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Review Article

A comprehensive review of oral hypoglycaemic drugs and their oral health correlates

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ABSTRACT

Oral hypoglycaemic drugs (OHDs) are vital in the effective management of type 2 diabetes mellitus (T2DM), a widespread metabolic disorder that affects millions globally. While these medications excel at controlling blood glucose levels, they can also lead to significant oral health challenges. This article delves into the various pharmacological classes of OHDs and highlights their potential impacts on oral health, including issues such as dry mouth (xerostomia), periodontal disease, taste changes, delayed healing, and a higher susceptibility to oral infections. It is imperative for healthcare providers, especially dental professionals, to understand these connections, as recognizing the oral health implications of diabetes is essential for delivering comprehensive and effective care to diabetic patients. Proper awareness and proactive management can make a substantial difference in the overall well-being of those living with diabetes.

Keywords: Oral hypoglycemic drugs, Diabetes mellitus, Oral health

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels due to defects in insulin secretion, insulin action, or both. The most prevalent form, T2DM, is largely associated with insulin resistance and relative insulin deficiency. According to the International Diabetes Federation, over 537 million adults were living with diabetes globally in 2021, a number projected to increase to 643 million by 2030 (IDF, 2021). As the global incidence of T2DM continues to rise, it has become a major public health concern, affecting millions worldwide. The management of T2DM often involves lifestyle modification, dietary regulation, and pharmacological therapy, most notably through the use of oral hypoglycaemic drugs (OHDs).[1]

OHDs are a diverse group of medications that help regulate blood glucose levels in individuals with type 2 diabetes. They work through various mechanisms such as enhancing insulin secretion, increasing insulin sensitivity, decreasing glucose absorption from the intestines, or promoting urinary glucose excretion. These medications are critical in delaying or preventing the microvascular and macrovascular complications of diabetes, such as retinopathy, nephropathy, neuropathy, cardiovascular disease, and more recently acknowledged, oral health complications.[2]

Despite the systemic focus in diabetes management, there is growing recognition of the bidirectional relationship between diabetes and oral health, particularly periodontal disease. Poor glycaemic control has been shown to worsen periodontal outcomes, and conversely, chronic oral infections can adversely affect blood sugar regulation.[3] OHDs, while indispensable in managing diabetes, may also contribute directly or indirectly to oral health challenges. Side effects such as dry mouth (xerostomia), altered taste (dysgeusia), increased risk of fungal infections, and hypoglycaemic episodes during dental

procedures are some of the concerns that need to be addressed by dental professionals.[4] Moreover, the long-term use of certain hypoglycaemic agents may influence salivary gland function, immune response in the oral cavity, and the overall microbial balance, creating a more susceptible environment for oral disease. These implications underscore the importance of integrating dental care into the comprehensive management plan for diabetic patients.[5]

Understanding the effects of OHDs on oral tissues is essential for both medical and dental practitioners. It facilitates better coordination of care, improves patient outcomes, and enhances quality of life. As the use of these medications continues to grow alongside the diabetes epidemic, increased awareness and research into their oral health implications remain vital.[6]

CLASSIFICATION OF OHDS

OHDs encompass several classes, each with distinct mechanisms of action (Table 1).

Table 1: Classification of OHDs.

Drug class	Agents	Mechanism of action
Sulphonylureas	First generation agents: Chlorpropamide, tolazamide, tolbutamide Second generation agents: Glipizide, glibenclamide	Stimulates insulin secretion from β-cells
Biguanides	Metformin	Inhibits hepatic glucose production; increase insulin sensitivity
Thiazolidinediones	Pioglitazone	Enhances insulin sensitivity via PPAR-γ activation
Dipeptidyl peptidase-4 (DPP-4) inhibitors	Sitagliptin, Saxagliptin	Prolongs incretin activity; increase insulin secretion
Sodium-glucose cotransporter 2 (SGLT2) inhibitors	Canagliflozin, dapagliflozin	Promotes glucose excretion in urine.
Alpha-glucosidase inhibitors	Acarbose	Delays carbohydrate absorption in the intestines.

ORAL MANIFESTATIONS ASSOCIATED WITH DIABETES

Uncontrolled diabetes is associated with several oral complications, including: Periodontal disease, xerostomia (dry mouth), oral candidiasis, delayed wound healing, burning mouth syndrome and dental caries.

The effects of OHDs may influence the above conditions directly or indirectly.

