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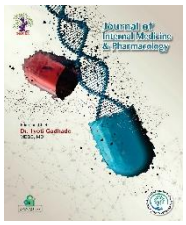

Research Article

Current Approaches in the Treatment and Prevention of Oral Submucous Fibrosis: A Chronic Disease Perspective

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ABSTRACT

Oral Submucous Fibrosis (OSMF) is a chronic, progressive, and scarring disease of the oral cavity, often extending to the pharynx and upper esophagus, primarily caused by the chewing of areca nuts, betel quid, ghutka, mawa, and similar substances. This review highlights the potential role of antioxidants such as lycopene, curcumin, spirulina, and β-carotene in managing OSMF. It explores the synergistic effects of these antioxidants in combating oxidative stress and proposes the development of buccal oral patches as a novel therapeutic approach. These patches are designed to adhere to the affected oral mucosa, providing a controlled release of antioxidants directly to the lesion site, offering a promising direction for future treatment strategies. This approach may help alleviate symptoms, slow disease progression, and improve patient outcomes in OSMF management.

Keywords: Chronic Disease, Collagen, Fibrotic Bands, Areca Nuts, Antioxidants, Oral Patches

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1. Introduction

Oral submucous fibrosis (OSMF) stands as a significant connective tissue disorder and a premalignant condition, predominantly associated with the habitual chewing of areca nut. The addition of tobacco to this habit further exacerbates the incidence of OSMF [1]. This complex disorder progresses through distinct stages, with initial manifestations involving inflammation within the oral cavity and a distinctive blanching of the oral mucosa, resembling a marble-like appearance.

As OSMF advances, the formation of fibrotic bands becomes prominent, leading to a consequential restriction in the range of jaw motion, clinically identified as trismus. Beyond the evident physiological impact, OSMF gives rise to numerous challenges in oral hygiene, affecting essential functions such as communication, dietary habits, speech, swallowing, and even routine activities like tooth brushing [2].

The pathological development of fibrous bands within the connective tissues of the oral cavity results in increased thickness and a rubbery texture, marking a distinctive characteristic of OSMF [2]. Recognized since 1952 when Schwartz described it as "Atropica idiopathica mucosae oris," OSMF has since been acknowledged as an insidious and chronic disease affecting various parts of the oral cavity and, at times, extending to the pharynx, as articulated by Jens Pindborg in 1966 [3].

Beyond the physical manifestations, OSMF is notably characterized by diminished oral movement, depapillation of the tongue, a shrunken uvula, progressive reduction in mouth opening, and an overall increase in the leathery texture of the oral mucosa [4]. These clinical features underscore the intricate nature of OSMF, not only as a physical health concern but also as a potential precursor to malignancy, demanding a comprehensive understanding of its pathophysiology and effective strategies for both treatment and prevention.

2. Causative Factors for Oral Submucous Fibrosis (OSMF)

Oral submucous fibrosis (OSMF) is intricately linked to several causative factors that collectively contribute to its onset and progression. Chief among these is the habitual chewing of areca nut, with the alkaloids, particularly arecoline, identified as potent agents inducing fibrotic changes. The addition of tobacco further compounds the risk, as the synergistic effect of tobacco's carcinogenic compounds intensifies the inflammatory and fibrotic processes. The composition of betel quid, a common preparation involving areca nut, betel leaf, and slaked lime, plays a crucial role in releasing harmful substances that promote fibrosis and inflammation. Additionally, genetic predisposition adds another layer to the complexity, with certain individuals being more susceptible to OSMF due to their genetic makeup. A comprehensive understanding of these causative factors is essential for developing effective preventive measures and targeted therapeutic interventions against OSMF.

3. Symptoms of Oral Submucous Fibrosis (OSMF)

The initial stages of OSMF manifest with a distinct leathery sensation in the oral mucosa, accompanied by visible fibrotic bands. As the condition progresses, the mucosa undergoes a transformation, losing its natural elasticity and assuming a stiff, blanched appearance. This progression typically originates in the posterior regions of the mouth and gradually extends towards the outer areas. Notably, the symptoms of OSMF encompass a range of oral manifestations, as illustrated in Figure 1, including:

Reduced Mouth Opening (Trismus):A significant symptom of OSMF is the gradual reduction in the

ability to open the mouth fully, often referred to as trismus.

Depapillation of the Tongue:OSMF can lead to changes in the tongue's surface, resulting in depapillation, where the normal papillary structures diminish.

Shrunken Uvula:The uvula, a fleshy projection in the back of the throat, may exhibit shrinkage as a consequence of OSMF.

Limited Jaw Movement:The development of fibrotic bands restricts the normal range of jaw motion, causing difficulties in activities such as speaking, chewing, and swallowing.

