



RESEARCH ARTICLE

SALIVARY HYPOFUNCTION, XEROSTOMIA AND ITS PROSTHODONTIC MANAGEMENT

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Abstract

Saliva is a multipurpose fluid secreted by three major pairs of salivary glands. Saliva constantly bathes all the oral hard and soft tissues and helps to maintain the oral homeostasis. Saliva has manifold functions in protecting the integrity of the oral tissues. It is of crucial importance for both dentulous as well as edentulous patients. Dysfunction in the salivary flow produces negative effect on the oral environment, can lead to severe consequences in the overall patient's health and in their quality of life. Saliva acts as a mainstay for the success of the removable prosthodontic therapy. Thus, a knowledge regarding saliva is essential for providing efficient prosthodontic treatment and after care. This article aims to provide a brief overview of salivary hypofunction, xerostomia and its prosthodontic implications.

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Introduction:-

Saliva is a multifunctional, versatile substance produced by the body and plays a pivotal role in the preservation of oropharyngeal health. Saliva provides a fluid environment that aids in the lubrication of oral cavity. Saliva is required for normal speech, swallowing, and cleansing of the oral tissues. Various salivary proteins such as amylase, lipase, proteases, nucleases, mucins, gustin aid in the digestive process. Saliva also possess antibacterial properties for hydrolysis of microbial cell membranes (lactoferrin, lysozyme, lactoperoxidase); and inhibit microbial adherence (immunoglobulins). The saliva acts as an anticarcinogenic agent by dilution and clearance of dietary sugars, buffering of plaque acids, and by providing ions like calcium and phosphate for tooth remineralization (Ana, 2002; Turner, 2016).

The rate of secretion follows a circadian rhythm, thus maintaining the saliva flow during the waking hours and decreasing during sleep. Mean daily salivary output ranges from 500 to 1500 mL, or per day- 0.3 to 0.4 mL per minute. On an average, approximately 1ml of saliva present in the oral cavity; a flow rate less than 0.1 mL per minute has been determined to be significantly abnormal. The quantity of saliva 0.2 -0.4 ml/min indicates oligosialia. A resting saliva flow rate less than 0.01 mL per minute or stimulated salivary flow rate of less than 0.10 ml per min has been determined to be significantly abnormal (hyposalivation). "Salivary hypofunction," is the reduced salivary output from all the salivary glands while the subjective complaint of a dry mouth is termed "xerostomia" (Ana, 2002; Turner, 2016).

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Etiology of xerostomia:

Etiology of xerostomia is multifactorial. Few causes are described as follows: Salivary gland diseases and disorders like agenesis of the salivary glands, sialadenosis, sialadenitis, sialolithiasis, Sjogren's syndrome, Mikulicz syndrome, or tumours of salivary glands. Endocrinal diseases like diabetes mellitus, hyperthyroidism, hypothyroidism, Cushing's syndrome, Addison's disease are also commonly associated with xerostomia. Neurologic disorders like stroke, Parkinson's disease, Bell's palsy and Alzheimer's disease are also associated with xerostomia. Psychogenic conditions that can lead to xerostomia include anxiety, depression, nervousness, stress, and eating disorders like anorexia nervosa, bulimia. Other diseases like rheumatoid arthritis, SLE, scleroderma, sarcoidosis, amyloidosis, Crohn's disease, ulcerative colitis, cystic fibrosis, hypertension, burning mouth syndrome, primary biliary cirrhosis, liver transplant candidates, renal diseases and renal dialysis, anaemia, fibromyalgia, chronic fatigue syndrome, and atrophic gastritis also may also lead to xerostomia. Infections such as HIV/AIDS and tuberculosis are also associated with salivary hypofunction (Ana, 2002; Brennan, 2002; Dugal, 2010; Turner 2016; Joanna, 2014; Han, 2015; Gupta 2006).

More than 400 drugs are known to produce xerogenic effects. Few drugs that can lead to xerostomia are listed in Table 1 (Turner, 2016; Gupta, 2006; Tanasiewicz, 2016).

Radiation-induced hyposalivation can occur when the salivary glands are within the field of radiation, and leads to a permanent degeneration of the salivary gland. Following radiation, the glands atrophy and become non-functional and fibrotic. This damage typically occurs when the exposure dose is 60 Gy or more. The most radiosensitive glands are parotid, followed by the submandibular, sublingual, and minor glands (Ana, 2002; Turner 2016).

