Review

# Dental implants for patients with oral mucosal diseases: A narrative review and clinical guidance

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## Abstract

Oral mucosal diseases are a group of conditions that affect the oral mucosa with variable severity and include recurrent aphthous stomatitis (RAS), oral lichen planus (OLP), pemphigus vulgaris (PV), mucous membrane pemphigoid (MMP), and systemic lupus erythematosus (SLE). These may manifest clinically as painful oral ulcerations, reticulations and/or erosions, with differences between each. Management protocols often include initial topical and/or systemic corticosteroid (CS) therapy to control the patient's acute symptoms, followed by CS-sparing agents for long-term maintenance therapy. Patients with oral mucosal diseases often require dental implants to replace missing teeth. However, data on potential complications and success rates for these cases is still lacking. Considering the steady increase in the incidence of immune-related systemic conditions in the general population globally, dentists are expected to have the needed knowledge and ability to safely place dental implants in this group of patients. Therefore, this review aims to discuss the underlying pathogeneses of common oral mucosal diseases, clinical presentations, best practice approaches, and recommendations for the placement of dental implants in patients with similar conditions.

**Keywords:** dental implants, oral lichen planus, recurrent aphthous stomatitis, systemic lupus erythematous, vesiculobullous diseases

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# Background

For the past several decades, replacing missing teeth with dental implants has become the first choice for patients in need of better predictability, longevity and esthetics.[1] This preference can be attributed to factors such as the ability to preserve neighboring teeth, improved quality of life and the high survival rate of placed implants.[1] When compared to other available treatments, dental implants continue to be the closest option to mimicking natural teeth and restoring lost function.

Although the reported success rate of dental implants is approx. 95–98% in healthy subjects, the outcome data in patients with oral mucosal diseases is still lacking.[2–4] Oral mucosal diseases include a wide range of conditions that have a significant impact on the patient's quality of life, ranging from mild to more severe, such as recurrent aphthous stomatitis (RAS), oral lichen planus (OLP) and pemphigus vulgaris (PV).[2] Management protocols for these conditions often involve initial topical and/or systemic corticosteroid (CS) therapy to control the patient's acute symptoms, followed by CS-sparing agents for long-term maintenance therapy.[5] In some clinical scenarios, combinations of more than one agent with long-term follow-up are indicated for an optimal outcome.

Considering the steady increase in the incidence of immune-related systemic conditions in the general population globally, dentists are expected to have the needed knowledge and ability to safely place dental implants in this group of patients.[3] Therefore, this review aims to discuss the underlying pathogeneses of common oral mucosal diseases, clinical presentations, best practice approaches, and recommendations for the placement of dental implants in patients with these conditions.

# Recurrent aphthous stomatitis

## Overview

Recurrent aphthous stomatitis is a common chronic inflammatory disease characterized by recurrent, painful ulcerations of the oral mucosa.[6] The estimated prevalence of RAS ranges from 5% to 25% in the general population and can reach up o 60% in selected groups with higher stress levels, such as students or professionals in demanding jobs.[6,7] Recurrent aphthous stomatitis is most commonly diagnosed in young patients, with a peak onset between 10 and 29 years of age and a female predominance.[6] The etiology of RAS is still unknown but it is reported to be hereditary with multiple implicating factors such as stress levels, oroantral microbiota, and deficiencies in iron and vitamin B complex.[8] Clinically, RAS manifests as a painful ulcer or multiple ulcers, covered by a grey-yellowish pseudomembrane, and surrounded by an erythematous halo on the non-keratinized oral mucosa (Fig. 1).[9] There are several types of RAS, including minor, major, herpetiform, or complex type. The type of RAS determines the selection of the most suitable treatment approach (Table 1).

## Management

In order to diagnose RAS, other potential causes (e.g., iron, vitamin $B_{12}$ or folate deficiencies and trauma) and underlying medical conditions such as Crohn's disease, ulcerative colitis, Behçet's disease, and systemic lupus erythematosus (SLE), which may present clinically with

