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Titanium biocompatibility in oral tissues - A systematic review

(Biocompatibilidad del titanio en los tejidos orales: una revisión sistemática)

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Abstract(english)

Over the past decade, dental implants have gained widespread acceptance and adoption as a solution for replacing missing teeth and supporting various types of dental prostheses, including fixed and partially removable ones. Despite their generally high long-term success rates, with 96.1% survival after ten years and 83.8% after 25 years, implant failures remain a possibility. Major databases such as Medline were explored detailed literature search in resulting in a systematic review pertaining to titanium implants. Six scientific articles dated between 2020 – 2024 pertaining to titanium implants were highlighted. Discussion - Recent years have seen a significant increase in evidence suggesting that inflammation induced by bacterial biofilms around implants can lead to complications affecting both soft and hard tissues, ultimately resulting in implant failure. This inflammatory state is identified as peri-implant mucositis and peri-implantitis, highlighting the importance of vigilant periodontal and prosthetic maintenance in implant care.

Keywords(english)

Titanium, prosthodontics, implant, dentistry, maxillofacial.

Resumen(español)

Durante la última década, los implantes dentales han ganado una amplia aceptación y adopción como solución para reemplazar dientes faltantes y soportar diversos tipos de prótesis dentales, incluyendo las fijas y parcialmente removibles. A pesar de sus tasas de éxito a largo plazo generalmente altas, con un 96,1% de supervivencia después de diez años y un 83,8%

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después de 25 años, los fracasos de los implantes siguen siendo una posibilidad. Se exploraron importantes bases de datos como Medline mediante una búsqueda bibliográfica detallada que resultó en una revisión sistemática relacionada con los implantes de titanio. Se destacaron seis artículos científicos fechados entre 2020 y 2024 relacionados con implantes de titanio. Discusión: En los últimos años se ha visto un aumento significativo en la evidencia que sugiere que la inflamación inducida por biopelículas bacterianas alrededor de los implantes puede provocar complicaciones que afectan tanto a los tejidos blandos como duros, lo que finalmente resulta en el fracaso del implante. Este estado inflamatorio se identifica como mucositis periimplantaria y periimplantitis, lo que resalta la importancia del mantenimiento periodontal y protésico vigilante en el cuidado de los implantes.

Palabras clave(español)

Titanio, prótesis, implantes, odontología, maxilofacial

Introduction

Titanium, an illustrious transition metal boasting atomic number 22, stands as a cornerstone in the creation of dental implants (1,2). Its biocompatibility, first acknowledged by Gottlieb Leventhal in 1951, stems from its inert behaviour within living tissue (1). Bengt Kasemo expanded upon this, attributing titanium's superior qualities as an implant material to the ultra-thin oxide layer, measuring 2–10 nanometers thick, that swiftly forms upon exposure to oxygen. This oxide layer endows titanium with high polarization resistance, shielding it against corrosion and preventing the release of metallic ions into the body (3,4). Additionally, the surface oxide film's high dielectric constant makes it an ideal site for chemical bonding and the attachment of various biomolecules (5).

Materials and methods

“Titanium” AND “implant” AND “biocompatability’’ were the words used in MEDLINE database using advance search strategy targeting different article categories between 2020 to 2024. The result was 41 articles, out of which we selected 6 articles based in the inclusion criteria. Inclusion criteria was of scientific literature between 2020-2024. Exclusion criteria was of scientific literature devoid of scientific literature irrelevant to the specific search ‘Titanium’. This systematic review was conducted to determine importance of podoplanin following the guidelines of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). PubMed, Lilacs, Embase, Scopus, and Web of Science were the source of electronic databases. The search strategy used Boolean operators (AND and OR): [ALL (“Titanium”) AND (implant OR biocompatability OR prosthodontics OR oral OR rehabilitation OR dentistry) AND (prostheses)]. The following data were collected: first author, year, country of study, type of study and outcome. The quality of studies was assessed using the STROBE (Strengthening the Reporting of Observational Studies) checklist.

Results

Six articles were included in this systematic review based on the selection criteria and PRISMA flow chart. We analyzed and mentioned in the articles reviewed. This included only relevant research articles and excluded articles pertaining to non specific search terms (table 1).

