Implants and Autoimmune Diseases

Implantlar ve Otoimmün Hastalıklar

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ABSTRACT

Osseointegration describes the process by which dental implants integrate and become fixed within bone. This process occurs following the placement of the implant into the bone and is characterized by the direct contact between the implant and the surrounding bone. Osseointegration is critical for the long-term stability and durability of implants.

Autoimmune diseases, particularly their effects on bone metabolism, can have an impact on osseointegration. In autoimmune diseases, immune responses can alter bone remodeling. This can negatively affect the osseointegration process, increasing the risk of implant failure.

For instance, autoimmune diseases such as Sjögren's syndrome, systemic lupus erythematosus, and systemic sclerosis are associated with dry mouth, mucosal inflammation, and periodontal diseases. As a result, bone loss may occur around dental implants.

However, it has been shown that dental implants can successfully osseointegrate in individuals with autoimmune diseases. Therefore, patients considered for implant treatment should be evaluated, individually taking into account the status and management of their autoimmune conditions. Additionally, regular follow-ups and maintaining proper oral hygiene after implant placement can enhance the success of the osseointegration process.

Keywords: *Dental implants, osseointegration, autoimmune diseases, oral mucosal diseases*

ÖZ

Osseointegrasyon, dental implantların kemikle bütünleşerek sabitlenmesi sürecini tanımlar. Bu süreç, implantın kemik içine yerleştirilmesini takiben gerçekleşir ve implantın çevresindeki kemik ile doğrudan temas kurmasıyla karakterizedir. Osseointegrasyon, implantların uzun vadeli stabilitesi ve dayanıklılığı için kritik öneme sahiptir.

Otoimmün hastalıkların, özellikle kemik metabolizması üzerindeki etkileri, osseointegrasyon sürecini etkileyebilir. Otoimmün hastalıklarda, bağışıklık sistemi yanıtı anormal şekilde aktive olabilir ve kemik remodelleme süreçlerini değiştirebilir. Bu durum, implantın kemikle bütünleşme sürecini olumsuz etkileyebilir ve implantın başarısız olma riskini artırabilir.

Örneğin, Sjögren sendromu, sistemik lupus eritematozus ve sistemik skleroz gibi otoimmün hastalıklar ağız kuruluğu, mukozal inflamasyon ve periodontal hastalıklar ile ilişkilidir. Buna bağlı olarak dental implantların çevresinde kemik kayıpları meydana gelebilir.

Ancak, otoimmün hastalığı olan bireylerde dental implantların başarılı bir şekilde osseointegre olabileceği gösterilmiştir. Bu nedenle, implant tedavisi düşünülen hastaların, otoimmün hastalıklarının durumunu ve tedavi planlamasını dikkate alarak implant tedavisine uygunlukları değerlendirilmelidir. Ayrıca, implant sonrası düzenli kontroller ve uygun ağız hijyeni sağlanarak osteointegrasyon sürecinin başarısı artırılabilir.

Anahtar Kelimeler: *Dental İmplantlar, osseointegrasyon, otoimmün hastalıklar, oral Mukozal Hastalıklar*

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INTRODUCTION

The importance of scientifically validated dental implant therapy is steadily increasing. Dental implants are frequently used in edentulous patients to ensure prosthetic stability and maintain oral health. The presence of sufficient bone quality and volume, as well as general health influence implant success.

Over the past two decades, increased life expectancy has led to a continuously growing elderly population and, consequently, an expansion of the medically at-risk group.[1] In this age group, the prevalence of chronic diseases such as cardiovascular disease, diabetes, hypertension, autoimmune disorders, and cancer has risen. These conditions may serve as relative contraindications during implant placement. Among these medical conditions, a subset of autoimmune diseases poses specific risks for oral mucosal health.

Autoimmune diseases are characterized by an abnormal immunological response to autoantigens, leading to organ-specific or systemic inflammatory tissue destruction. The hallmark features of autoimmunity include the presence of circulating T cells, autoantibodies, and chronic inflammation.