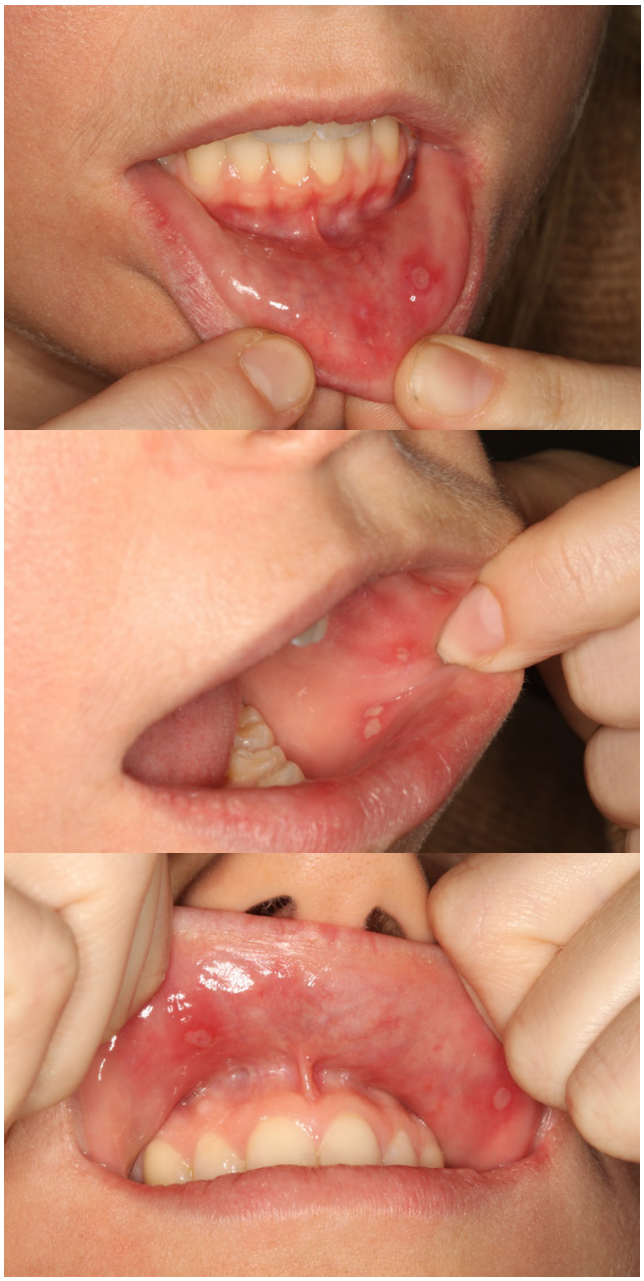

Fig. 1. Patient with severe and minor recurrent aphthous stomatitis (RAS) involving the maxillary and mandibular labial and buccal mucosa

**Table 1.** Clinical types of recurrent aphthous stomatitis (RAS)[8,51]

| Characteristic | Type of RAS | | | |
|---|---|---|---|---|
| | minor | major | herpetiform | complex |
| Prevalence | 80–90% | 10% | 1–10% | 1–5% |
| Size | <1 cm | >1 cm | multiple 2–3-mm aphthae that coalesce into a large one | 3 mm or more, oral or genital aphthae |
| Shape | oval | ragged oval, crateriform | oval | combination of all 3 forms (oval, ragged oval and crateriform) |
| Location | non-keratinized mucosa | non-keratinized mucosa | any intra-oral site | depend on the RAS form present |
| Healing | 4–14 days | up to 6 weeks | 10–14 days | |

aphthous-like oral ulcerations, should be excluded.[6,9] In addition to a clinical examination, laboratory investigation (e.g., colonoscopy for possible Crohn's disease) and medical consultations may be needed to rule out secondary RAS.

As of today, there is no cure for RAS. However, it is a self-limiting condition that takes from 4 to 14 days to heal completely. In some situations, longer periods of healing are observed, particularly in cases of major RAS, resulting in scarring at the ulcer site.[8] Several options are available to manage the patient's symptoms, including topical administration of lidocaine (i.e., gel, spray, or suspension) for pain control and cyanoacrylate-based sealing agents such as isoamyl-2-cyanoacrylate to create a protective layer over the ulcer and improve function.[10] Mild to moderate symptoms may respond to topical CS therapy in the form of gel or ointments (i.e., fluocinonide or clobetasol propionate), or elixir (i.e., dexamethasone or compounded clobetasol) for cases with multiple ulcers (Table 2). Intralesional injections of triamcinolone acetonide provide a useful option for painful, larger ulcers to expedite the healing process. Cases with more acute and severe symptoms may require a short course of systemic CS therapy.[6] Long-term prophylaxis therapy with colchicine, pentoxifylline or dapsone can be considered for patients with few or no ulcer-free days to keep the disease in a remission state.[11]

## RAS and dental implants

Literature on the impact of RAS on dental implant success is lacking. However, several factors should be considered in such cases. Placement of dental implants is often associated with increased anxiety and stress levels, which could trigger a RAS episode in the first days post-surgery.[12] As sites with active oral ulcerations are more likely to have friable and less resilient soft tissues, it is advised to initiate RAS treatment before attempting to place a dental implant, with the aim of keeping the disease in a remission state. Careful tissue management during the surgery is also recommended to prevent dehiscence and delayed wound healing at ulcer sites.