Altered Texture of Oral Mucosa:The oral mucosa undergoes a noticeable change in texture, becoming increasingly leathery as fibrous bands develop.

These symptoms collectively underscore the progressive nature of OSMF and its impact on various aspects of oral health and functionality. Early recognition of these signs is crucial for timely intervention and effective management of the condition.

Fig 1: Symptoms of oral submucous fibrosis

4. Other clinical symptoms

Oral Submucous Fibrosis (OSMF) presents a myriad of clinical symptoms that extend beyond the oral cavity, reflecting the systemic impact of the condition. Trismus, characterized by the incapability of fully opening the mouth due to oral fibrosis, is a hallmark symptom. Changes in taste perception, dryness of the mouth, and earache are additional manifestations. OSMF may lead to stenosis of the eustachian tubes, resulting in loss of hearing. Nasal intonation of the voice, increased salivation, and difficulty in swallowing solid foods are common challenges. The condition also hampers essential activities such as eating, talking, and blowing due to reduced movement of the soft palate. Other observable effects include a small tongue, shrinking of the uvula, and the stiffening and thinning of the lips. This comprehensive array of symptoms underscores the intricate nature of OSMF, emphasizing the need for thorough clinical assessment and intervention strategies tailored to the multifaceted impact of the disorder.

5. Characterization of Possible Diseases in OSMF Patients

The association between areca nut, a prominent component in the etiology of Oral Submucous Fibrosis (OSMF), and its potential to contribute to various diseases underscores the complex health challenges faced by individuals with this condition. Areca nut, known for its carcinogenic properties, significantly contributes to the disease burden among OSMF patients. Despite its association with life-threatening conditions, areca nut remains easily accessible and is consumed freely across age groups. A substantial number of OSMF patients not only engage in the habitual chewing of areca nut but also concurrently use tobacco, consume unhealthy amounts of alcohol, and may be involved in drug abuse. These behavioral patterns, coupled with potential dietary deficiencies, place OSMF patients at a heightened risk of developing co-morbidities. These may include but are not limited to metabolic syndromes, respiratory disorders, gastrointestinal complications, liver diseases, and cardiovascular conditions, as depicted in Figure 3 [11]. The intricate interplay of these factors necessitates a comprehensive approach to patient care, considering the multifaceted impact of OSMF on overall health and well-being.

Effect on the cardiovascular system

Areca nut usage resulted in increased heart rate, irrespective of the frequency of usage, due to central sympathetic response, but the effect on blood pressure is more varied, leading to a fall of the diastolic component due to the peripheral cholinergic effect and increase in the systolic component in non-habitual users. Areca nut does not alter the cerebral blood flow as there is not much significant increase in blood flow of the internal carotid artery and middle cerebral artery [12].

Effect on gastrointestinal system and food metabolism

Areca nut has diverse effects on the digestive system and metabolism of food in the human body. It leads to lowering of plasma cholesterol by up to 25% due to inhibition of intestinal acetyl co- enzyme acyltransferase (ACAT) and pancreatic cholesterol esterase (PACE), resulting in decreased cholesterol absorption. [13] Areca nut chewers have increased gastrointestinal motility due to stimulation of colonic M3 receptors, which is dose dependent, and increased saliva secretion due to the presence of AChE inhibitors and arecoline, leading to laxative and sialagogue effects, respectively, which explains its use in the rural population [14].

Effect on the respiratory system

Various case reports from different parts of the world have shown that the areca nut metabolite arecoline causes aggravation of disease in asthmatics by increasing bronchoconstriction in a dose-dependent manner and decreasing the forced expiratory volume in 1 second (FEV1) by 30%; also, the rate of hospitalization is higher in asthmatics who chew areca nut [15].

Effect on blood

Areca nut causes platelet aggregation associated with phospholipase C activation, mobilization of Ca++, TXB2, which leads to release of growth factors, and increased fibrogenesis that plays a crucial part in its effects on the oral mucosa and cardiovascular system [16].

6. Etiopathogenesis of OSMF

Understanding the etiopathogenesis of Oral Submucous Fibrosis (OSMF) involves a comprehensive exploration of major causative factors and contributing elements, as outlined in Table 1 and depicted in Figure 4. The intricate nature of OSMF's pathogenesis is yet to be fully elucidated, although several mechanisms have been proposed. Notably, areca nut-chewing in various formulations stands out as the primary causative agent, with Figure 4 illustrating its central role in the disease process.