Salivary gland atrophy for example, as seen during liquid diet feeding, may also lead to decreased salivary flow and can occur when there are prolonged periods of autonomic denervation. However, there is regenerative capacity in the glands and they regain normal function upon reintroduction of feeding by mouth. Salivary duct ligation, institutionalisation, compromised masticatory function, disability (cognitive and physical) and old age are often associated with salivary hypofunction. Some temporary causes of dry mouth are heavy snoring, mouth breathing, upper respiratory tract infections, dehydration and fear. Chronic stress and menopause are also commonly associated with symptoms of dry mouth. Improper prosthesis design eg extended denture flanges which may cause obstruction to the flow of saliva can also lead to hyposalivation.

Risk factors for salivary hypofunction or xerostomia:

Studies have demonstrated that female gender has a higher prevalence of developing a dry mouth sensation or xerostomia than males do at all ages. This may be commonly attributed to the fact that female patients are likely to take more medications which can induce xerostomia than the male patients. However, even in non-medicated females the prevalence of xerostomia remains high compared to their male counterparts. Some common habits such as smoking; alcohol use and the drinking of caffeine containing beverages such as coffee and soft drinks can cause dry mouth. However, these are reversible conditions and avoiding or reducing the habit or consumption may remove the xerostomic effects (Han, 2015; Petrusic, 2015).

Signs and symptoms of hyposalivation and xerostomia

When salivary hypofunction occurs, it leads to a plethora of sequelae. Table 2 describes the major clinical features of hyposalivation and xerostomia (Ana, 2002; Joanna, 2014; Turner, 2016; Gupta, 2006).

Diagnosing salivary gland hypofunction and xerostomia:

Patient's history and clinical examination of the oral cavity acts as an important diagnostic aid. The reliable clinical predictors of salivary gland hypofunction are: dryness of the lips, dryness of the buccal mucosa, absence of saliva production during the milking of parotid gland, and high decayed/missing/filled teeth (i.e., DMFT) score (Dugal, 2010). There are some specific instruments used to assess dry mouth symptoms: The Xerostomia Questionnaire (XQ) and the Xerostomia Inventory (XI). The XI consists of an 11-questions (Table 3) which can be assigned a score between 1 and 5 and the combined total score calculated into a sum ranging from 11 to 55, that represents the severity of the underlying xerostomia (Table 4). A score of 11 is characterized as very mild xerostomia and 55 represents severe xerostomia (Han, 2015).

Sialometry can be used to measure the salivary flow rate (both stimulated and unstimulated) for the objective assessment of xerostomia severity. Unstimulated salivary flow rates are determined by collecting all saliva that is

produced without any salivary stimulation while patients are at rest. In contrast, simulated salivary flow rates are obtained while a patient chews on paraffin wax or some other material. In healthy people, the unstimulated whole saliva rate exceeds 0.15 mg/min. When saliva production decreases by about 50%, subjective symptoms of dry mouth appears. The best strategy is to monitor a patient's salivary health (objectively and subjectively) over time (Gupta, 2006). The Modified Schirmer test can also be used to diagnose xerostomia. It is quick, inexpensive, does not need sophisticated equipment and has acceptance from the patients. Additionally, sialography may be used to identify calcification or stones in salivary gland. Salivary scintigraphy can be used in assessing salivary gland function. Minor salivary gland biopsy is used for diagnosis of Sjögren's syndrome, HIV salivary gland disease, sarcoidosis and amyloidosis. Biopsy or fine-needle aspiration biopsy of major salivary glands is an option when malignancy is suspected (Dugal, 2010; Gupta, 2006).

Management of xerostomia

Prosthodontists often acts as primary care givers in the management of xerostomia. Treatment of salivary hypofunction or xerostomia requires identification of the etiological factor and then appropriate therapy (such as antibiotics for bacterial infections and surgery for neoplasm). Most of the cases requires replacement of lost fluid with artificial salivary substitutes and salivary stimulation with pharmacological drugs (sialagogues), sugar-free gums and mints. Some useful tips for managing salivary hypofunction and xerostomia includes advising the patients to sleep on their side to reduce mouth breathing and to frequently apply petroleum-based lubricants to their lips during the day as well as at the bedtime. It is advisable to place a cool-air humidifier in the bedroom, 1 hour before bedtime (Ana, 2002).

Dental management of these patients begins with thorough patient education. To compensate for intraoral dryness, patients usually avoid chewing and prefer a liquid or semiliquid diet that is usually rich in fermentable carbohydrates. As decreased mastication worsens the condition, patients should undergo nutritional counselling to limit the harmful effects of diet modifications. Patients should be emphasized to chew, because periodontal mechanoreceptors and mechanical stimulation of the tongue and oral mucosa act as a vital stimuli for salivation. The use of citrus sweet drinks or candies accelerates the caries process and should be avoided. Sugar-free candies and gum are highly recommended (Ana, 2002).