# Oral lichen planus

## Overview

Oral lichen planus is a common, chronic T-cell-mediated mucocutaneous disease that affects the oral cavity, skin and/or genitalia.[9,13,14] The estimated prevalence of OLP ranges from 0.22% to 5% worldwide. The condition is more prevalent in females and the age of onset ranges between 40 and 80 years.[13,15,16] The pathogenesis of OLP has been linked to the apoptosis of epithelial basal cells induced by $CD8^+$ cytotoxic T-cells as a result of endogenous or exogenous

**Table 2.** Common therapies used for the management of oral mucosal diseases

| Treatment | | Dose/concentration | Formulation | Frequency | Indication |
|---|---|---|---|---|---|
| Topical CS therapy | fluocinonide | 0.05% | gel | 2–3 times daily | localized oral ulcers |
| | clobetasol propionate | 0.05% | gel | | |
| | dexamethasone | 0.5% | elixir | | multiple oral sites involved |
| | compounded clobetasol | 0.05% | elixir | | |
| | prednisolone | 15 mg/5 mL | syrup | | |
| Systemic CS therapy | prednisone<br>prednisolone | 0.5–1 mg/kg/day | tablets | once daily | moderate to severe OLP, VBDs, SLE |
| CS-sparing agents/ immunosuppressive agents | hydroxychloroquine | 200 mg | tablets | twice daily | maintenance therapy for OLP |
| | azathioprine | 1 mg/kg/day | tablets | once daily | maintenance therapy for OLP, VBDs |
| | mycophenolate mofetil | 500 mg | tablets | 1–4 times daily | maintenance therapy for OLP, VBDs |

CS – corticosteroid; OLP – oral lichen planus; SLE – systemic lupus erythematosus; VBDs – vesiculobullous diseases.

antigens.[17] Common triggers include local and systemic inducers of cell-mediated hypersensitivity (such as a local reaction to dental restorative material or flavoring agents), stress, and microorganisms such as hepatitis C virus, which remain controversial among OLP experts.[16] Clinically, OLP may present as a multifocal disease, often with symmetrical distribution on the buccal mucosa, tongue, lips, gingiva, palate, and, rarely, the floor of the mouth.[13] Several forms of OLP have been described in the literature, including reticular, erythematous, erosive, papular, plaque, and bullous types (Fig. 2).[14] The plaque form, in particular, may mimic other oral pathological conditions, including leukoplakia, which must be excluded by the treating dentist and biopsied if needed.[18] Desquamative gingivitis is often an early sign of OLP in active disease and presents as desquamation (peeling) of the gingival margin with erythema and bleeding on brushing.[13] Patients with oral lichen planus may also experience discomfort, pain and sensitivity with acidic and spicy foods or drinks and/or a burning sensation in the oral cavity of varying severity. In addition to the oral cavity, OLP patients may report other body sites affected by the same process, such as skin, scalp and genitalia, presenting with purplish, scaly and itchy plaques.[19] Diagnosis of OLP is usually given based on a combination of the patient's reported history and clinical manifestations; however, a biopsy may be indicated for less classical presentations, suspicious for pre-malignant or malignant lesions.[19]

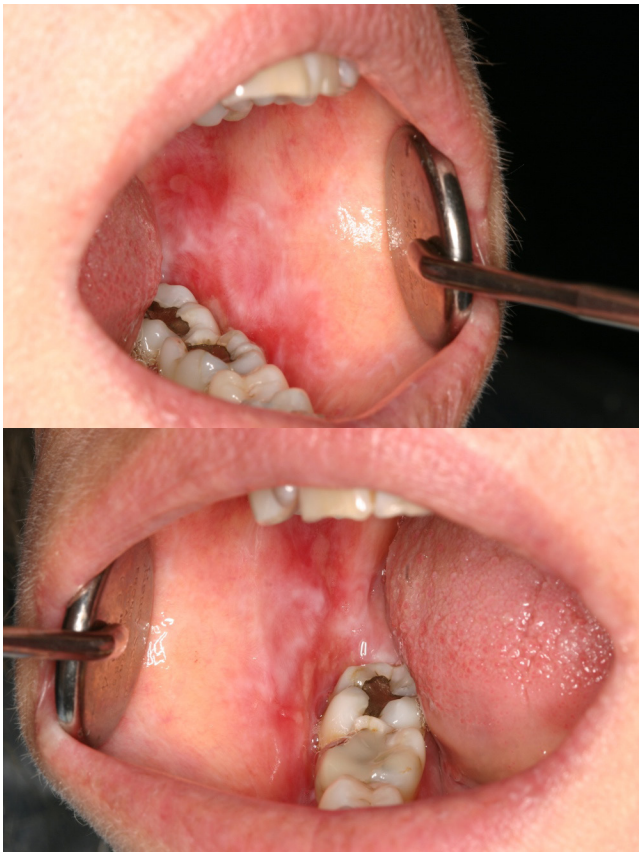

Fig. 2. Patient with reticular, erythematous and ulcerative forms of oral lichen planus (OLP) affecting buccal mucosa on both sides