Contributory risk factors include the consumption of smokeless tobacco, elevated intake of chilies, exposure to toxic levels of copper in both foodstuffs and masticatories, deficiencies in essential vitamins, and malnutrition leading to reduced serum protein levels, anemia, and genetic predisposition [19]. These multifactorial contributors collectively contribute to the initiation and progression of OSMF. The intricate interplay of these elements underscores the need for ongoing research to unravel the precise mechanisms and interactions involved in the etiopathogenesis of OSMF, facilitating the development of targeted therapeutic strategies and preventive interventions.

7. Market Preparations for OSMF

Several marketed preparations cater to the treatment of Oral Submucous Fibrosis (OSMF), offering diverse dosage forms to address the complexities of the condition:

Mouthwashes and Gels: Formulations containing antioxidants, analgesics, or anti-inflammatory agents aim to alleviate symptoms and enhance oral health. These products provide localized relief and can be incorporated into daily oral care routines.

Oral Medications: Tablets or capsules may contain antioxidants, vitamins, or specific medications

prescribed by healthcare professionals. These oral medications play a crucial role in managing OSMF symptoms and addressing underlying issues associated with the condition.

Topical Applications: Creams or ointments designed for topical application directly to the affected areas inside the mouth provide localized relief. These formulations aim to target specific symptoms and improve the overall condition of the oral mucosa.

Injections: In severe cases, steroid injections may be administered to reduce inflammation and control the progression of OSMF. This intervention is typically employed under the supervision of healthcare professionals to address the more advanced stages of the condition.

Buccal Films: Innovative buccal films, incorporating antioxidants like curcumin, offer a targeted approach to OSMF treatment. These films provide a localized and controlled release of therapeutic agents, contributing to the management of the condition.

While these marketed preparations contribute to the therapeutic arsenal for OSMF, it is imperative that individuals seek guidance from healthcare professionals for an accurate diagnosis and personalized treatment plan tailored to their specific needs. Ongoing research and advancements in treatment modalities are essential to continually enhance the efficacy and accessibility of interventions for individuals affected by OSMF.

8. Future Prospective

The significant toll on human lives and economic resources resulting from morbidity and mortality associated with areca nut and Paan masala addiction necessitates urgent attention and comprehensive measures. The economic burden surpasses the revenue generated by the industry, underscoring the need for a government-led areca nut control program. Implementing stricter laws to regulate areca nut consumption and mandating pictorial warnings on products can contribute to public awareness and prevention.

Innovative approaches in treatment are also on the horizon, aiming to enhance patient experience and treatment outcomes. The development of oral patches utilizing a Novel Drug Delivery System presents a promising avenue to mitigate patients' pain during intralesional injections in the oral cavity. Incorporating antioxidants such as lycopene, beta-carotene, carotenoids, curcumin, and spirulina into these patches could potentially enhance treatment efficacy.

Looking forward, the landscape of Oral Submucous Fibrosis (OSMF) treatment appears optimistic, with ongoing research exploring various modalities, including medications, surgical interventions, and emerging therapies like stem cell treatments and gene therapy. Advances in understanding the underlying mechanisms of the disease hold the potential to drive the development of more targeted and efficacious treatments, with the ultimate goal of alleviating symptoms, halting disease progression, and, ideally, reversing the pathological conditions. This collective effort towards prevention, innovative treatment strategies, and continued research signals hope for a more effective and comprehensive approach to managing OSMF in the future.

Conclusion

In conclusion, Oral Submucous Fibrosis (OSMF) presents a complex and challenging health issue with multifaceted implications for affected individuals and society at large. The habit of chewing areca nut, often compounded by tobacco use, remains a pivotal factor in the initiation and progression of this premalignant disorder. OSMF manifests with a spectrum of symptoms, affecting various aspects of oral health and overall well-being, and may lead to a heightened risk of co-morbidities. The etiopathogenesis of OSMF involves a combination of genetic predisposition, nutritional

deficiencies, and environmental factors, with areca nut emerging as a central causative agent. The interconnectedness of these elements underscores the need for comprehensive preventive measures, including government-led control programs, stricter regulations, and public awareness campaigns.

Looking to the future, innovative treatment approaches, such as the development of oral patches utilizing a Novel Drug Delivery System, show promise in enhancing patient comfort during therapy. Ongoing research into medications, surgical interventions, and advanced therapies like stem cell treatments and gene therapy holds the potential to revolutionize OSMF management.

To address the significant health and economic burden posed by OSMF, a concerted effort is required from healthcare professionals, policymakers, and the community. Implementing effective preventive strategies, advancing treatment modalities, and fostering public awareness will be instrumental in mitigating the impact of OSMF and improving the overall oral health landscape. Through collective action and ongoing research endeavors, we strive towards a future where the burden of OSMF is minimized, and affected individuals receive timely, effective, and compassionate care.

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