Discussion

The bioactivity, osseointegration, and biocompatibility properties of titanium play pivotal roles in fostering bone formation directly onto the metal surface following dental implant placement, thus contributing to the exceptional survival rate and effectiveness of titanium dental implants (6,7). Osseointegration, crucial for implant success, involves the interplay between living bone and titanium/titanium alloy dental implants, particularly within the interfacial zone measuring 21 to 50 nanometres. Here, bone cells release essential growth factors, facilitating bone formation around the implants.Moreover, blood plasma proteins deposit onto the surface oxide layer of titanium dental implants post-implantation, triggering the formation of fibrin matrices. These matrices act as scaffolds, providing a conducive environment for bone-forming cells to reside and promoting bone formation to anchor the implants (8,9).An exemplary titanium dental implant, the OsseoSpeed implant from DENTSPLY Implants, debuted in 2004. Its unique surface texture is achieved through two sequential manufacturing steps: titanium oxide blasting followed by hydrofluoric acid etching (10–12). Ellingsen et al. conducted studies on OsseoSpeed implants using a rabbit model, revealing significantly greater removal torque, shear strengths, and bone-to-implant contact levels compared to controls after 1 and 3 months of healing (13).Clinical trials further underscore the success of OsseoSpeed implants. Mertens and Sterling evaluated 42 implants over five years, reporting an impressive 97% survival rate and minimal marginal bone loss. Raes et al. documented a one-year survival rate of 98% with OsseoSpeed implants in the anterior maxilla, while Collaert et al. observed a two-year survival rate of 100% in edentulous patients treated with OsseoSpeed mandibular implants (14,15). These findings reinforce the efficacy and longevity of OsseoSpeed implants in clinical practice.Despite the successful application of titanium implants, research has constantly aimed to develop advanced titanium alloying techniques to optimize biocompatibility and mechanical properties. However, Ti implants usually cannot be placed in narrow bones such as the anterior alveolar ridge (16). In addition, close proximity between the implant and neighbouring teeth could cause bone loss. Thus, different titanium alloys have been developed to improve the mechanical strength for applications requiring small-diameter implants (≤3.5 mm) (17). Titanium–6aluminum–4vanadium is one of the most commonly used titanium alloys. Ti alloy's most commonly used product in dental implants is Ti–6Al–4V, known as Grade V titanium alloy, composed of 6 and 4% aluminium and vanadium with the addition of a maximum of 0.25% of iron and 0.2% of oxygen. Ti–6Al–4V yields better strength and fatigue features, excellent corrosion resistance, and an improved elastic modulus compared to cp-Ti. Specifically, vanadium has been demonstrated with high cytotoxicity, and aluminium might play a role in inducing senile dementia. However, a safety risk is posed due to the release of toxic vanadium and aluminium ions. Titanium–nickel is also limited due to nickel hypersensitivity (18).When compared, titanium alloys incorporating other beta-phase stabilizers such as tantalum, molybdenum, niobium, and zirconium have garnered increased attention as materials for medical applications due to their non-toxic and non-allergenic properties (19). Zirconium shares the same crystal structure as titanium and exhibits complete mutual solubility with it (20). Titanium–zirconium alloys (TiZr) have exhibited enhanced corrosion resistance, improved tensile and fatigue strength, and comparable biocompatibility to titanium (21,22) Notably, titanium and zirconium are the only metals that do not inhibit osteoblast growth, making a combination of both well-suited for implants (3).One such TiZr alloy, known as Roxolid®, developed by Straumann AG (Basel, Switzerland), contains 13 to 17% zirconium. Its surfaces undergo pretreatment involving large-grit (0.25–0.5 mm) aluminium oxide sandblasting and acid etching using hydrochloric and sulfuric acid. In a study by Gottlow et al., significantly