## Management

Oral lichen planus is a chronic disease with no approved cure to date. Patients with drug-induced lichenoid reactions may benefit from switching to an alternative agent after consultation with their physician. Otherwise, the management of OLP is typically tailored to address the symptoms reported by the patient. Education regarding the overall disease and its prognosis should be offered to asymptomatic patients. Patients with more symptomatic diseases need CS therapy as the first line of treatment in a topical formulation, which requires multiple daily applications, such as clobetasol or fluocinonide. In clinical situations where multiple oral sites are involved, topical dexamethasone elixir can be prescribed. Similar to RAS, intralesional triamcinolone injections expedite the healing process of single and large painful ulcerations. Systemic CS therapy is a viable and effective option with a rapid onset for achieving the remission in moderate to severe disease. Prednisone or prednisolone can be administered at a dose of 0.5–1 mg/kg/day. In most cases, OLP tends to have a favorable prognosis with less impact on the person's quality of life. However, a small number of cases could progress to more severe forms or continue to be symptomatic for a longer period of time, requiring maintenance therapy.[20] For these cases, steroid-sparing agents such as hydroxychloroquine, azathioprine and mycophenolate mofetil are often considered.[19,21] However, patients with more frequent episodes of exacerbated symptoms during the year may be treated with topical agents, with or without short-term systemic CS therapy.

## OLP and dental implants

As of today, there are no guidelines or recommendations for the management of OLP patients with dental implants. In general, OLP patients can undergo dental procedures with a low risk of complications.[22] Yet, data on dental implant placement in OLP patients and potential complications has been scarce. A systematic review reported that patients with controlled OLP had a mean dental implant survival rate of 98.3%, with a mean follow-up of 44.6 months.[2] However, a prospective study involving 55 dental implants placed in patients with active OLP showed that 42 (76%) dental implants failed and were successfully replaced after controlling disease activity with systemic CS therapy.[23] Moreover, the marginal bone loss of implants placed in active OLP patients was compared to that in controlled OLP patients on systemic CS therapy and healthy individuals. During a 4-year follow-up, more bone loss was observed in the active OLP group (2.53 ±0.44 mm) than in the controlled OLP group and healthy individuals (0.75 ±0.56 mm and 0.79 ±0.73 mm, respectively).[24] However, a retrospective study that included 66 short implants placed in patients with controlled OLP showed the reported success rate of 98.5%, with marginal bone loss of 0.96 mm mesially

and 0.99 mm distally within a mean follow-up period of 68 months.[25] No significant differences were observed between the reticular and erosive forms of OLP, and the study did not include a control group.[25] In a prospective study comparing 18 patients with controlled erosive OLP to 18 healthy subjects who received dental implants, the implant survival rate was 100% in both groups; however, OLP patients with desquamative gingivitis had higher rates of peri-implant mucositis and peri-implantitis.[26] Studies indicate that OLP patients in remission are likely to have more predictable outcomes with dental implant treatment than those with uncontrolled disease.

# Vesiculobullous diseases

## Overview

### Pemphigus vulgaris

Pemphigus vulgaris is a rare mucocutaneous vesiculobullous disease (VBD) and the most common subtype of the pemphigus group. It is an autoimmune condition characterized by autoantibodies targeting desmoglein 1 and/or 3, which results in loss of adhesion between keratinocytes and the suprabasal layer with blister formation.[27] The estimated global prevalence of PV is approx. 0.1–0.5% and tends to be more common in certain ethnic groups, such as Ashkenazi Jews, Japanese and populations of Mediterranean descent.[28] It primarily affects adults with a female predilection, and the age of onset ranges from 50 to 60 years. In addition to the skin, PV can also affect the pharynx and the oral cavity. The condition is usually chronic and frequently causes blisters, erosions and ulcers at the affected sites (Fig. 3).[29] The oral cavity is often the first site to be affected, causing a series of examinations. These include a biopsy for hematoxylin and eosin (H&E) and direct immunofluorescence (DIF) examination in addition to serum testing using indirect immunofluorescence (IDIF) to make an accurate diagnosis followed by disease management.

