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Oral Adverse Drug Reactions of Antidepressants and Their Periodontal Implications: A Narrative Review

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Abstract
Background: *The global rise in antidepressant prescriptions has led to an increasing prevalence of drug-induced oral complications in dental practice. Antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs), are associated with a range of oral adverse effects that carry significant periodontal implications.*
Objective: *This narrative review aims to consolidate current evidence on the oral manifestations of antidepressants, with a focused analysis of their impact on periodontal health, and to outline evidence-based clinical management strategies for dental practitioners.*
Methods: *A literature search was conducted across PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar using the keywords: "antidepressants," "oral adverse effects," "xerostomia," "periodontal disease," "bruxism," and "SSRIs."*
Results: *Xerostomia, induced by the anticholinergic mechanisms of TCAs and, to a lesser degree, SSRIs, is the most prevalent oral complication. It directly contributes to plaque accumulation, gingivitis, dental caries, and progression of periodontitis. SSRI-associated platelet dysfunction increases bleeding tendency during periodontal procedures. Bruxism, oral candidiasis, burning mouth syndrome, and taste disturbances further compromise periodontal health. Polypharmacy and advanced age amplify the severity of these effects.*
Conclusion: *Comprehensive dental assessments integrating thorough medical and pharmacological histories are essential for patients on antidepressant therapies. A multidisciplinary approach involving periodontists and psychiatrists is recommended to mitigate drug-induced oral complications and optimize patient outcomes.*
Keywords: *Antidepressants; Oral Adverse Effects; Xerostomia; Tricyclic Antidepressants; Bruxism; Drug-Induced Oral Reactions.*

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I. INTRODUCTION

Depression is one of the most prevalent mental health disorders globally, estimated to affect 280 million people worldwide, according to the World Health Organization[1]. Antidepressant medications represent the cornerstone of pharmacological management for depression, anxiety disorders, and a growing range of psychiatric and pain-related conditions. Global antidepressant utilization has risen substantially over the past two decades, with SSRIs representing the most widely prescribed class[2,3]. As a result, dental practitioners increasingly encounter patients undergoing long-term antidepressant therapy.

Although antidepressants are generally regarded as safe within their therapeutic ranges, they are associated with a spectrum of adverse drug reactions. Oral complications may involve the salivary glands, oral mucosa, dentition, and periodontal tissues[4,5]. From a periodontal perspective, drug-induced changes in salivary composition and flow rate, coagulation dynamics, and neuromuscular activity have direct consequences for gingival and periodontal health[6,7,8]. Saliva plays a critical homeostatic role in maintaining oral pH, buffering bacterial acids, and providing both mechanical and immunological protection against pathogenic microorganisms. Qualitative and quantitative salivary deficiencies compromise oral defence mechanisms, increasing vulnerability to oral diseases[9].

Despite their clinical significance, the periodontal implications of antidepressants and their associated oral adverse effects remain underrecognized in routine dental practice. A 2024 systematic review by Alcazar-Hernandez et al., published in the Journal of Clinical Medicine, documented a consistent association between antidepressant use and elevated risks of xerostomia, dental caries, and periodontal disease across 11 observational studies[10]. A parallel narrative review by Taccardi et al. in 2024 further elucidated the bidirectional relationship between depressive disorders and periodontitis, highlighting the role of antidepressant drugs in modulating periodontal inflammatory pathways[11]. Given this growing evidence base, the present review aims to provide a

comprehensive, periodontics-focused appraisal of oral adverse drug reactions attributable to antidepressant therapy and to offer evidence-informed management recommendations for the dental team.

II. LITERATURE REVIEW

2.1 Classification of Antidepressants and Mechanisms of Oral Toxicity

Antidepressants are classified according to their primary mechanism of action into four major categories: (i) selective serotonin reuptake inhibitors (SSRIs), including fluoxetine, sertraline, and escitalopram; (ii) serotonin–norepinephrine reuptake inhibitors (SNRIs), including duloxetine and venlafaxine; (iii) tricyclic antidepressants (TCAs), including amitriptyline, imipramine, and desipramine; and (iv) miscellaneous agents, such as mirtazapine and bupropion[12]. Each drug class carries a distinct pharmacological profile with a corresponding adverse-effect signature relevant to oral health (Table 1).