Table 1. An overview

S.NO.	Author	Year	Journal	Outcome
1	Kheder W, Al Kawas S, Khalaf K, Samsudin AR.	2021	Jpn Dent Sci Rev.	Relation between the presence of titanium particles and ions, biological complication, and corrosion
2	Eftekhar Ashtiani, Reza et al.	2021	*Evidence-based Complementary and Alternative Medicine*	Dental pulp regeneration, the healing process, and antibacterial and anti-inflammatory effects.
3	Dr Madiha Umar, Tayyaba Bari, Dr. Fahimullah, Rimsha Qasim, Hadia Khursheed, Dr. Robina Tasleem, & Dr. Hafiz Mahmood azam.	2024	Journal of Population Therapeutics and Clinical Pharmacology	Improved patient outcomes and enhanced clinical practices.
4	Roy M, Corti A, Dominici S, Pompella A, Cerea M, Chelucci E, Dorocka-Bobkowska B, Daniele S.	2023	*Journal of Functional Biomaterials.*	Do not produce cytotoxic or proinflammatory effects on gingival fibroblasts,
4	Silva RCS, Agrelli A, Andrade AN, Mendes-Marques CL, Arruda IRS, Santos LRL, Vasconcelos NF, Machado G.	2022	Materials (Basel).	Nanobiotechnological surface modifications
5	Hoornaert A, Vidal L, Besnier R, Morlock JF, Louarn G, Layrolle P.	2020	Clin Oral Implants Res	Favorable surface modification, phase control, and mechanical properties.
6	W. Nicholson J.	2020	Prosthesis	Alloys cpTi and Ti-6Al-4V

higher removal torque and bone area were observed in vivo for a titanium–zirconium alloy compared to commercially pure (cp) titanium (23).Furthermore, it was observed that the oxides on titanium–zirconium alloy surfaces are more stable and have favourable corrosion resistance (24). Moreover, the alloying of titanium with zirconium improves the mechanical strength, especially for applications in small-diameter implants (22). While the mechanical strength is high for titanium–zirconium alloys, they are well suited for implantation in the cortical bone due to a low Young's modulus, which prevents stress shielding (25). The effect of Zr on the increase in mechanical properties and its ability to influence the etching process were identified as causes for these differences (26). Increased mechanical properties were responsible for fewer structural changes on TiZr during sand blasting. TiZr increased integrin-beta3 mRNA and protein levels compared with Ti in an in vitro study by Gomez et al. Cells on TiZr surfaces showed higher MMP1 protein levels than Ti surfaces, although similar TIMP1 protein production was observed (27), suggesting that TiZr is a potential clinical candidate for soft tissue integration (28).

Moreover, the incorporation of zirconium into titanium alloys has been noted to impact their corrosion resistance and serve as a catalyst in the generation of hydrogen during etching and hydridation processes. Additionally, the mechanical characteristics of titanium–zirconium alloys permit the placement of small-diameter implants in critical implantation sites, such as the anterior region of the mandible, where bone volume is limited, and crestal bone thickness is substantial. An alternative alloy formulation may involve titanium, tantalum, niobium, and zirconium, exhibiting cytocompatibility similar to commercially pure titanium (cpTi) but eliciting a reduced inflammatory response and enhanced osseointegration. For instance, titanium–tantalum–niobium–zirconium (with possible additions of silicon and iron) demonstrated improved cytotoxicity compared to the Ti–6Al–4V alloy. (29).Although adverse effects of these components have yet to be observed when utilized in the form of titanium alloys for dental implants, it is advisable to exercise extra caution and conduct long-term evaluations to address safety concerns. Animal studies have indicated the superior mechanical properties of titanium alloy compared to titanium alone when employed as a material for tooth implants. The biological responses to these alloys have been investigated in vitro (30). It has been observed that the composition of the alloy has favourable effects on its microstructure, consequently influencing its mechanical properties. However, there remains a scarcity of randomized, controlled clinical trials concerning the alloying of titanium. A review conducted by Wennerberg et al. found limited clinical evidence thus far to support a preference for alloying titanium over using zirconia or titanium alone.