### Mucous membrane pemphigoid

Mucous membrane pemphigoid (MMP) is a VBD that predominantly affects body mucosal surfaces, resulting in the formation of subepithelial blisters.[27] It typically affects the oral mucosa, conjunctiva, anogenital tissues, and upper aerodigestive tract with occasional skin involvement. The pathogenesis of MMP is driven by autoantibodies targeting various autoantigens in the basement membrane zone (BMZ), including collagen XVII (COL17, also known as BP180), BP230, laminin 332, integrin α6/β4, and collagen VII (COL7), which results in the separation between the epithelium and connective tissue.[5] Mucous membrane pemphigoid has an incidence rate of approx. 5–7.5 cases per 10,000 adults, with a female predilection

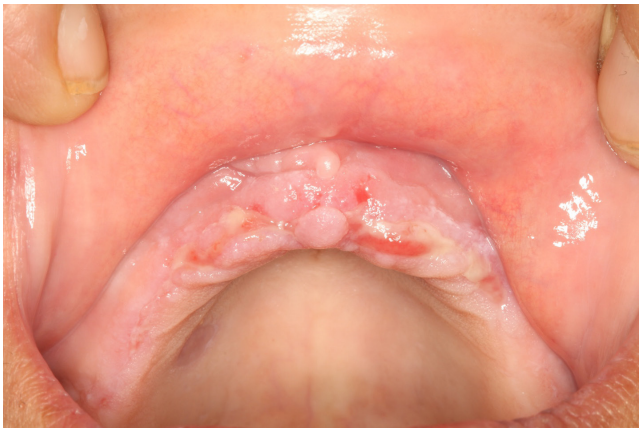

Fig. 3. Patient with pemphigus vulgaris (PV) on the anterior maxillary alveolar ridge presenting as erythema with ulceration

and an age range of 50–80 years.[30] Clinical manifestations of MMP include painful blisters and erosions on mucosal surfaces and skin, often healing with scar formation (Fig. 4). Similar to PV, obtaining a biopsy for H&E and DIF examination is the gold standard for diagnosing MMP and facilitating treatment.

## Management

Most VBD cases can achieve disease remission with proper treatment, based on affected sites. Longstanding, untreated disease may result in life-threatening events such as dehydration, infections and sepsis.[31] The treatment options available for both PV and MMP start with topical and systemic CS therapy to achieve disease remission. Systemic immunosuppressive treatments are recommended for moderate to severe cases with multi-system involvement to control disease activity. For long-term maintenance purposes, patients are commonly treated with CS-sparing agents to reduce the total dose and duration of CS therapy while still controlling the patient's symptoms. Several agents with evidence-based benefits are available and include mycophenolate mofetil, rituximab and intravenous immunoglobulins (IVIG).[30]

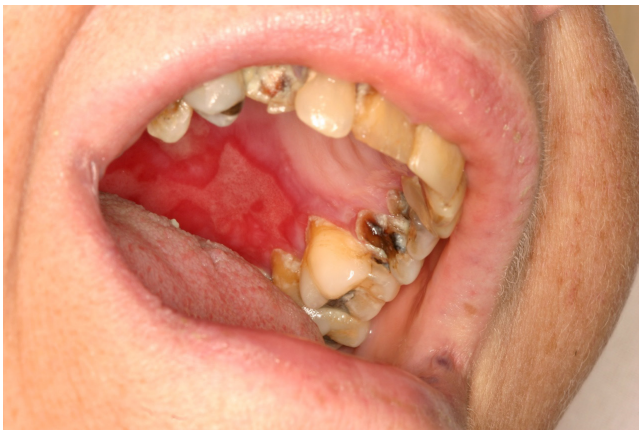

Fig. 4. Oral erythema with large ulceration in the soft palate in a patient with mucous membrane pemphigoid (MMP)

## Vesiculobullous disease and dental implants

Similar to other previously discussed mucosal diseases, few studies have evaluated the success of dental implants in patients with VBD. In active VBD, the presence of autoantibodies against hemidesmosomes, as part of the disease pathogenesis, may jeopardize the formation of the junctional epithelium between the gingival epithelium and the implant surface.[32] This can result in plaque and bacterial accumulation, increasing the risk of peri-implant mucositis and implant failure. A single case of an edentulous female patient diagnosed with PV on low-dose systemic CS therapy who received 2 dental implants to support the denture was reported. The patient was followed up every 6 months for 32 months and demonstrated 100% implant survival rate after at least 24 months.[29]

# Systemic lupus erythematosus

## Overview

Systemic lupus erythematosus is a chronic, autoimmune multi-system disease that affects the joints, tendons, kidneys, skin, blood vessels, and other organs such as the heart, lungs and brain, with a broad spectrum of clinical manifestations.[30] The oral mucosa can be affected in 40% of SLE patients, with symptoms including desquamative gingivitis, erosions, xerostomia, and/or temporomandibular joint symptoms such as edema and pain (Fig. 5). The incidence rate of SLE is estimated to range between 0.3 and 23 cases per 100,000 individuals per year, with the disease most commonly affecting those aged from 16 to 55 years.[33] Systemic lupus erythematosus is 10 times more likely to affect women than men.[30] The pathogenesis of SLE has been linked to B- and T-cell dysfunction with the production of antinuclear antibodies (ANA).