Consultation with physicians and pharmacists is recommended if elimination or substitution of an offending medication is considered. The timing of the dose may be changed to correspond with meals, thus enabling salivary stimulation through the process of eating to counteract the drying effect of the drug. The use of medication before bedtime should be avoided as this time period is associated with minimum salivary flow rate (Ana, 2002).

A change in fluid intake is recommended. Patients should be advised to sip cool water throughout the day and drink milk with their meals. Water will cleanse and hydrate the oral tissues but, it cannot act as a substitute for saliva. Whole milk serves as a better substitute as it contains moisturizing properties. Olive oil can also be swabbed onto the mucosa to provide lubrication. Citrus fruits that can irritate the oral mucosa; caffeine and alcohol (including alcohol-containing mouthwashes) may cause additional dryness of the mucosa and must be avoided (Ana, 2002).

Sialagogues used for the treatment of xerostomia are of two type- gustatory sialagogues and pharmacological sialagogues. At a primary level of management, gustatory sialagogues may adequately promote a flow of saliva. Towards this end, the sugar-free chewing gums have been of substantial value. They stimulate saliva flow by their continued release of flavour over at least 30 minutes as well as by the action of mastication. Pharmacological sialagogues (drugs) that can be used in the treatment of xerostomia are mentioned in Table 5 (Ana, 2002; Turner, 2016; Gupta, 2006).

Levine et al defined the ideal artificial saliva substitute as long-lasting, capable of providing lubrication, to wet and protect oral tissues, and able to inhibit the colonization of cariogenic bacteria (Ana, 2002). However, an ideal saliva substitute is not available till date. Commercially available products contain –salts, carboxymethyl cellulose derivatives, or animal mucins - to increase viscosity, parabens to inhibit bacterial growth, and sugar-free flavouring agents (sorbitol or xylitol). These are available in the forms of sugarless chewing gums, tablets, discs, patches, mouth rinses, solutions, spray, gel, infusion pumps, pastilles and canisters. However, the current commercial saliva substitutes are short-acting, require constant reapplication and are not cost effective. Various available saliva substitutes are listed in Table 6 (Ana, 2002; Turner, 2016; Fergusson, 1994; Gupta, 2006).

An ideal salivary reservoir is a device that stores the saliva and doesn't impede with the normal oral functions. It should be simple to use and easy to clean. Saliva reservoirs are divided into three types: Based on the arch into which they are incorporated- maxillary or mandibular reservoirs. Based on cleansability of salivary reservoir they can be classified as cleansable reservoir and non-cleansable reservoir. Based on functional aspect of stomagnathic system: functional salivary reservoir, where the patient can control the release of saliva by functional movement of the oral structures and nonfunctional salivary reservoir where release and flow rate are not under the control of patient. The salivary reservoirs can be filled with artificial saliva. The volume of an average salivary reservoir ranges from 2.3-5.3 ml and the duration of flow ranges from 2-5 hours (Bushan, 2016).

Acupuncture is capable of increasing parasympathetic activity, which results in neuropeptide release that stimulates salivary gland blood flow and secretions (Blom, 1992; Dawidson, 1997). Gamma-linoleic acid (evening primrose oil, 2000 units daily, ingested over a minimum of 6 weeks) also has been recommended to increase parotid and submandibular gland salivary flow, although its mechanism of action is not clearly understood (Ana, 2002). Hyperbaric oxygen therapy increases stimulated saliva output, decreased sensation of dry mouth, and hence trend toward improvement in quality of life (Fox, 2015). Artificial salivary gland fabricated based on the principles of tissue engineering (Sood, 2013) and salivary gland transfer also have been implicated as treatment modalities for xerostomia.

Prosthodontic considerations in xerostomia:

General considerations:

The lips should be coated with petroleum jelly to help retraction and access to the oral cavity. The operator's gloved fingers should be wetted to prevent them from sticking to the soft tissues. As the mirror is less bulky than fingers, it should be used to facilitate tray insertion. Silicone impression materials should be used as they are best tolerated and least traumatic to the mucosa. Zinc oxide eugenol paste adheres to and burns the mouth and materials such as plaster of Paris will adhere to the mucosa and abrade it and hence should be avoided (Jacob, 2013).