TCAs exert pronounced anticholinergic activity by blocking muscarinic acetylcholine receptors in the salivary glands, resulting in reduced salivary secretion—the principal mechanism of TCA-induced xerostomia[13]. SSRIs, while lacking significant anticholinergic properties, inhibit platelet serotonin uptake, thereby impairing platelet aggregation and prolonging bleeding time—a mechanism of direct clinical relevance during periodontal instrumentation[14]. SSRIs are also associated with an altered dopaminergic–serotonergic balance, contributing to drug-induced bruxism[15]. SNRIs share elements of both SSRI and TCA profiles, although their oral adverse effects tend to be milder. Understanding these mechanistic distinctions is essential for anticipating drug class–specific oral complications in periodontal patients.

Table 1: Classification of Antidepressants and Their Oral/Periodontal Adverse Effect Profiles

Drug Class	Examples	Primary Mechanism of Oral Toxicity	Key Oral/Periodontal Effects
SSRIs	Fluoxetine, Sertraline, Escitalopram	Platelet serotonin depletion; altered dopamine–serotonin balance	Increased bleeding tendency, bruxism, mild xerostomia
TCAs	Amitriptyline, Imipramine, Desipramine	Anticholinergic blockade of muscarinic receptors	Severe xerostomia, dental caries, oral candidiasis
SNRIs	Duloxetine, Venlafaxine	Combined SSRI + mild anticholinergic activity	Moderate xerostomia, mild bleeding tendency
Miscellaneous	Mirtazapine, Bupropion	Variable; histaminergic blockade (mirtazapine)	Dry mouth, taste disturbances

2.2 Oral Adverse Drug Reactions

Oral adverse drug reactions associated with antidepressants encompass a broad clinical spectrum. The following subsections review the major manifestations and their mechanistic underpinnings.

III. MATERIALS AND METHODS

This narrative review was conducted by systematically searching PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. The search was restricted to peer-reviewed articles published between 2021 and 2024. The following MeSH terms and free-text keywords were employed: “antidepressants,” “oral adverse effects,” “xerostomia,” “periodontal disease,” “bruxism,” “SSRIs,” “tricyclic antidepressants,” and “dental caries.” Eligibility criteria included studies reporting oral adverse effects of antidepressant medications in human subjects—encompassing systematic reviews, meta-analyses, randomized controlled trials, observational studies, and authoritative narrative reviews. Studies were excluded if they were case reports, conference abstracts, non-English publications, or focused solely on non-dental systemic effects. Reference lists of included articles were manually screened for additional relevant sources. Data synthesis was performed narratively, with findings organized thematically by drug classification and type of oral adverse effect.

IV. RESULTS

4.1 Xerostomia and Salivary Hypofunction

Xerostomia—the subjective sensation of oral dryness—is the most frequently reported oral adverse effect of antidepressant therapy[10,16,17]. It is most pronounced with TCAs owing to their anticholinergic mechanisms, but is also observed in SSRI users[18]. A comparative cross-sectional study demonstrated a xerostomia prevalence of

57.4% in SSRI users compared with 29.4% in non-users ($p = 0.002$); SSRI users additionally showed significantly higher caries experience (mean DMFT 9.39 vs. 6.48, $p < 0.001$) and worse periodontal indices[10,13,16]. A survey-based study reported that 83.9% of patients on antidepressants experienced xerostomia or dental caries, with salivary flow reductions more severe in TCA users (58%) than in SSRI users (32%)[17].

Saliva serves essential periodontal protective functions: it maintains oral pH, reduces enamel demineralization, limits pathogenic microbial colonization, and facilitates mechanical cleansing of tooth surfaces[18]. Reduced salivary flow impairs all these functions, creating an environment conducive to supragingival and subgingival plaque accumulation—the primary etiological factor for gingivitis and periodontitis[18,19]. Clinically, xerostomic patients demonstrate increased plaque index, gingival index, probing depths, and bleeding on probing, indicating a clear and direct association between drug-induced salivary hypofunction and deteriorating periodontal status[10,20].

4.2 SSRI-Associated Bleeding Tendency

Serotonin stored within platelets plays an integral role in primary haemostasis. SSRIs inhibit serotonin reuptake not only at neuronal synapses but also at platelet membranes, thereby depleting intraplatelet serotonin and attenuating platelet aggregation[14]. Multiple meta-analyses have confirmed an elevated bleeding risk associated with SSRI use, with the risk particularly heightened when SSRIs are combined with anticoagulants or nonsteroidal anti-inflammatory drugs[7,14,21]. In the periodontal context, patients receiving SSRI therapy may exhibit exaggerated gingival bleeding during routine scaling and root planing, periodontal surgery, and implant procedures. This effect does not necessitate discontinuation of SSRI therapy in most cases, but it does require appropriate precautionary measures, including patient counselling, use of haemostatic agents, and close intraoperative monitoring[7,14].

