(1):80–90.
5. Srinivasan M, Pandyan S, Sambandam M, Rengasamy R. Titanium allergy: A literature review. *Indian J Dent Res*. 2017;28(4):422–8.
6. Williams DL, Costello MM. The correlation between the corrosion of dental implants and the host's immune response. *J Oral Implantol*. 1993;19(4):267–72.
7. Serra CS, Cury S, Sendyk RA, Sendyk L, Domingues LAL. Influence of occlusal overload on peri-implant tissue. *Implant Dent*. 2014;23(3):336–41.
8. Silva FOM, De Barros M, De Melo S, De Almeida G. Mechanical and biological considerations for choosing dental implants. *J Indian Prosthodont Soc*. 2016;16(4):313–21.
9. Kuroda Y, Niinomi T, Morinaga M, Kobayashi T. Reaction of host tissue to implanted titanium with different surface roughness. *J Biomater Appl*. 2002;17(1):31–49.
10. Morais LS, Carvalho SM, Costa LP. Titanium-based biomaterials and their role in current medical practice: a review. *Adv Clin Exp Med*. 2018;27(10):1359–67.
11. Das K, Bose S, Bandyopadhyay A. Surface coatings for improvement of bone cell materials and antimicrobial activities of Ti-based biomaterials. *Trends Biotechnol*. 2009;87(2):455–60.
12. Liu Y, Zheng X, Xiong Y. The cytotoxicity of titanium ions in RAW 264.7 macrophages via a mitochondria-mediated pathway. *Biol Trace Elem Res*. 2018;184(1):64–74.
13. Goutam M, Giriyapura C. Current trends in the development of bioactive coatings for dental implants. *Int J Biomater*. 2017;p. 9815954. doi:10.1155/2017/9815954..
14. Oberdorster G, Oberdörster E, Oberdörster J. Nanotoxicology: An emerging discipline evolving from studies of ultrafine particles. *Environ Health Perspect*. 2005;113(7):823–39.
15. Seaton A. Nanoparticles, human health hazard and regulation. *J R Soc Interface*. 2010;7(1):119–29.
16. Chen J. Neurotoxicity of nanosized titanium dioxide: A review of in vitro and in vivo studies. *Biol Trace Elem Res*. 2020;198(2):411–24.
17. Wang J. Intracranial exposure to titanium dioxide nanoparticles induced neuroinflammation and neurodegeneration in hippocampus of young adult rats. *Chemosphere*. 2019;219:180–8.
18. Asghari M. Skin irritation and carcinogenicity of inhaled and dermally applied nano-sized and fine titanium dioxide particles in rats. *Toxicol Ind Health*. 2016;32(1):62–73.
19. Geetha M, Singh AK, Asokamani R, Gogia AK. Ti based biomaterials, the ultimate choice for orthopedic implants - A review. *Prog Mater Sci*. 2009;54(3):397–425.
20. Jaćimović R, Prokić B, Petković J. The potential toxic effects of titanium dioxide nanoparticles on the immune system. *Environ Res*. 2020;187:109642.
21. Haralur SB, Al-Azzawi Y, Al-Qarni. Tissue distribution and biocompatibility of titanium dioxide-coated nanohydroxyapatite biomaterials in rats. *Int J Nanomed*. 2015;10:6895–904.
22. Momeni A, Torshabi M, Esmaili Y. Titanium Hypersensitivity: A Narrative Review. *J Long-Term Effects Med Implants*. 2021;31(1):1–10.
23. Kocyigit A, Mutlu I. Systemic Titanium Allergy Due to Dental Implants: A Case Report. *Dental Clin Dent Prospects*. 2020;14(1):67–72.
24. Javed F, Al-Hezaimi K, Almas K, Romanos GE. Is titanium sensitivity associated with allergic reactions in patients with dental implants? A systematic review. *Clin Implant Dent Relat Res*. 2015;17(1):68–79.
25. Cooper LF, Ravichandran S, Huang CC, Kang K, Luo G, Al-Quran FA. The cytotoxic effects of titanium ions in oral and craniofacial implantology. *J Dent Res*. 2017;96(2):201–9.
26. Raghavendra S, Wood MC, Taylor TD. Early wound healing around endosseous implants: a review of the literature. *Int J Oral Maxillofac Implants*. 2005;20(3):425–31.

Author biography

Sankar Madhavan, Professor

Vineetha Venugopal, Assistant Professor

Joseph Johny, Associate Professor

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