

ETIOPATHOGENESIS OF XEROSTOMIA: A CONCISE REVIEW

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Abstract

Xerostomia, or dryness in mouth is usually concerned with decrease in the amount of saliva flow causing severe discomfort to the patients. As saliva is the most beneficial fluid which play a very important role in the sensation of flavour perceived in the mouth and lubrication of tongue. Along with this it also contributes in defending of the oral mucous membranes by providing bactericidal action such as proteolytic enzymes, lysozyme, lacto-peroxidase and IgA, IgG antibodies.

The significant risk factors for xerostomia may be systemic or be iatrogenic– demonstrated by many types of pharmacologically active agents or chemotherapy, ionized radiation which is used as adjuvant in destroying malignant cells and aging issues. The related syndrome to this group include Sjogren's syndrome manifested primarily by lacrimal and salivary glands inflammation producing various clinical symptoms. This is a typical problem for diabetes patients which is correlated with inadequate salivary flow followed by alterations in the microcirculation. Several treatment strategies for the management of such condition include medications for lubrication of mucosa and saliva substitutes. But, understanding the primary cause of xerostomia enables quicker diagnosis and a most effective treatment strategy. The intent of this article is to briefly review the etiology of xerostomia along with risk factors.

Keywords: Saliva, Sjogren's syndrome, Xerostomia, Xenogeneic drugs.

INTRODUCTION

Xerostomia or literally dry mouth is more often avoided complaint of the individuals that can apparently affect the patient's well-being of life. It is an unusual chronic state which is important to diagnose as it produces variety of symptoms. It is measured by explicitly asking people about their experiences with the disorder, which affects roughly one-quarter of adults and 40% of older persons.¹

More often than males, women have xerostomia, complain about it, and are impacted by it. The extent of this condition has been appeared to advance with age which may be associated to the growing use of medicines for various diseases by the elderly people. A number of recent studies mentioned that nearly one in five older people has dry mouth. Furthermore, it is responsible for infections of the oral cavity and carious tooth which result in declining the health due to lack of nutrition.(Figure 1) The most essential element of the mouth for maintaining the oral homeostasis is salivary fluid.²

The boosting incidence of reduced saliva is originating due to the consequences of some systemic diseases and mostly by prescribed medications. Such condition can be for short period of time, usually subside after stoppage of medicine. This decline in the amount of saliva can have depreciated effect on oral function.

Moreover, it may affects the constant eating patterns, the pleasure of flavour due to defective taste sensation. Such patients should elude certain type of foods, like dry foods and sticky foods (butter peanut) because of inefficiently mastication or swallowing.

In addition, it may also obstacle the speaking ability of the individuals and give rise to cracks and fissures in the oral mucosa and foul-smelling breath.(Figure 2) In denture wearing patients it exacerbates chewing difficulties and unbearable denture which is principally due to a reduced surface tension among the dehydrated mucosa and the denture. A coupling of all of these factors can sequel to a poor or insufficient diet of the affected person.³

ROLE OF SALIVA

Saliva is outlined as the most beneficial fluid which is usually taken for granted. Nevertheless, its diminution may significantly affect taste, promote irrigation, lubrication and defending of the oral mucous membranes.⁴ The salivary secretion produced is protein-rich providing bactericidal action including-proteolytic enzymes, lysozyme, lacto-peroxidase and IgA, IgG antibodies. Furthermore, it acts as a vehicle for transportation of various nutrients, enzymes (amylase). The buffering system is continuously helping in maintaining the oral pH of 7 directed by bicarbonate and phosphate buffer systems.⁵



Figure 1: Rampant Caries

Figure 2: Dry, red fissured tongue

ETIOLOGY

A. Local Causes

1 Medications

Xerostomia is presented in most of the situations by the reason of salivary gland dysfunction, but it is also associated with non salivary origin in which patients presenting completely with entirely normal salivary gland function. The most noticeable adverse effect to the therapeutic drug is xerostomia which manifests as dry mouth and quantifiable salivary hypofunction. Only a few of more than 500 medications attributed to this symptom have been revealed to significantly lower salivary production.⁶

The exact mechanism responsible for these symptoms has not yet been fully determined. But, it is postulated that changes in systemic or mucosal hydration are thought to be possible contributors.⁷

1.1 Mechanisms of action of xerogenic drugs

Drug-related dry mouth is caused by a variety of processes, although many of them are mediated by an anticholinergic effect. Muscarinic acetylcholine receptors in the periphery convey cholinergic impulses to autonomic organs, although the precise physiological roles of each subtype are still poorly understood. The parasympathetic cholinergic neurotransmission to the salivary gland and many other glands is responsible for reducing fluid release and amylase secretion. It is mainly mediated by the M3-muscarinic receptors.⁸

1.2 Drugs with actions on the cholinergic system

1.2.1 Tricyclic antidepressants

These drugs mediate both serotonergic or noradrenergic mechanisms which has prohibiting effect on full mouth drying along with some other symptoms. Certain drugs with pronounced effect are zimelidine, nortriptyline, mianserin & amitriptyline which is documented in up to 27% of patients consuming these drugs.