IMPLICATIONS OF OHDS ON ORAL HEALTH

Increased risk of infections (periodontal disease)

Diabetes itself predisposes individuals to a higher risk of infections, including periodontal disease, due to impaired immune responses and poor wound healing. Periodontal disease is considered the "sixth complication" of diabetes. Diabetes, particularly when poorly controlled, increases susceptibility to chronic periodontitis. Elevated blood glucose levels promote the formation of advanced glycation end-products (AGEs) which activate inflammatory pathways via receptor for AGEs (RAGE), intensifying periodontal destruction.[7] OHDs like metformin have been found to exert anti-inflammatory effects and osteogenic effects, improving periodontal outcomes when used as an adjunct to scaling and root planning.[8,9] Studies show that locally delivered 1% metformin gel in periodontal pockets leads to improved clinical attachment level and bone fill in chronic periodontitis patients with diabetes because it reduces pro-inflammatory cytokines like TNF-α and IL-6 and promotes osteoblast differentiation.[10]

Xerostomia (dry mouth) and salivary gland dysfunction

Several oral hypoglycaemic agents, particularly metformin, have been associated with dry mouth, either due to dehydration or altered salivary gland function. Xerostomia can lead to difficulty in swallowing or speaking, increased dental caries and oral mucosal lesions. Sulfonylureas and DPP-4 inhibitors are more commonly associated with dry mouth symptoms.[11]

Taste alterations (dysgeusia)

Some patients report taste disturbances with medications such as metformin and sulfonylureas, which may affect appetite, nutrition, and oral hygiene practices.

DPP-4 inhibitors and immune modulation in the oral cavity

DPP-4 is expressed on various immune cells, and its inhibition might alter host responses. DPP-4 inhibitors may impair chemotaxis and neutrophil activity, potentially increasing susceptibility to infections like periodontitis or

candidiasis.[12] However, evidence remains inconclusive, and further research is warranted.

Oral candidiasis

Hyperglycaemic conditions and dry mouth create a favorable environment for *Candida albicans* colonization. Furthermore, SGLT2 inhibitors, through their glycosuric effect, can predispose not just to genital infections but also to oral candidiasis, particularly in immunocompromised individuals.[13] Some reports suggest a higher risk of oral candidiasis, particularly in patients with poor glycaemic control or dentures.[14]

Burning mouth syndrome

Burning mouth syndrome (BMS) is often reported by diabetic individuals and is often associated with peripheral neuropathy or altered salivary composition. Some OHDs, particularly sulfonylureas and meglitinides, may contribute to neuropathic changes in predisposed individuals. Moreover, poor glycaemic control increases BMS risk.[15]

Delayed wound healing and increased susceptibility to infection

Thiazolidinediones like pioglitazone, due to their immunomodulatory action, might delay healing by affecting cytokine production. They may also impair osteoblast differentiation, affecting bone healing post dental extractions or implants.[16] Diabetic patients also exhibit impaired collagen synthesis, reduced neutrophil function, and microangiopathy, all contributing to delayed wound healing.[17]

Hypoglycaemia and dental emergencies

Sulfonylureas and meglitinides can cause hypoglycaemic episodes, especially in patients with irregular meal patterns or during long dental procedures. Symptoms such as sweating, confusion, and syncope require prompt recognition and management by dental professionals.[18,19]

Drug-induced oral lesions

Rarely, certain medications (e.g., pioglitazone**)** have been implicated in causing oral mucosal changes or ulcerations. Though uncommon, such lesions should be evaluated for potential drug-related etiology.[5,20]

RECOMMENDATIONS FOR DENTAL PRACTITIONERS

Medical history review

Thoroughly review patients diabetic status, including medications, glycaemic control (HbA1c), and any history of hypoglycaemia.

Preventive care

Emphasize oral hygiene, regular dental check-ups, and early intervention for periodontal disease.

Saliva management

Recommend saliva substitutes or sugar-free gum to manage xerostomia. Encourage hydration.

Emergency preparedness

Keep glucose tablets or gels in the clinic for potential hypoglycaemic events.

Patient education

Educate diabetic patients on the importance of oral health and the impact of diabetes and its medications.

FUTURE DIRECTIONS IN RESEARCH

Further investigation is needed into long-term oral health outcomes associated with newer antidiabetic agents like GLP-1 receptor agonists and dual SGLT1/2 inhibitors. Studies on the reversal of oral manifestations through optimal glycaemic control and OHD adjustment are warranted. Development of clinical guidelines for dental practitioners managing diabetic patients on OHDs.

CONCLUSION

The relationship between OHDs and oral health is intricate and clinically significant. OHDs play a pivotal role in managing type 2 diabetes, but they are not without oral health implications. While these medications are essential for metabolic control, their potential to influence oral pathophysiology must not be underestimated. A collaborative approach between medical and dental professionals is essential to ensure comprehensive care for diabetic patients, enhancing both systemic and oral health outcomes.

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