Dry mouth and complete dentures:

Salivary hypofunction and xerostomia can cause devastating effect in the denture-wearing patients because of multiple factors that affect chewing, swallowing, tasting and speaking. Saliva plays a crucial role for the retention and comfort in wearing removable prostheses. Saliva is required to create adhesion, cohesion and surface tension that aids in increased retention of removable prostheses. Diminished salivary flow causes a lack of lubrication and can produce denture sores in the denture mucosal interface. Hyposalivation or xerostomia may lead to dislodgement of the prosthesis due to decreased stability and retention during common functions and can cause social embarrassment; ultimately impairing a person's ability or willingness to speak or eat, particularly in public. Patients can be advised to spray/wet their prostheses with artificial saliva before denture insertion and before meals. Increasing the wetting of the prosthesis enhances retention and stability during function, and this will aid in mastication and swallowing. Patients should be instructed to wet their prostheses before applying adhesive, and a combined use of denture adhesive and artificial saliva appears to be beneficial. During mealtime, greater intake of liquids, specially water, is recommended; to aid in mastication and speech. Metal denture bases can be preferred due to their better wettability. When resin denture bases are used, soft relining may be done to improve comfort (Turner, 2008).

Patients with salivary hypofunction are more susceptible to mucosal candidiasis due to lack of lubricating and protective action of saliva. It manifests as a combination of a pseudomembranous covering, erythema of the underlying tissues and a burning sensation of the tongue, surrounding soft tissues or of the whole mouth (stomatopyrosis). Burning sensation can be common over the oral structures that contacts the denture area. The oral mucosa sometimes may appear normal clinically, but the lack of lubricating effect of saliva in xerostomia along with the microfriction of the denture against the mucosal surface usually induces dysesthesia. Although treatment regimens have been recommended for burning mouth syndrome, there has been little documentation on the condition in denture-wearing patients who have dry mouth (Turner, 2008). Patients with complete dentures and hyposalivation experiencing fungus-associated denture stomatitis can be diagnosed by means of clinical findings, although microscopy can be used to confirm the clinical diagnosis by showing mycelia or pseudohyphae in a direct smear. Dentures supporting tissues can be treated by applying topical antifungal agents, such as nystatin cream and azole gel onto the tissue surface of the denture before placement. Dentures may be cleaned with 0.2% chlorhexidine solution overnight or a 1% chlorhexidine gel twice a day. In cases of severe infection, systemic antifungal treatment is required. If refractory, systemic therapy with fluconazole may be provided. Denture use at night should be

discouraged. Regular maintenance of denture hygiene is recommended with brushing and denture cleansers (Turner, 2008; Gupta, 2006).

In the patient with decreased salivation, the lack of salivary lubrication can also produce traumatic ulceration of the mucosa. The ulcerations typically manifest as small, painful lesions with elevated circumferential fibrous tissue. If ulceration is left untreated, a frictional reactive hyperplasia can occur that develops into an epulisfissuratum. An epulisfissuratum appears as redundant tissue in the alveolar vestibule. Treatment of an epulisfissuratum or a fibro-epithelial polyp requires complete surgical excision, and after surgery, the dentures must be refabricated, rebased or relined (Turner, 2008).

Although there is insufficient scientific evidence regarding the use of denture adhesives in general, their use to enhance retention of well-made prostheses is acceptable and, at times, necessary. Moistened denture adhesives improve adhesion and cohesion and create a uniform fill of material, particularly on well-made prostheses, that improves surface tension. In patients with hyposalivation, the use of adhesives can lead to enhanced denture function and patient comfort. The patient should be educated regarding the daily use of adhesives and should be advised to visit the dentist annually to evaluate the adequacy of the prosthesis and the health of the underlying denture-bearing tissues (Turner, 2008).

Fixed partial denture (FPD):

In the dry oral environment, fixed non tissue bearing prosthesis are preferred where indicated. Full coverage retainers with supragingival margins and easily cleaned pontics are recommended when xerostomic patients are provided with FPDs (Dugal, 2010).

Removable prosthodontics:

In case of partially edentulous patients using removable prosthesis special attention should be given to residual teeth and periodontal tissues. Gingivally approaching clasps should be avoided as they may impinge onto the cheeks. Tooth supported denture with minimal tissue coverage, whenever possible are advisable. Metal denture bases should be preferred because of their better wettability (Dugal, 2010).

Conclusion:-

Xerostomia is a debilitating condition and may occur due to a variety of underlying etiologies including systemic diseases, medications, head and neck radiation, and improper lifestyle. Taking a thorough medical history, including the patient's past medical history, medication list, and social history, is of utmost importance for the diagnosis of dry mouth. The vulnerable elderly denture-wearing population with salivary hypofunction and xerostomia is at risk of experiencing social withdrawal, malnutrition and a host of oropharyngeal problems. There are few adequate treatments for these common oral problems, and new therapies are required that will enhance denture retention, reduce dryness and enhance oropharyngeal health in older edentulous patients who have xerostomia.