Although the exact etiology of autoimmune diseases remains largely unknown, genetic, endocrinological, and environmental factors such as diet, lifestyle, and exposure to infections are believed to play a role in their development. It is estimated that autoimmune diseases affect approximately 3% to 5% of the global population and occur more frequently in women. However, the underlying reason for this gender disparity remains unclear.[2]

In individuals with autoimmune diseases, wound healing and osseointegration may be adversely affected due to alterations in the immune system. Although many conditions in medically compromised patients are still considered as risk factors for dental implant prognosis, there are only a few absolute contraindications for this treatment modality. [3]

The aim of this article is to review, the potential risks and complications that can affect the outcomes of dental implant therapy in patients with autoimmune diseases.

DISEASES

Oral lichen planus

Oral lichen planus (OLP) is a chronic mucocutaneous inflammatory disease that can affect the skin and/or mucous membranes.[4] The etiology of OLP remains unclear; however, it is thought to involve a cell-mediated immune dysregulation triggered by genetic and environmental factors. Secondary contributing factors may include local irritants (such as metal dental restorations, trauma, smoking, and alcohol consumption), systemic diseases (including diabetes, hypertension, and anxiety), and the use of certain medications (such as antimalarials, antihypertensives, diuretics, and nonsteroidal anti-inflammatory drugs).[5] OLP is more commonly observed in women aged 40–60, with a reported global adult prevalence of approximately 1.01%.[6]]. Due to its 1.40% risk of malignant transformation, close follow-up is essential.[7] While a high prevalence of OLP has been reported in patients with hepatitis C infection in Japan and the Mediterranean, no such association has been observed in France and the United States.[8]

It is recommended that dental implant procedures be performed during the remission phase of OLP.[9]

Regular follow-up is crucial not only for the early diagnosis and treatment of conditions such as peri-implant mucositis and peri-implantitis, but also for the timely detection of malignant transformation. Delayed diagnosis of peri-implantitis may compromise the long-term success of the implant, while diagnostic delays in malignant lesions can significantly increase the malignancy associated mortality and morbidity.[9]

In a systematic review conducted by Moya et al. in 2020, the implant survival rate in patients with OLP was reported to be 93.88% and this figure is not statistically significant when compared to healthy individuals. The review emphasizes the importance of regular follow-up and oral hygiene practices in maintaining these high survival rates.[10] The same review also recommends a prophylactic glucocorticoid (deflazacort) regimen for implant placement in OLP patients: 30 mg of glucocorticoid (deflazacort) for two days prior to the procedure, 15 mg of glucocorticoid (deflazacort) daily for three days following the procedure, and 7.5 mg of glucocorticoid (deflazacort) daily for the subsequent three days.[10]

In a study comparing the marginal bone loss around dental implants placed in patients with active OLP, controlled OLP (receiving systemic corticosteroids) and healthy individuals, it is reported that bone loss is significantly higher in the active OLP group (2.53 ± 0.44 mm) compared to the controlled OLP group (0.75 ± 0.56 mm) and the healthy group (0.79 ± 0.73 mm).[11]

In a systematic review published by Chrcanovic et al. in 2020, the five-year implant failure rate in patients with OLP was reported to be 2.7%. The same publication noted that in OLP patients who developed squamous cell carcinoma, the implant failure rate was 90.6%; however, in none of these cases was osseointegration lost. Instead, the implants were removed along with the tumor.[9]

Patients with OLP can be rehabilitated with dental implants. Potential risks and complications that may affect treatment outcomes should be carefully evaluated by the clinician and clearly communicated to the patient.[10]

Sjögren's syndrome

Sjögren's syndrome (SS) is a chronic autoimmune disorder characterized by dry eyes and dry mouth due to an immune-mediated attack on the body's exocrine glands. SS is more prevalent in women than in men and is considered to be the second most common rheumatic autoimmune disease after rheumatoid arthritis.[12] Medications commonly used by this patient group, such as hydroxychloroquine, cyclosporine, and corticosteroids, should be taken into consideration during treatment planning.