4.3 Dental Caries

The reduction in salivary flow rate associated with antidepressant use increases cariogenic risk through multiple pathways: diminished buffering of bacterial acids, reduced salivary immunoglobulin A (IgA) and other antimicrobial proteins, impaired calcium–phosphate remineralization, and enhanced retention of fermentable carbohydrates on tooth surfaces[9]. Older adults and patients on polypharmacy represent a particularly vulnerable population, as age-related decline in salivary gland function compounds drug-induced hypofunction[9,16]. Root surface caries—a distinct carious pattern observed in xerostomic patients, particularly those with gingival recession—has been reported with increased prevalence in antidepressant users[9,10]. Dental caries indirectly worsens periodontal status by creating plaque-retentive areas, elevating the bacterial load at the gingival margin, and contributing to tooth loss.

4.4 Oral Candidiasis

Oral candidiasis arises as an opportunistic infection when immunological or mechanical mucosal defences are disrupted. Antidepressant-induced salivary hypofunction creates a microenvironment favouring Candida albicans proliferation by eliminating the mechanical flushing action of saliva and depleting salivary antifungal proteins such as histatins and lactoferrin[9,22]. Patients may present with pseudomembranous (white patches), erythematous, or angular cheilitis variants, typically accompanied by burning discomfort. Poorly controlled oral candidiasis perpetuates mucosal inflammation, impairs the patient's ability to maintain adequate oral hygiene, and exacerbates pre-existing periodontal disease[22,23].

4.5 Bruxism

Drug-induced bruxism is a rhythmic or sustained involuntary jaw muscle contraction leading to tooth grinding and clenching. It is recognized as a specific adverse effect of SSRIs and, to a lesser extent, SNRIs[15,24]. The pathophysiology is attributed to drug-induced alterations in dopaminergic and serotonergic neurotransmitter balance within the basal ganglia, analogous to the extrapyramidal side effects of antipsychotic medications[24,25]. Clinically, bruxism results in tooth surface attrition, cusp fractures, increased tooth mobility, and temporomandibular joint (TMJ) dysfunction. From a periodontal perspective, bruxism generates occlusal trauma that exceeds the adaptive capacity of the periodontium, contributing to widening of the periodontal ligament space, alveolar bone loss, and accelerated progression of pre-existing periodontitis[15,19]. A comprehensive review by Lobbezoo et al. confirmed bruxism as a multifactorial entity with significant pharmacological contributions[15].

4.6 Burning Mouth Syndrome and Taste Disturbances

Burning mouth syndrome (BMS) is a chronic orofacial pain condition characterized by persistent burning sensations in the oral mucosa without identifiable organic pathology[26]. Its aetiology is considered multifactorial, encompassing neuropathic, hormonal, and pharmacological components. Antidepressants have been implicated both as precipitating factors and, at low doses, as therapeutic agents in BMS management[27,28]. Taste alterations—including metallic taste (dysgeusia) and diminished taste acuity (hypogeusia)—are also reported in patients on

TCA and SSRI therapy, attributed to disruption of gustatory receptor transduction and altered salivary composition[9,10,29]. These sensory disturbances can adversely affect dietary behaviour, reduce nutritional intake, and indirectly compromise both systemic and periodontal health.

4.7 Periodontal Implications

The cumulative oral adverse effects of antidepressant medications converge to produce significant deterioration in periodontal health through multiple synergistic mechanisms. Xerostomia-driven salivary hypofunction is the primary driver of enhanced plaque accumulation, gingival inflammation, and subsequent progression from gingivitis to periodontitis[9,10,19]. A 2024 systematic review by Taccardi et al. highlighted that certain antidepressants—particularly fluoxetine and imipramine—demonstrate anti-inflammatory effects on periodontal tissues in animal models, reducing alveolar bone loss and suggesting a nuanced, potentially bidirectional pharmacological interaction between antidepressant agents and periodontal pathology[10,30].

