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Exploring Xenobiotic Sensing in Implant Dentistry: A Literature Review

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ABSTRACT:

Implant-supported rehabilitation is a well-supported evidence-based therapeutic strategy for replacing missing teeth in partially or completely edentulous patients, with predictable long-term success rates.[(1)] Dental implants are biomaterials used to regain lost chewing function and aesthetic in various edentulous cases. Dental implant materials are required to be non-allergic, sterilizable, biocompatible, and resistant to corrosion and occlusal loads[(2)]. Different materials have been used in the fabrication of dental implants; however, commercially pure titanium (Ti) is still the material of choice in implant dentistry.[(3)] Titanium is a transition metal with a silver colour, known for high strength and resistance to corrosion. Its outstanding capacity to incorporate into bone is a phenomenon termed "osseointegration".[(4)] Titanium has been considered a biological modulator of oral health. The ions and metal particles released may alter the interior physiological oral environment and initiate peri-implantitis or trigger a peri-implantitis flare[(5)]. Nevertheless, concerns have been raised regarding titanium's potential to induce hypersensitivity or inflammatory reactions in the host tissues which could lead to various complications in certain cases. It was reported that titanium ions may lead to systemic side effects such as hypersensitivity or allergy, and may disseminate to lymph nodes, liver and spleen in individuals with hip and knee prosthesis [(6,7)]. The purpose of this review was to compile the current evidence regarding the association between the release of titanium particles from dental implants and its biologic complications

Introduction

Xenobiotics are any substance foreign to the body. Xenobiotics include chemicals, infectious agents, bioaerosols, dusts, and other agents, such as proteins and allergens, to which the body responds[(4)].

Dental implants have emerged as transformative solutions for the rehabilitation of edentulous patients, restoring oral function and aesthetics. Titanium, due to its exceptional biocompatibility, mechanical strength, and corrosion resistance, remains the gold standard in implantology[(8)]. Despite its widespread acceptance, concerns regarding the release of titanium particles and ions from implants have gained increasing attention, necessitating a deeper understanding of their interactions with peri-implant tissues and systemic health.

The mechanisms behind implant-induced degradation and foreign body reactions are multifaceted, intertwining the fields of bioengineering, immunology, and materials science. The foreign body response has been explained, emphasizing the inflammatory reactions occurring at the tissue-implant interface.[(9)] This response is further compounded by oxidative stress, which plays a significant role in the generation of free radicals and tissue damage [(10)] Biocorrosion mechanisms lead to the release of titanium particles that accumulate in peri-implant tissues, triggering immune responses and potentially influencing implant longevity. [(11,12)] Titanium particles have been further highlighted for their detrimental effects on peri-implant health and survival, as they contribute to inflammation, bone loss, and potential implant failure[(13)].

Zirconia implants present potential benefits, such as enhanced biocompatibility and improved aesthetics, making them an appealing alternative to titanium. However, titanium remains the preferred choice in implant dentistry due to its well-documented clinical success, mechanical strength, and long-term stability.[14,15]

Beyond localized effects, systemic implications of implant-related degradation products warrant consideration. Detectable levels of trace metals (e.g., titanium, nickel) have been reported in saliva, posing questions about long-term exposure risks.[16] Oral inflammation has been identified as a key factor in the development of systemic diseases, reinforcing the strong connection between oral and overall health[17]

The role of oxidative stress is pivotal in understanding the broader biological impacts of titanium particles.[18] . The complex interplay between inflammation and immune responses to foreign materials has been thoroughly investigated, challenging conventional views on peri-implantitis and presenting alternative perspectives on implant-related complications[19,20]

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.[21]

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. [22]

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. [23]

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

This review aims to synthesize the wealth of evidence surrounding oral xenobiotics in implant dentistry. The goal is to provide a comprehensive understanding of the detection, sensing, and biological implications of titanium degradation products. Ultimately, this work seeks to inform future innovations in implant materials and techniques, improving patient outcomes and advancing the field of prosthetic dentistry.

Titanium Dental Implants and Biocorrosion

Titanium implants have long been regarded as the gold standard in prosthetic dentistry due to their superior biocompatibility, mechanical strength, and resistance to corrosion. However, research has illuminated critical aspects of titanium degradation in the oral environment, primarily due to biocorrosion mechanisms. Biocorrosion results from chemical, electrochemical, and mechanical processes, which are further exacerbated by the oral environment's unique challenges, such as fluctuating pH levels, bacterial biofilm activity, and enzymatic processes. The release of titanium particles and ions during this degradation process can lead to their accumulation in peri-implant tissues, potentially impacting implant success and patient health[11,12]

Titanium particles act as a contributing factor to peri-implant tissue inflammation and marginal bone loss, raising concerns about long-term implant stability[13] This insight underscores the importance of developing a deeper understanding of the environmental conditions and external factors that influence titanium's behaviour within the oral cavity.

