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Titanium Dental Implant Hypersensitivity: A Review Article

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ABSTRACT

Titanium and its alloys have been the material of choice for dental implants since decades. Although, titanium is considered a biocompatible element reports of allergic reactions to titanium and its alloys have emerged over time. Whether dental implants can potentially induce hypersensitivity reactions or not is still debatable. The present paper discusses available literature on metal hypersensitivity including that induced by titanium and its alloys. It also discusses available tests for detection of metal hypersensitivity and the mechanisms through which titanium and its alloys may trigger hypersensitivity reactions in tissues, including that in the oral environment.

Key words: Allergy, Dental Implant, Titanium, Hypersensitivity

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INTRODUCTION

Titanium has been used widely in the field of medical as well as dental science especially as an intraosseous material, owing to its remarkable biocompatibility [1-3]. Apart from being biocompatible, titanium possesses several other favorable properties, one of which is its high resistance to corrosion [4]. Titanium when exposed to the external environment develops a thin oxide layer which makes it resistant to corrosion [5]. Biocompatibility and corrosion resistance coupled with other useful mechanical properties like low thermal conductivity, good ductility, high strength and low weight as compared to other metals,4 has helped titanium maintain its status as the material of choice in orthopedic as well as dental implants [6,7]. Though, it has been believed widely that titanium is non-allergenic material in nature, instances of hypersensitivity to titanium have been reported in the literature.

Roitt et al. [8] have defined a hypersensitivity reaction as “an acute immunological response that occurs when coming into contact with a known antigen.” Type IV hypersensitivity reactions have been seen to be associated with implant related allergic reactions [9]. It is a T-cell mediated response and may occur in hours to days of contact with the allergen, hence called delayed hypersensitivity.10 Hypersensitivity to implants has not been discussed much in dentistry, but some common symptoms which have been reported in the medical literature include edema, redness, urticaria, pruritus, and eczema [10-13]. Advanced symptoms include atopic dermatitis [14] and necrosis [13].

DENTAL AND OROFACIAL ALLERGIC REACTIONS

Dental and Orofacial allergic reactions usually manifest themselves in the form of oral mucosal erythema, purpura of the palate, hyperplastic gingivitis, loss of papillae of the tongue, angular cheilitis and lichenoid reactions [15,16]. In dental implants, facial erythema and proliferative hyperplastic tissue along the dental implant have been reported [17-20].

Titanium dental implants may release titanium ions into the periodontal ligament tissue, which is capable of causing inflammatory changes at and surrounding the area of the dental implant. This inflammatory reaction leads to the activation of macrophages which in turn release cytokines which are known biomarkers of diseases. These titanium ions combine with endogenous proteins to form antigens which lead to Type IV or delayed hypersensitivity reactions [16,21]. Several diagnostic tests have been introduced to test for allergens. Some of which are as follows:

Patch test: It is the most commonly used test to detect allergies to substances. It is also called the epicutaneous test. In this test the presumed allergen is applied on the skin of the patient preferably at the back. The skin exposed to the allergen is usually examined after 48 to 72 hours for the presence of any changes like redness, edema, vesicle formation etc. Titanium oxide has been used for such patch tests. 0.1-0.2% titanium sulfate solution and titanium chloride have also been suggested to be used as reagents in place of titanium oxide. Not many such studies have been conducted on dental implants and such tests have limited applicability due to their poor sensitivity in Type IV hypersensitivity reactions [16,22,23].

Prick test: It is usually employed to test Type I hypersensitivity reactions and gives quick results. The presumed allergen is injected intradermally and the area around the injection site is examined after 15 to 30 minutes. It lacks application in checking dental implant sensitivities [16,24].

Lymphocyte transformation test (LTT)/ Memory Lymphocyte Immuno Stimulation Assay (MELISA): Cells of the patients in vitro are exposed to the presumed allergen and T cell proliferation is observed.25 It relies on the incorporation of tritiated thymidine by the T cells.23 Some studies have also reported the occurrence of false-positive results in such tests. This tests had been greatly popularized in testing metal allergies in the past, but studies suggest otherwise [25,26].

Blood test: It may aid in detection of allergy to titanium [23].

Since, all these tests lack applicability in testing hypersensitivity to implant materials, there is a need to develop newer methods to detect allergies to metals used as implant materials.