SS has numerous effects on oral health, including xerostomia (dry mouth) due to reduced salivary flow, widespread dental caries, chronically inflamed mucosa, hypertrophic salivary glands, chronic candidiasis, angular cheilitis, increased plaque accumulation, and difficulties in swallowing and using prostheses. Because of their high susceptibility to dental caries, SS patients tend to experience tooth loss at an earlier age compared to the general population. Dental implants represent a prominent treatment option for SS patients who struggle with removable prostheses due to dry and sensitive oral mucosa.[13]

In a prospective cohort study published by Maarse et al. in 2022, 37 implants were placed in 17 patients with SS, and 26 implants were placed in 17 patients without SS for comparison. After 18 months of follow-up, implant survival was reported as 100% in the SS group and 96.2% in the control group. Marginal bone loss was observed to be 1.10 ± 1.04 mm in SS patients and 1.04 ± 0.75 mm in the control group. No statistically significant difference was found between the two groups in terms of clinical outcomes. Despite similar probing depths, SS patients demonstrated stronger signs of peri-implant soft tissue inflammation compared to non-SS patients. These inflammatory findings were suggested to be associated with decreased salivary flow in SS patients and the consequent reduction in the oral cavity's self-cleansing ability.[12]

Another review evaluated a total of 712 implants placed in 186 patients. Over a mean follow-up period of 72.5 ± 59.2 months, a failure rate of 4.1% was reported. Most implant failures were noted to occur within a few months following the surgical procedure. Consequently, due to the relatively low failure rate, dental implant therapy can be considered as a valid treatment option for patients with SS; however, the possibility of increased peri-implant bone loss compared to the general population should be taken into account.[13]

Rheumatoid arthritis

Rheumatoid arthritis (RA) is a chronic systemic disease that leads to cartilage damage and bone destruction. RA may be accompanied by comorbidities involving the cardiovascular, respiratory, hepatic, muscular, and skeletal systems.[14] This condition is commonly observed in individuals with the HLA-DR4 genotype. In RA patients, connective tissue disorders affecting the soft and hard tissues surrounding teeth and implants may also be present.[15] Although the pathogenesis and exact mechanism of RA remain unclear, several molecular factors that modulate its progression have been identified. At the molecular level, a range of cytokines and cyclooxygenase enzymes are known to trigger the inflammatory process. Tumor necrosis factor-alpha (TNF-α), interleukin (IL)-1β, and IL-6 have been reported to play significant roles in disease progression.[14]

In a study published by Alenazi et al. 3 groups of patients, each consisting of 14 individuals, were analyzed. The first group included systemically healthy individuals, the second group consisted of patients with only RA, and the third group included patients with RA accompanied by another connective tissue disease (7 diagnosed with systemic sclerosis, 4 with Sjögren's syndrome, and 3 with dermatomyositis). Bleeding on probing was found to be significantly higher in the second and third groups compared to the first group. Additionally, in patients with RA and a secondary connective tissue disorder, levels of IL-6 and TNF-α in peri-implant crevicular fluid were reported to be higher than in patients with RA alone and in healthy individuals.[14]

In a prospective study comparing implant survival rates between RA and non-RA patients, El-Sherbini et al. reported no significant differences between the two groups.[16]

A systematic review examining 12 studies on implant placement in RA patients reported a mean survival rate of 97.2% (353 out of 363 implants) after an average follow-up period of 50.8 months. These findings underscore the importance of close clinical monitoring in patients with RA.[2]

Systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is a chronic, autoimmune, multisystemic disease with a wide spectrum of clinical manifestations, affecting joints, tendons, kidneys, skin, blood vessels, as well as major organs such as the heart, lungs, and brain.[17] It has been reported that oral mucosal involvement occurs in approximately 40% of patients with SLE.[18]

SLE is more common in women and is typically diagnosed between the ages of 20 and 40.[19] Current treatment approaches include antimalarial agents such as hydroxychloroquine, nonsteroidal anti-inflammatory drugs, glucocorticoids, immunosuppressive agents (cyclophosphamide, methotrexate, azathioprine, mycophenolate mofetil), and biologics such as belimumab and rituximab[20] As with many autoimmune

diseases, the primary goal in managing SLE is to achieve disease remission or maintain low disease activity without flares.[17] Before prescribing new medications, a comprehensive medical consultation should be conducted to avoid organ damage and potential drug interactions.