SSRI-induced platelet dysfunction complicates periodontal procedures by increasing intraoperative and postoperative bleeding, necessitating modified surgical protocols[7,19]. Bruxism-induced occlusal trauma exacerbates attachment loss in patients with pre-existing periodontitis and may compromise the long-term prognosis of periodontal treatment outcomes[15,19,31]. Oral candidiasis and mucosal burning further reduce compliance with home oral hygiene regimens, creating a vicious cycle of deteriorating periodontal status. The interplay between depressive behavioural factors—including reduced self-care motivation, irregular dental attendance, and altered dietary patterns—and pharmacological oral changes amplifies the periodontal disease burden in this patient population[10,23,32].

4.8 Risk Factors Modifying Severity

Several clinical variables modulate the severity of antidepressant-associated oral adverse effects. Advanced age is a significant risk amplifier, as reduced salivary gland reserve in older adults synergizes with drug-induced hypofunction. Polypharmacy—the concurrent use of multiple xerogenic medications—substantially elevates the xerostomia burden[9,10,16]. A systematic review confirmed that polypharmacy was independently associated with increased xerostomia severity in older adults[16,33]. Duration and cumulative dosage of antidepressant therapy correlate positively with the degree of salivary gland impairment[16,19,33]. Comorbid systemic conditions, including diabetes mellitus, Sjögren's syndrome, and autoimmune disorders, further compromise salivary and periodontal resilience. Poor baseline oral hygiene and irregular dental attendance exacerbate the progression from drug-induced xerostomia to clinically manifest periodontitis.

V. DISCUSSION

The management of antidepressant-associated oral adverse effects requires an integrated, multidisciplinary approach encompassing preventive, therapeutic, and collaborative strategies.

A comprehensive medical and pharmacological history—including the type, dosage, and duration of antidepressant therapy—should be obtained at the initial periodontal assessment and updated at every recall visit[10]. Communication with the prescribing psychiatrist is recommended for complex cases in which dose modification may be considered to mitigate severe oral side effects without compromising psychiatric therapeutic outcomes.

Xerostomia management centres on salivary stimulation and substitution. Patients should be advised to maintain adequate hydration, use sugar-free chewing gum or lozenges to stimulate residual salivary function, and consider topical saliva substitutes or mouth rinses containing carboxymethylcellulose or xylitol[9,22,26]. Prescription-strength fluoride applications—such as 0.5% sodium fluoride varnish or 1.1% sodium fluoride dentifrice—are indicated to reduce cariogenic risk in xerostomic patients[9,22]. Antifungal therapy (topical nystatin or miconazole; systemic fluconazole for recalcitrant cases) should be initiated promptly upon diagnosis of oral candidiasis[22,23,34].

Patients on SSRI therapy undergoing periodontal surgery or implant placement require haemostatic precautions. Local haemostatic measures, including absorbable gelatine sponge, oxidized cellulose, and tranexamic acid mouthwash, may be employed[14,22,35]. Routine coagulation screening is not mandated for patients on SSRIs alone; however, it is advisable when SSRIs are combined with antiplatelet or anticoagulant agents[17,14,35]. Bruxism management through custom-fabricated occlusal splints is recommended to reduce occlusal loading on periodontally compromised teeth, prevent further attachment loss, and protect prosthetic restorations[15,31,36]. Referral for behavioural or pharmacological bruxism management may be warranted in severe cases.

Patient education is a cornerstone of management. Patients should be informed of the oral side effects of their medications, instructed in meticulous oral hygiene techniques, and motivated to attend regular periodontal maintenance at shortened recall intervals—typically every three months for patients with established periodontitis[10,31].

VI. CONCLUSION

Antidepressant medications are associated with a broad spectrum of oral adverse drug reactions that carry significant periodontal implications. Xerostomia is the most prevalent manifestation; it directly promotes plaque accumulation, gingival inflammation, and periodontal disease progression. SSRI-induced platelet dysfunction and bruxism further complicate periodontal management. The interactions among pharmacological, behavioural, and systemic factors in this patient population create a complex clinical challenge requiring coordinated dental and medical care. Early identification of at-risk patients, timely implementation of preventive and therapeutic strategies, and multidisciplinary collaboration are essential to optimizing periodontal outcomes in individuals receiving long-term antidepressant therapy. Future prospective studies with standardized periodontal assessment protocols are warranted to better quantify the periodontal disease burden attributable to specific antidepressant agents and to evaluate the efficacy of targeted management interventions.

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