Diagnosis of SLE is often based on clinical characteristics and detecting serological abnormalities, including elevated ANA, anti-Ro antibodies (Abs), anti-La Abs, anti-Smith Abs, anti-U1-ribonucleoprotein Abs, anti-rheumatoid factor Abs, anti-dsDNA Abs, anti-cardiolipin Abs, lupus anticoagulant, and beta2-glycoprotein-I. In addition, the serum of SLE patients may show low C3 and C4, which helps reach the proper diagnosis.[30] Other imaging modalities are indicated on a case-by-case basis to assess organ involvement.

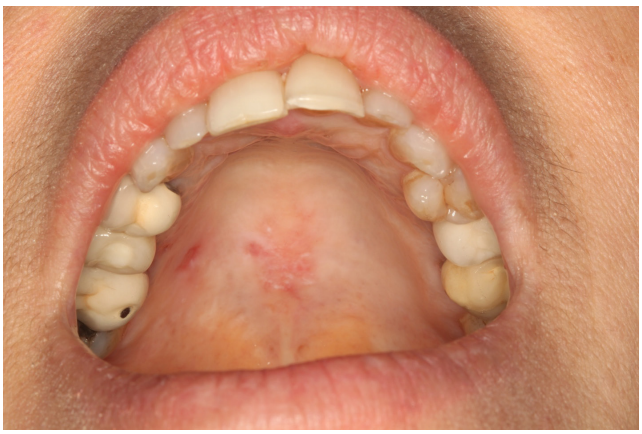

Fig. 5. Patient with systemic lupus erythematosus (SLE) presenting with islands of reticulation and erythema in the mid and right hard palate

## Management

Similar to most autoimmune conditions, the main goal in managing SLE is to reach disease remission or low disease activity with no flares. In general, the treatment of SLE is customized based on the severity and number of organs involved. Patients with acute symptoms may require a short course of systemic CS therapy to achieve rapid disease remission.[34] Hydroxychloroquine is commonly prescribed to stabilize SLE activity and reduce flares and other constitutional symptoms. In some cases, long-term use of low-dose systemic CS therapy is indicated. Several biological agents with promising efficacy are now available for the treatment of SLE, including rituximab and belimumab.[35] In the oral cavity, ancillary topical CS therapy is an effective tool to treat persistent or non-responsive lesions.

## SLE and dental implants

As of today, only a single case of implant placement in a patient with SLE treated with hydroxychloroquine 200 mg/day and low-dose CS (4 mg/day) therapy has been reported in the literature. In this case, the placed implant survived for 2 years without complications.[36] Other studies examined periodontal health in SLE patients. A cross-sectional study found no differences in periodontal parameters between SLE patients and systemically healthy individuals.[37] In addition, no significant correlation was found between SLE biomarkers and periodontal parameters assessing disease activity and prognosis.

# General considerations

Currently, there are no established guidelines for the management of patients with oral mucosal diseases who are receiving dental implants (Table 3). Hence, most of the needed clinical decisions made in dental practice today are based on expert opinions. Therefore, to minimize potential dental and medical complications, several factors should be considered for this group of patients when planning dental implant therapy. In general, asymptomatic patients with disease remission can be treated as healthy subjects without special precautions. For all other patients, comprehensive assessment and evaluation of related risk factors, in addition to medical consultations and careful handling of oral tissues, are crucial for successful treatment.

**Table 3.** Current literature on dental implant placement in patients with oral mucosal diseases

| Oral mucosal disease | Study | Study type | Patients, *n* | Implants placed, *n* | Mean age [years] | Mean follow-up [months] | Implant survival rate (%) |
|---|---|---|---|---|---|---|---|
| OLP | Aboushelib and Elsafi 2017[23] | prospective | 23 OLP | 55 (uncontrolled disease)/42 (after controlling the disease activity with systemic CS therapy) | 56.7 | 36 | 13 (uncontrolled disease)/100 (after controlling the disease activity with systemic CS therapy) |
| | Khamis et al. 2019[24] | prospective | 42 OLP/59 controls | 59 | 56.7 | 48 | 100 |
| | Anitua et al. 2018[25] | retrospective | 23 OLP | 66 | 58 | 68 | 98.5 |
| | Hernández et al. 2012[26] | prospective | 18 OLP/18 controls | 56 OLP/62 controls | 52.2 | 52.3 | 100 |
| PV | Altin et al. 2013[29] | case report | 1 | 2 | 70 | 32 | implant survived with mean peri-implant bone resorption of 0.9 mm at follow-up |
| SLE | Ergun et al. 2010[36] | case report | 1 | 6 | 49 | 24 | success at 2 years of follow-up |

PV – pemphigus vulgaris.