Before initiating implant treatment, the possibility of avascular necrosis (osteonecrosis) due to steroid use, as well as potential reductions in bone quality and/or quantity, should be considered.[18]]. The femur is reported to be the most commonly affected site of avascular necrosis resulting from interrupted blood supply to the bone. The prevalence of symptomatic avascular necrosis ranges from 0.8% to 33%, while asymptomatic avascular necrosis has been reported in 29% to 45% of patients with systemic lupus erythematosus (SLE).[21] The mandible, due to its compact structure and limited vascularity, is also considered a susceptible site for necrosis.

Nevertheless, a separate systematic review examining the success of implant therapy in SLE patients reported a 100% implant survival rate.[18] In a cross-sectional study conducted on both SLE patients and systemically healthy individuals, no significant differences were found between the two groups in terms of periodontal parameters.[22]

Due to the use of corticosteroids and immunosuppressive medications, patients with SLE may have an increased susceptibility to infections. Therefore, surgical antibiotic prophylaxis should be considered in such cases.

Systemic sclerosis

Systemic sclerosis, an autoimmune disease, affects blood vessels and connective tissues through a series of pathophysiological processes including obstructive vasculopathy in small vessels, fibroblast inflammation, and subsequent immune dysregulation, ultimately resulting in the accumulation of extracellular matrix. The heart, lungs, kidneys, gastrointestinal tract, mucosa, and skin may be involved in the disease process.[23–25] Excessive collagen deposition in the skin and perioral tissues can lead to restricted mouth opening due to involvement of the orbicularis oris muscle.[26] Fibrosis of the salivary glands reduces salivary flow (xerostomia), impairing its antibacterial activity and buffering capacity, thereby contributing to dental erosion, caries, and periodontal disease. As a result, the use of mucosa-supported prostheses, oral hygiene practices, and dental treatments become increasingly difficult.[27,28]

In a systematic review published in 2023, implant survival rates were reported as 100% in case reports and 89.2% in case series. The review indicated that implant survival does not appear to be significantly affected by systemic sclerosis in patients who maintain good oral hygiene. The same publication also suggested that the use of short implants may serve as a viable alternative during implant surgery to facilitate manipulation in cases where mouth opening is restricted due to fibrosis.[29]

Crohn's disease

Crohn's disease is a progressive condition characterized by chronic inflammation of the gastrointestinal tract, which may also involve the oral cavity. It can affect any segment of the gastrointestinal system. In a typical clinical presentation, patients seek medical attention with complaints of abdominal pain, chronic diarrhoea, weight loss, and fatigue. The primary goal of current treatment strategies is to prevent complications and halt disease progression.[30] The prevalence of Crohn's disease is reported as 322 per 100,000 individuals in Europe, 319 per 100,000 in Canada, and 214 per 100,000 in the United States.[31]

In individuals with Crohn's disease, inadequate bone formation around implants may occur due to nutritional deficiencies and autoimmune inflammatory processes at the surgical site.[32]

In their study, Peron et al. reported successful osseointegration following the placement of implants measuring 11.5 mm in length and 3.75 mm in diameter. No signs of peri-implantitis were observed during the 2-year follow-up period. [33]

Further prospective clinical studies are needed to draw definitive conclusions regarding the effects of Crohn's disease on implant therapy.

CONCLUSION

It is evident that autoimmune diseases and their treatments can significantly influence the outcomes of implant therapy. Dental implant placement in individuals with autoimmune disorders requires special attention. Due to the inherent nature of these diseases characterised by immune system dysregulation, chronic inflammatory processes, and the use of immunosuppressive therapies implant success may be directly affected. According to the literature, each patient's individual immune status, systemic medication use, and tissue healing capacity should be carefully considered, and consultation with medical specialists is strongly recommended.

In this context, a multidisciplinary approach should be adopted when planning dental implants for individuals with autoimmune diseases. Patients' systemic conditions must be thoroughly evaluated, and long-term follow-up is imperative. Future large-scale clinical studies will contribute to the development of more specific clinical approaches aimed at improving implant success rates in this patient population..

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