CORROSION IN DENTAL IMPLANTS

Titanium and its alloys have been considered to be fairly resistant to corrosion, yet reports of corrosion in titanium alloys have been documented in the literature. The different types of corrosion that titanium alloys may be prone to are as follows:

Galvanic corrosion: This is a common type of corrosion occurring in titanium implants which occurs due to contact of the titanium implant with that of other metallic restorations in the oral cavity. This results in the production of galvanic current and may also result in pain [27-30].

Crevice corrosion: It generally occurs due to the geometry of implant assembly. Localized crevice assault may occur on exposure of the implant to heat or solutions containing chloride, bromide or iodide ions during various procedures. There is increase in the concentration of these ions around the crevice which leads to decrease in the pH and finally degradation of the protective oxide layer around titanium, leading to the corrosion of the implant [30,31].

Erosion corrosion: This type of corrosion occurs when saliva containing corrosive compounds like food particles and certain enzymes, comes in contact with high velocity [32]. Titanium is relatively resistant to saliva and other fluids carrying suspended solids, therefore this type of corrosion occurs due to continuous attack of such corrosive fluid inducing local changes and removal of metal or cement material of the implant. This may additionally give rise to crevice or galvanic corrosion [27].

Stress corrosion cracking: This type of corrosion relies on a combination of three factors for its occurrence, namely tensile stress, an alloy susceptible to corrosion, and an environment conducive to corrosion. Tensile stresses may develop as a result of residual stresses during implant fabrication/ machining and functional/ occlusal loading. Implants may have minute crevices or pits which may be differentially exposed to stresses leading to stress corrosion cracking [27,33].

Even though it has been proved that titanium alloys exhibit better corrosion resistance as compared to Co–Cr and stainless steel alloys, their corrosion over time may result in dissolution and leaching out of titanium ions and other alloy materials like aluminium and molybdenum into the oral environment which may provoke a host response. This host response may induce cytokine production and hence hypersensitivity reactions [27,34].

DISCUSSION

Titanium has become the material of choice for the fabrication of appliances in medical as well as dental field due to its extraordinary properties, especially. its biocompatibility. But, it is worth remembering that there exists no material which can be said to be 'universally biocompatible' [27,35]. When it comes to materials that are used in dentistry including implants it has been noted that dental biomaterials have the capacity to release certain substances that can potentially affect the oral environment and hence induce hypersensitivity reactions [27,36,37]. Therefore, the release of such substance, which are usually in the form of ions into the oral environment, their redistribution into the body of the patient and accumulation are major concerns related to the choice of material in dental implants. Also, the potential toxicity and risks associated with the release of ions in the oral environment and the body raise genuine health concerns since these implants are intended for lasting a lifetime. Such reactions will also affect the longevity of the implants [22,38]. Therefore, studies are now being increasingly conducted to check the hypersensitivity or allergic reactions caused by materials used for dental implants, esp. titanium and its alloys.

Allergic reaction to a metal is spawned by the reaction of metal ions with skin and mucosa or by corrosion of the concerned metal used, particularly in case of an implant. Metal ions often form bonds with native proteins to produce haptens which can elicit antibody production and hence allergic reactions. These ions also possess the potential to precipitate the degranulation of mastocytes and basophiles, which again may induce allergic reactions [9,39]. Foussereau et al. [40] were the first to report hypersensitivity in a patient to a steel orthopaedic fracture implant. Many identical reports of hypersensitivity reactions have been reported thereafter [5].

Bone loss induced by corrosion has been speculated to be a major cause of late loosening of implants [41] Lalor et al. [42] in their study discovered presence of huge amounts of titanium ions in failed hip implants of patients. They concluded that the primary factor behind the failure of these implants was allergic reaction to the titanium alloy used in the implants. They also found evidence of T-lymphocytes at the reaction site suggestive of Type IV hypersensitivity reaction. Witt et al. also documented failed hip implants due to corrosion. They reported that in the titanium implants another layer of TiO_2 was formed rapidly following corrosion, a phenomenon termed as 'repassivation'. A lot of TiO_2 was formed at the implant site, so much so that the surrounding tissue turned black [42,43]. Huber et al. [41] established a link between implant corrosion and hypersensitivity. They performed microscopic examination of perimplant tissue from 11 patients with loose articular implants with unusual deposits. Evidence of hypersensitivity reaction was found in all the cases indicating a possible relationship between the two. Instances of allergic reaction to implanted pacemakers with titanium casing have also been documented by Yamauchi et al. [24], Sicillia et al. [1] used the cutaneous tests (Prick technique) to test Type I Hypersensitivity to titanium and epicutaneous tests to test for Type IV/ Delayed hypersensitivity on 35 patients. In the cutaneous tests, a drop of 1% and 5% titanium oxide was introduced to the skin on the forearm of the patient and a puncture in the skin was made using a lancet. Reaction to the titanium oxide was noted. In the epicutaneous tests, the same concentrations of titanium oxide were placed on the skin at the back of the patient and covered with a waterproof dressing. Reaction to the substance was noted at 24, 48 and 72 hours to check for signs of Type IV hypersensitivity. Eight patients in the study displayed positive tests.1However, it has been reported that cutaneous and epicutaneous tests are only effective in testing contact sensitivity to allergens and no standard patch test has yet been developed to test allergy to titanium [27].