Long-term use of several medications for oral mucosal diseases should be considered, as it may have a direct or indirect effect on the osseointegration and success of dental implants. For instance, systemic CS therapy is used to treat VBD and SLE.[11] There is no consensus on the direct effect of CS therapy on the osseointegration of dental implants.[38] However, some studies have discussed the negative effect of CS therapy on osteoblasts via induction of cellular apoptosis and reducing the number of pre-osteoblasts while promoting the differentiation of bone marrow stromal cells to adipocytic lineage cells.[38] In addition, CS has the potential to extend the life span of osteoclasts and promote bone resorption. On the contrary, a systematic review found no association between lower implant survival and systemic CS therapy.[39]

Medication considerations and other risk factors should be discussed with the patient before treatment. In addition, potential complications must be explained in detail. Once all questions have been addressed, obtaining the patient's consent to the procedure is the last step before initiating treatment and should be documented in medical records. In the next section, we will discuss specific considerations for pre- and post-dental implant surgery as well as the long-term maintenance phase and follow-up (Table 4).

## Before dental implant surgery

Several points have to be considered for patients with oral mucosal diseases before dental implant surgery. First, a complete medical history, including current medications and allergy history should be obtained in detail during the consultation visit. It is recommended to obtain oral mucosal disease history and status and to discuss the proposed dental plan with the oral medicine specialist/oral pathologist of the patient. Consultation with the

**Table 4.** General considerations regarding patients with oral mucosal diseases receiving dental implants

| Treatment phase | Considerations |
|---|---|
| Before implant placement | – if the patient is asymptomatic and in a remission stage, no specific intervention is needed;<br>– if oral lesions and/or ulcerations are present, initiate indicated treatment to achieve disease remission;<br>– consult with the treating physician for updated treatment regimen and considerations;<br>– maintain good oral hygiene to avoid the risk of infection or exacerbation of oral mucosal disease;<br>– implement a stress-reduction protocol;<br>– ensure gentle handling of soft tissue during dental surgery;<br>– initiate antibiotic therapy (e.g., amoxicillin, clindamycin) the day before or on the day of surgery |
| Postoperative phase | – prescribe systemic antibiotics, as indicated, or continue previously initiated antibiotic therapy;<br>– antimicrobial, alcohol-free mouthwash (chlorhexidine 0.12% solution) twice daily until wound healing is complete; alternatively – Betadine 1%;<br>– effective pain control measures;<br>– continue to maintain good oral hygiene;<br>– close and frequent follow-up;<br>– instruct the patient to avoid irritating food items, specifically for OLP and VBD patients |
| Long-term maintenance | – regular follow-up and maintenance visits;<br>– close monitoring of OLP patients for early detection of malignant transformation process |

treating physician is also recommended for a complete understanding of the patient's medical status and active medications, as well as any necessary recommendations and precautions. It is also recommended that all patients receive dental prophylaxis for complete removal of accumulated local deposits (i.e., plaque and calculus) as these can act as a trigger for disease activity in VBD.

In general, dental implants should be placed when the mucosal disease is in partial or complete remission (i.e., minimal or no mucosal ulceration, absence of signs of inflammation). This approach applies to all conditions included in this report that have been demonstrated to improve dental implant outcomes.[23] On a case-by-case basis, antibiotic coverage may be considered for patients on long-term (>6 weeks) systemic CS therapy or immunosuppressive therapy who are prone to infection.[40] Eligible patients usually begin antibiotic therapy (e.g., amoxicillin, clindamycin) the day before or on the day of surgery, continuing for 5–7 days during the initial healing phase.

Adrenal suppression is another potential complication in patients on the long-term systemic CS therapy due to the increased stress and pain levels associated with dental procedures.[41] Even with the reduced risk of adrenal crisis in dental clinics, the indication for perioperative CS therapy as a prophylaxis measure remains controversial.[41] Few studies have suggested an increased risk of adrenal insufficiency for patients receiving more than 7.5 mg prednisolone/day or equivalent for more than 30 days, or more than 20 mg prednisolone/day for more than 2 weeks.[42] Other studies recommended CS supplementation regimens based on the surgery type and anticipated stress.[41] For instance, minor surgeries require 25–75 mg of hydrocortisone, while major surgeries given on the same day would require 100–150 mg of hydrocortisone. However, the World Workshop on Oral Medicine VI indicated insufficient evidence to support the use of supplemental perioperative CS therapy for most dental procedures performed under local anesthesia, except for the most stressful procedures, procedures performed under general anesthesia, patients with poor health, or patients on medications that metabolize cortisol or inhibit its synthesis.[43] Consultation with the treating physician on a case-by-case basis before the day of the surgery is recommended.