Inflammation and Oxidative Stress: Localized and Systemic Effects

Inflammation and oxidative stress are central to the biological response to titanium degradation products. When titanium particles are released into the peri-implant environment, they can activate immune cells, leading to the release of pro-inflammatory cytokines and the recruitment of macrophages and neutrophils.[9] This immune response is a critical aspect of the foreign body reaction, which can significantly influence the healing process and long-term integration of the implant. Moreover, the inflammatory response can manifest in conditions such as peri-implantitis, characterized by tissue inflammation, bone loss, and ultimately, implant failure.[19]

Oxidative stress, a byproduct of inflammatory responses, involves the excessive production of reactive oxygen species (ROS) that can damage cellular structures, including DNA, proteins, and lipids.[10] This oxidative damage not only affects peri-implant tissues but can also

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have systemic consequences such as cardiovascular conditions, further highlighting the need for proactive measures to monitor and mitigate the release of titanium particles. [17]

Comparative Analysis: Zirconia vs. Titanium Implants

While titanium remains the preferred choice for dental implants, alternatives such as zirconia have garnered attention for their potential to address some of titanium's limitations. Zirconia, a ceramic material, is noted for its aesthetic qualities, biocompatibility, and resistance to corrosion. Zirconia implants exhibit comparable or even superior performance in terms of osseointegration and peri-implant tissue health.[14] However, the long-term clinical outcomes and cost implications associated with zirconia implants remain areas of active investigation, limiting their widespread adoption in implant dentistry.

Detection of Titanium Degradation Products

Advancements in analytical techniques have improved the ability to detect and quantify metal particles and ions released from dental implants. Utilizing salivary analysis to detect trace metals, including titanium, nickel, and vanadium is providing valuable insights into the localized and systemic exposure of patients to these xenobiotics.[16] These findings raise important questions about the potential toxicological effects of prolonged exposure to titanium degradation products, emphasizing the need for rigorous monitoring protocols.

Prevention of 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.[2]

Future Directions in Implantology

Emerging research has identified the need for interdisciplinary approaches to address the challenges associated with titanium implants. Innovations such as surface modifications, coatings, and nanostructured materials are being explored to enhance the bioactivity and corrosion resistance of implant surfaces. [20] Furthermore, the development of real-time sensing technologies for monitoring titanium ion release and oxidative stress in the peri-implant environment could pave the way for more precise and personalized implant care.

FUTURE SCOPE

Advancing Material Science Research should focus on developing implant materials with enhanced resistance to xenobiotics and reduced particle release. Zirconia surfaces and innovative coatings offer promising alternatives that warrant further exploration

Long-Term Toxicology Studies Comprehensive longitudinal studies evaluating the systemic and local effects of titanium degradation products are critical.

Integrating Multidisciplinary Research Addressing the challenges posed by xenobiotics and implant degradation requires interdisciplinary collaboration among materials scientists, toxicologists, microbiologists, and clinicians. Such efforts are essential for developing innovative solutions and improving patient care

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CONCLUSION

The interaction between xenobiotics, titanium implants, and peri-implant health represents a complex and multifaceted area of research. While titanium implants remain the gold standard in dental rehabilitation, addressing challenges posed by degradation products and foreign substances in the oral cavity is critical for advancing the field. Several studies have shown that the released Ti particles/ions might contribute to peri-implantitis through different mechanisms, such as foreign body reaction, cellular response of epithelial, gingival, inflammatory, and bone cells, epigenetic mechanisms namely DNA methylation and shaping the oral microbiome by favouring dysbiosis.(24) The concentration and size of these particles/ions depend on the implant's chemical composition and surface treatment applied to the dental implant. Innovations in surface coatings, material science, and digital workflows, combined with interdisciplinary research efforts, hold the potential to revolutionize implantology and ensure safer, longer-lasting solutions for edentulous patients.(25) However, further studies are urgently required to elucidate the complex interactions between all these mechanisms and Ti particles/ions in the pathogenesis and progression of peri-implantitis.(26)

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