Both M2 and M3 muscarinic receptors has prohibition on cholinergically smooth muscle contractions which is recommended to treat overactive bladder.⁹

1.2.2 Antipsychotics

Adverse drug reaction of conventional phenothiazine presented as dry mouth including other symptom such as sleep issues, movement abnormalities, and excess weight. Treating schizophrenia patients, one atypical antipsychotic medication, clozapine and olanzapine is said to be more effective and to have less motor side effects than standard antipsychotics. Patients on lithium co-therapy with olanzapine may cause significantly higher effect which presumably act via its diuretic effect.¹⁰

1.2.3 Diuretics

According to one study on older individuals, it was suggested that diuretic agents, thiazides and psychotropics were the most often prescribed medications that have equally effective at lowering the mean salivary flow rate. Also, when compared to the placebo, xerostomia was felt ten times more likely to occur after consuming furosemide.¹¹

1.2.4 Antihistamines

The older antihistamines were associated with sedating effects on the central nervous system (CNS) and antimuscarinic effects also leads to dryness of mouth. Its degree varied from drug to drug and therefore non-sedating antihistamines have been developed. However, some antihistamines medications include acrivastine, cetirizine, fexofenadine, mizolastine, astemizole, and terfenadine produces less symptoms.⁸

1.3 Drugs with actions on the sympathetic system

1.3.1 Antihypertensives

Some antihypertensive drugs are centrally acting produces prominent ADRs and therefore now little used. These mainly include reserpine, methyldopa and clonidine which is associated with stimulation of salivary gland alpha 2-adrenergic receptors. Salivary content is affected by treatment with beta 1-selective adrenoceptor antagonists but not saliva flow velocity. The amylase action and total protein content showed the most obvious impacts, both of which were considerably reduced. Approximately 12% of those using ACE inhibitors have such symptoms.¹²

1.3.3 Opioids, benzodiazepines, and drugs of abuse

The long-term consumption of opioids, particularly atropine, hyoscine and atropinics, can produce dry mouth by suppressing secretions. Moreover, release of morphine sulphate, alfentanil & dihydrocodeine cause tiredness and dry mouth in 80% of user. Diazepam and Zopiclone which comes under benzodiazepines leads to mild decreased salivation, mainly recommended as anxiolytics.¹³

1.4 H2 receptor antagonists and proton-pump inhibitors

Most of the time the classic triple therapy is advised to exterminate ulcer producing bacteria-*Helicobacter pylori* which is consist of amoxicillin or tetracycline, metronidazole and a bismuth derivative. Incorporation of an H2-receptor antagonist increase the rate of destruction such ulcer producing bacteria, reduces the time period and leads to dry mouth. In addition, Omeprazole also results in dryness of mouth which is demonstrated in 41% of patients.⁸

1.5 Retinoids

Although there is a lack of concrete evidence, systemic retinoids are widely recognised to produce mouth dryness and disturbances in the oral mucosa, as demonstrated with the introduction of etretinate and 13 cis-retinoic acid. The researcher assesses the mean flow rate of stimulated saliva which was considerably lower over the treatment period of 3 months with oral isotretinoin.¹⁴

1.6 Anti-HIV drugs

A considerable number of individuals receiving protease inhibitor medication may have oral or peri-oral adverse effects. After consuming didanosine up to 7% of people may experience tongue dryness.¹⁵

1.7 Cytokines

Interferon which comes under Cytokines used for the management of Sjogren's syndrome along with chronic hepatitis C infection can impair salivation result in significant dryness. When Interleukin-2 used for control of haematological and nasopharyngeal carcinoma malignancies then it significant diminished both the resting and stimulated saliva flow.¹⁶

2. Radiotherapy- induced salivary dysfunction

In spite of several modern technologies the early diagnosis of oral cancer is challenging and as it progresses, the treatment modalities also advance which results in developing certain complications. So, the modified treatment of tumors eventually is combination of surgery along with radiation therapy and chemotherapy as an adjuvant that leads to compromised life's quality.