In a split-mouth study comparing titanium alloying with titanium alone, utilizing early loading protocols in irradiated patients, one hundred and two implants were placed in twenty patients across both jaws. Following a one-year follow-up, excellent yield strength and fatigue properties were observed for all implants, resulting in higher survival rates and minimal marginal bone loss (<0.4 mm) in all patients, with no significant difference noted between the groups. However, it was noted that alloying with titanium exhibited low wear resistance, a higher elastic modulus approximately 4–10 times that of human bone, and lower shear strength, potentially impacting its utility as implants or in screw form. (1)The surface treatment of titanium holds paramount importance in ensuring the successful osseointegration of implants into bone tissue. Inadequate healing of the implant can lead to severe complications such as infection, inflammation, aseptic loosening, or the stress-shielding effect, necessitating reoperation. Following the implantation of a titanium graft, various interactions are critical for establishing a robust bone-implant interface. Cell adhesion to the implant surface is essential, with surface roughness playing a pivotal role in enhancing and expediting osseointegration. Equally crucial factors include biocompatibility and resistance to bacterial colonization.(31)Titanium's bio-inertness is attributed to the spontaneous formation of a protective film of titanium oxides on its surface. This film acts as a barrier against the ingress of metal compounds while facilitating the adhesion of calcium and phosphate ions necessary for mineralized bone structure formation. However, the mere presence of this film does not ensure titanium's biocompatibility; an appropriate surface finish is imperative to establish a secure bone-implant connection. The methods utilised to enhance the cell adhesion by increasing the surface roughness encompass a range of techniques including plasma spraying, sandblasting, acid etching, laser treatment, and sol-gel, categorized into three overlapping groups based on the type of modification.(31)However, altering the surface morphology of titanium without affecting its chemical composition, and vice versa, presents a challenge. Etching processes applied to titanium for surface modifications increase the hydrogen content on the titanium surfaces, forming titanium hydride as hydrogen ions attach to the outer surface layer. The degree of this process depends on factors such as the acidity of the solution and the duration of etching. Studies suggest that higher hydrogen content facilitates faster healing and enhances osseointegration. Thus, cathodic polarization is employed to increase the thickness and concentration of the titanium hydride layer. Videm et al. demonstrated that surfaces with higher hydrogen content exhibit 60% greater retention in in vivo models. Moreover, hydridation enhances the attachment of biological molecules, which bind to the surface alongside hydrogen.(1)While the oxide layer on titanium is a significant feature, attempts to increase biocompatibility solely by thickening this layer through anodic oxidation in acidic solutions have not shown notable improvements. However, hydroxylation in alkaline solutions can increase the presence of hydroxide groups on the surface.(1)Modifying the chemistry of implant surfaces involves various chemical processes to enhance their physical and mechanical properties. Such alterations lead to improved performance and longevity of dental implants. Chemical treatments for surface modification can be categorized into acid treatment, alkali treatment, hydrogen peroxide usage, and anodic oxidation. Anodic oxidation aims to thicken the titanium oxide layer on implant surfaces, while hydrogen peroxide creates a porous outer layer and dense inner oxide layer, enhancing corrosion resistance. Alkali and acid treatments focus on improving biocompatibility.(1)Surface modification of titanium and its alloys, such as Ti–6A1–4V and cpTi (commercially pure titanium), involves oxidizing titanium (IV). These changes significantly boost the adhesion of osteoblasts and the oxide layer, thus improving their biological properties for dental implant applications. Nonetheless, such alterations may trigger an immune response and fibrosis around the implants as chemically modified surfaces can be more readily recognized by the body as foreign, leading to the release of fibrotic factors (32). Abrahamsson et al. conducted a comparative analysis of peri-implant tissues focusing on titanium and gold alloys. Thirty-two titanium implants were surgically placed in five dogs, with the distance from the abutment–implant junction to the first bone–implant contact serving as a measure of actual bone loss. Histometric findings revealed that bone loss was 0.78 mm around titanium (serving as the control implant), 0.80 mm around the alloy, 1.80 mm around zirconium, and 1.26 mm around the dental porcelain implant. Clinical assessment highlighted significant soft tissue recession around the alloy implant. Piattelli et al. noted a distinction in peri-implant tissue stability between titanium abutments versus those made of gold alloy, zirconia, and aluminum oxide. Their study, drawing on various sources including dental implants, prosthetics, and periodontal journals, encountered challenges regarding the accuracy of soft tissue measurements. Notably, peri-implant tissues around zirconia and titanium were primarily defined through histological and animal studies. Consequently, the heterogeneous nature of research methodologies, follow-up durations, and outcome variables hindered meta-analysis efforts. For instance, titanium abutments did not exhibit superior bone level maintenance compared to those made of gold alloy, aluminum oxide, or zirconia. Additionally, comprehensive clinical performance data comparing zirconia and alloy to titanium were lacking.A study comparing the reaction of peri-implant tissues to titanium and alloy implants was conducted in dogs. Bone loss, measured from the implant–abutment junction to the first bone–implant contact, revealed a bone loss of 0.78 mm around the titanium implant and 1.80 mm around the alloy implant (33). In another investigation, 12 implants were placed in six monkeys to compare zirconia and titanium implants. No discernible difference was observed between the treatment groups receiving either material implant. Furthermore, the capacity to establish stable peri-implant tissues was assessed using single-piece alloy and titanium implants. The findings demonstrated a vertical expansion of soft peri-implant tissues from the mucosal margin to the initial bone–implant contact (34). A histological examination investigating the soft tissue response to titanium and zirconium healing caps/abutments was conducted in a cohort of five patients. Six months post-implantation, gingival biopsy specimens were obtained from both test and control implant sites. Results indicated a higher prevalence of inflammation in titanium specimens compared to zirconium counterparts. Furthermore, the composition of peri-implant tissue among tested abutments was delineated through comparisons involving single-piece soft tissue samples from aluminium oxide and titanium implants in twenty patients (33). A four-year randomized trial employing a split-mouth design compared the response of peri-implant tissues to titanium and gold alloy implants restored with metal–ceramic crowns in twenty patients. Each patient received two implants, one gold alloy and one titanium. After four years, no significant difference was noted in the peri-implant tissue response to gold alloy or titanium implants. Additionally, a clinical randomized controlled multicentre study compared aluminium oxide and titanium implants. In the first phase, thirty-four test sintered aluminium oxide abutments were placed alongside thirty-five control implants and followed up for one year. Subsequently, fifteen patients underwent placement of ten test and ten control abutment implants, with a follow-up period of three years. Results indicated negligible bone loss around ceramic implants in the first group, while the second group exhibited a loss of 0.3 mm after one year and a gain of 0.1 mm after three years (35).Furthermore, a five-year study aimed to discern differences between ceramic and titanium implants. Thirty-two patients received a total of 103 implants, with fifty-three aluminum oxide ceramics being utilized. Notably, soft tissue around both implant types remained healthy. In terms of peri-implant mucosal bleeding, no distinction was observed between ceramic and titanium implants. However, less bone loss was observed with titanium abutment implants compared to ceramic implants (35).