Several factors contributing to oral implant failures have been reported in various studies. Tonetti et al. stated that peri-implant infection, biomechanical overload, or a combination of the two could be the possible factors involved in the late implant failures [44]. Piattelli et al. [45] proposed that infection of the surrounding implant tissue could be associated with early as well as late implant failures, loss of osseointegration without infection could be associated with late failures and fracture of the implants could be associated with late failures. Researchers over the years have classified implant failures in different ways. Esposito et al. [46] classified implant failure on the basis of biological, mechanical, iatrogenic and patient-related factors.5 Additionally, increased risk of implant failures has been reported in patients with diabetes mellitus and those undergoing head and neck radiation therapy [47,48]. Preez et al. [49] authored a case report of implant failure due to hypersensitivity reaction to titanium. Egusa et al. [50] also reported presence of facial eczema suggestive of allergic reaction to a titanium implant over-denture in a patient.

Titanium alloys are the preferred choice instead of pure titanium in the construction of dental implants due to their greater strength. These alloys preferably contain aluminium and vanadium in addition to titanium, but other elements in smaller amounts may also be present in these alloys. These elements may serve as impurities and have been speculated to induce allergic reactions in several cases [51]. Harloff et al. [52] in their study performed a spectral analysis to assess the percentage of additional elements in titanium alloys which may act as potential allergens. They concluded that in all the examined titanium alloys certain elements other than aluminium and vanadium were invariably present. Common elements discovered in the titanium alloys were Nickel, Cobalt, Chromium, Beryllium, Copper, Iron and Palladium. Forte et al. [53] have highlighted various studies shedding light on the allergic potential of elements present consistently in titanium alloys. Many other studies elucidate the allergic potential of nickel, aluminium and beryllium [54-56]. On the contrary, Hasoki et al. [57] in a recent study examined 270 patients that visited a Dental Metal allergy Clinic for hypersensitivity to different metal allergens used in dental alloys. This included 4 titanium allergens as well. They placed the allergens on the skin at the back of these patients and sealed them with adhesive plaster. The skin of the patients was examined for signs of hypersensitivity at 2, 3 and 7 days after placement of the allergen. 80.4% of the 217 patients displayed positive allergic reaction to at least one of the allergens. Out of 270 patients 16 had dental implants. 11 patients displayed a positive allergic reaction to at least one of the allergens while 4 patients exhibited allergy to titanium allergens. Among the 270 patients, only 6.3% of the patients displayed hypersensitivity to titanium allergens [57], further asserting that most of the allergies to titanium alloys are a product of other metal impurities present in the alloy. On the contrary, Pioletti et al. [58] conducted a study to determine the cytotoxicity of various concentrations of commercially pure titanium (cp) on osteoblasts. They postulated that corrosion of titanium caused decrease in viability of osteoblasts which would in turn produce cytotoxic effects. Studies by Kwon et al. [59] and Wang et al. [60] have reiterated that prolonged experience to commercially pure titanium may produce cytotoxic effects. Also, Mine et al. [61] in their study indicated that prolonged exposure to titanium ions may adversely affect cells responsible for osseointegration including osteoblasts and osteoclasts. There is a lack of availability of epidemiological studies that demonstrate the prevalence of titanium hypersensitivity or hypersensitivity to titanium alloys in the general population [7].

CONCLUSIONS

Although, evidence-based studies on hypersensitivity to dental implant materials, especially titanium and its alloys are insufficient to prove that titanium dental implants are not biocompatible, yet reported instances of hypersensitivity induced by titanium and its alloys cannot be overlooked. Also, there is a need to develop tests that may accurately detect hypersensitivity to metals and alloys including that of titanium in the oral environment so that further studies on implant hypersensitivity may be conducted with ease. Clinicians should also check for hypersensitivity to titanium and its alloys in cases of implant failures.

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