Radiation therapy injures the parenchyma of the salivary gland, and eventually leads to its fibrosis and secretory hypofunction which is usually related to dose.¹⁷

Pathogenesis of Radiation Induced salivary

There are very few studies have provided evidence of the functional impairments in the secretory system caused by head and neck radiation. Therefore, we still don't fully understand the precise processes behind this is unknown. Histologically, it was suggested that the residual tissue had fibrosis and that there had been a loss of salivary epithelial cells, mostly acinar cells. Additionally, it was thought that the local vasculature has also altered.¹⁸

Low proliferative activity in the parenchyma of gland makes it unlikely that radiation-induced reproductive mortality from DNA mutation will occur during or soon after treatment. Chemotherapy can also reduce salivation, however it's unclear which medications or doses cause such condition.¹⁹

3. Miscellaneous

3.1 Duct calculi

Sometimes, dryness on the afflicted side may result from an occlusion of a major salivary gland's duct, most often the Wharton's duct. If left untreated, the occlusion may result in hyposalivation and gradual gland fibrosis.¹¹

3.2 Sialadenitis

Mumps and post-operative parotitis are examples of acute infections, but nutritional poor nutrition oedema and iodide hypersensitivity are examples of chronic diseases which produces this condition.⁷

3.3 Psychogenic causes

The body enters "fight or flight" mode, certain hormones specifically adrenaline along with cortisol are secreted which several other autonomic nerve processes are altered. It causes decreased salivary flow during test periods, including fear, depression, tension.²

4. Systemic Causes

4.1 Sjogren's Syndrome

It is a systemic autoimmune exocrinopathy with an uncertain cause presented primarily by lacrimal and salivary glands inflammation. It is identified by invasion of clusters of encroaching lymphocytes substituting the normal glandular tissue and progressive loss of secretory epithelial cells. Furthermore, the salivary ductal epithelium undergoes hyperplasia and metaplasia, resulting in the distinctive epi-myoeptithelial islands formation located near normal acini. As an outcome, both the content and flow rate of saliva substantially effected. Clinical dryness symptoms, notably in the mouth and eyes are the consequence of such condition.²⁰

4.2 Diabetes mellitus

For ambulatory diabetes patients, experiencing a dry mouth is a typical problem. It has a high correlation with both inadequate salivary flow due to troubles in glycaemic control of the patients. The pathogenesis of diabetes mellitus is reduced salivary flow as a result of autonomic dysfunction, destruction to the gland parenchyma, or modifications in the micro-vessels of the salivary glands. The depressed salivary flow in diabetic patients could be due to autonomic dysfunction, damage to the glandular tissue or alterations in the microcirculation to the salivary glands.²¹

2.3 Others- Xerostomia may be brought on by hormonal imbalances associated with pregnancy and menopausal. Sometimes, a clinical pattern matching that of Sjogren's disease can develop when donor lymphocytes multiply and invade the recipient's salivary glands. Certain chronic inflammatory conditions mainly sarcoidosis and amyloidosis can introduce hyposalivation.²⁰

DISCUSSION

Xerostomia has frequently seen considered synonymous to impaired salivary flow. However, in dentistry it is important to diagnosed patients with such condition as it is insufficiency enhances the chances of infection. It frequently occurs in the older population by means of an adverse effect of medicines, systemic diseases, immunological conditions and radiotherapy for head and neck neoplasm. Saliva adds moisture for the action of oral mucosa and insufficient saliva increases the build-up of bacteria on oral surfaces. Signs of hypofunction of the salivary glands that all been thought to be considered are dryness during eating, insufficient tongue movement or trouble swallowing of dry foods.²

Several treatment strategies for the management of hyposalivation include medications for lubrication of mucosa and saliva substitutes. The US Food and Drug Administration-permitted sialogogues for the patients which incorporate few drugs- cevimeline and pilocarpine.²²

CONCLUSION

Xerostomia or dry mouth is a regularly seen symptom in day today life. It occurs as a consequence of many types of medication. Apart from this, it develops secondary to large number of diseases, as a side-effect of radiation therapy or as a manifestation of syndromes. Some infections, such as HIV infection, sarcoidosis, and TB, cause immunocompetent cells to invade salivary glands or cause granulomas to develop which further enhanced such condition. Therefore, it is a challenging oral health problem and should not be neglected as it can be transformed into chronic form. So, to maintain their overall health, these people require specialised treatment.

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