There is insufficient data on the impact of chronic hydroxychloroquine use on the success of dental implants. Hydroxychloroquine is an antimalarial and immunomodulatory agent used in SLE and OLP. A meta-analysis reported no significant delay in healing time after implant placement in patients on long-term hydroxychloroquine for specific medical conditions. The same applies to other CS-sparing agents, including mycophenolate mofetil, azathioprine, pentoxifylline, and dapsone. Therefore, no specific precautions are indicated for patients treated with one or more of these drugs.[44]

In addition to current medications, certain conditions may require further consideration. For instance, increased stress levels during implant placement may be a potential trigger for RAS. Therefore, the implementation of stress-reduction protocols, including early morning appointments and pain-free procedures, could be of potential benefit. Other measures include pre-emptive analgesia and implant placement under nitrous oxide or oral sedation before the day of the surgery using short-acting benzodiazepines (e.g., 0.5–1 mg diazepam or 0.125–0.25 mg triazolam given 1 h before the procedure). These may benefit high-risk patients without medical contraindications.

## Post-operative phase

After the placement of dental implants, patients are given specific post-operative instructions to reduce the risk of complications and facilitate healing. In the context of oral mucosal diseases, additional instructions are required. For instance, patients with OLP and VBD should be advised to avoid potentially irritating food items (i.e., citrusy and spicy agents) during the initial healing phase. In addition to wound care and oral hygiene instructions, proper pain control is crucial to reduce post-surgical stress that may trigger an acute episode of RAS or reactivation of the dormant herpes simplex virus. The treating dentist should pay special attention to potential drug interactions of the prescribed pain medications with the patient's current medications. For example, hydroxychloroquine is a known substrate for cytochrome P450 2D6 (CYP2D6), which is a liver enzyme involved in the body metabolism.[45] Therefore, hydroxychloroquine has the potential to undermine the effectiveness of codeine and tramadol, which use the CYP2D6 pathway for activation of the prodrug, as well as increase serum levels of metoprolol in patients with heart disease.[46] In addition, non-steroidal anti-inflammatory drugs (NSAIDs) combined with prednisolone may increase the risk of gastrointestinal tract (GI) bleeding and ulceration.[47] Moreover, ibuprofen, together with pentoxifylline, may also increase the risk of GI bleeding. Treatment with both ibuprofen and tacrolimus requires monitoring of renal functions in patients with compromised kidneys. Post-surgical prescription of amoxicillin also carries a risk for drug interactions as it has the potential to reduce the serum levels of mycophenolate mofetil and increase methotrexate levels in the blood.

Antimicrobial therapy is critical to the success of dental implants,[48] including systemic antibiotics prescribed for 5–7 days during the initial healing phase. In addition, less irritating antimicrobial mouthwash should be prescribed, such as alcohol-free chlorhexidine (0.12%). Alternatively, Betadine 1% has similar antimicrobial effects to chlorhexidine. Patients should be instructed to identify unusual symptoms following implant placement and to report them immediately in case an intervention or treatment is needed. The symptoms may include a sudden increase in their pain level, acute or persistent edema, progressive gingival inflammation, and/or bleeding and implant mobility.

After surgical placement of dental implants, prosthetic treatment should be considered carefully. Prosthetic components that maintain minimal contact with the surrounding mucosal surfaces through proper pontic design should be used. In addition, careful handling of soft tissues with minimal trauma and the use of tissue-compatible materials are recommended.[25] The excessive use of potentially irritating materials (e.g., retraction cords and acrylic materials for temporary restoration) may exacerbate the patient's symptoms or trigger an inflammatory gingival response.[49] Furthermore, the procedure time for the surgical and prosthetic parts should be kept to a minimum to reduce the risk of edema and tissue irritation.

## Long-term maintenance and follow-up

Similar to healthy subjects, patients with oral mucosal diseases who receive dental implants require regular follow-up to ensure treatment success and early detection of complications. In addition, meticulous oral hygiene regimens should be reinforced on a regular basis and may have to be conducted through scheduled office visits. Patients with OLP, in particular, should be followed up every 6–12 months for early detection and management of suspicious lesions due to the risk of malignant transformation.[20] Based on a recent report published by the World Health Organization (WHO), OLP has been classified as a pre-malignant disorder with a malignant transformation rate of 0.1–0.5%, which remains controversial.[50] However, patients should be educated about this risk and the process of self-examination to facilitate the surveillance process.

# Conclusions

Oral mucosal diseases are common conditions with variable severity in the general population. Currently, there are no contraindications for the placement of dental implants in patients with oral mucosal diseases. However, there are no established guidelines on best practices and protocols to increase the success rate of dental implants in such cases with minimal complications. The current review provides dentists with insight into special considerations for placing dental implants in patients with oral mucosal diseases.

## Ethics approval and consent to participate

Not applicable.

## Data availability

Not applicable.

## Consent for publication

Not applicable.


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