Conclusion

Dental implants, especially those crafted from titanium and its alloys, have transformed the landscape of tooth replacement therapy. Their remarkable longevity in clinical settings underscores their effectiveness in reinstating both oral function and aesthetics. Titanium's compatibility with biological tissues and its ability to integrate seamlessly into the surrounding bone make it an ideal choice for dental implants, with the protective oxide layer playing a pivotal role in preventing corrosion and fostering bone growth around the implant. However, ongoing research in titanium alloys seeks to improve their mechanical properties and broaden their applicability, especially in cases where bone volume is limited. Titanium-zirconium alloys, in particular, have emerged as promising alternatives, offering enhanced corrosion resistance and mechanical strength compared to pure titanium. Furthermore, surface modifications of these alloys contribute to their biocompatibility and facilitate better integration with the adjacent tissues. Studies focusing on peri-implant outcomes emphasize the critical role of material selection in influencing tissue response. While titanium implants generally exhibit positive results, comparative analyses with materials like zirconia and gold alloys reveal varying tissue reactions and rates of bone loss. Insights from clinical trials provide valuable guidance for treatment decisions, ultimately optimizing patient outcomes. Looking ahead, ongoing research efforts into implant materials and surface enhancements hold the promise of further improving implant success rates and enhancing patient satisfaction. Long-term clinical investigations and advancements in material science will continue to propel innovation in dental implantology, ensuring the delivery of optimal outcomes for individuals seeking tooth replacement therapy.

Conflict of interest

None to declare

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