Table 1:- List of xerogenic medications.

Sr.No	Category	Drug
1.	Sedative agents	Benzodiazepams: Alprazolam, Diazepam, Lorazepam, Oxazepam, Triazolam
2.	Antihistamines	Carbinoxamine, Clemastine, Dexchlorpheniramine, Diphenhydramine, Hydroxyzine, Meclizine, Promethazine, Cetirizine, Desloratadine, Fexofenadine, Levocetirizine, Loratadine
3.	Anti-Parkinsonian	Benzotropine, Bromocriptine, Carbidopa, Entacapone, Levodopa, Pramipexole, Rasagiline, Ropinirole, Selegiline, Trihexyphenidyl
4.	Antihypertensives	Alpha agonist: Clonidine, Guanabenz Beta-blockers: Acebutolol, Atenolol, Bebutolol, Betaxolol, Bisoprolol, Carvedilol, Esmolol, Labetalol, Metoprolol, Penbutolol, Pindolol, Propranolol, Stalol, Timolol Diuretics: Bumetanide, Furosemide, Torsemide Calcium channel blockers: Amlodipine, Diltiazem, Felodipine, Isradipine, Nifedipine, Nimodipine, Verapamil ACE inhibitors: Benazepril, Captopril, Enalapril, Fosinopril, Lisinopril, Moexipril, Perindopril, Quinapril, Ramipril, Trandolapril

5.	Antidepressants	Fluoxetine, Paroxetine, Venlafaxine, Mirtazapine, Trazodone, Amitriptyline, Clomipramine, Doxepin, Imipramine, Nortriptyline, Protriptyline, Trimipramine
6.	Cholinolytic agents	Atropine, Homatropine, Scopolamine
7.	Immunostimulants	Interferon-alpha
8.	Appetite suppressants	Sibutramine

Table 2:- Signs, symptoms and clinical features of salivary hypofunction and xerostomia.

Sr. No	Signs and symptoms
1	Increased incidence of dental caries
2	Susceptibility to candidiasis
3	Burning mouth
4	Erosion and ulceration of mucosal tissues
5	Glossodynia (sore tongue)
6	Altered taste sensation (dysgeusia)
7	Difficulty with speech
8	Difficulty with swallowing (dysphagia)
9	Difficulty with mastication
10	Gingivitis
11	Halitosis
12	Impaired use of removable prostheses
13	Extra orally- dry and cracked lips and angular cheilitis
14	Depapillation of tongue
15	Absence of or decrease salivary output from milking of parotid gland.
16	Food debris may stick to teeth or soft tissue and the normal pooling of saliva in the floor of mouth is absent.
17	A tongue depressor, used to examine the mouth, can stick to the buccal mucosa.
18	The dry mucosa is more susceptible to trauma and infection, and the patient may be suffering from painful mucositis.
19	Difficult to eat dry foods such as biscuits, nuts (crackersign).

Table 3:- Xerostomia inventory.

	Xerostomia inventory
1	My mouth feels dry
2	I have difficulty in eating dry foods
3	I get up at night to drink
4	My mouth feels dry when eating a meal
5	I sip liquids to aid in swallowing food
6	I have to suck sweets or cough lollies to relieve dry mouth
7	I have difficulties swallowing certain foods
8	The skin of my face feels dry
9	My eyes feels dry
10	My lips feel dry
11	The inside of my nose feels dry

Table 4:- Scoring criteria for xerostomia inventory.

Rating	Response
1	Never
2	Hardly ever
3	Occasionally
4	Fairly often
5	Very often

Table 5:- Drugs used for the treatment of xerostomia.

Drug	Form and dosage
Pilocarpine	5 to 10 mg administered 3 or 4 times daily, 30 minutes before meals.
Cemivaline	30 mg, 3 times a day.

Table 6:- Salivary Substitutes.

Saliva substitutes	Ingredients
Entertainer's Secret (spray)	NaCMC, Na ₂ HPO ₄ , KCl, parabens, aloe vera, glycerin
Moi-Stir (solution)	NaCMC, Na ₂ HPO ₄ , CaCl ₂ , MgCl ₂ , KCl, NaCl, parabens, sorbitol
MouthKote (spray)	xylitol, sorbitol, yerba santa, citric acid, ascorbic acid, sodium benzoate, sodium saccharin
Oralbalance (gel)	hydroxyethyl cellulose, hydrogenated starch, glycerate, polyhydrate, KSCN, glucose oxidase, lactoperoxidase, lysozyme, lactoferrin, aloe vera, xylitol
Saliva Substitute (solution)	NaCMC, sorbitol, methylparaben
Salivart (spray)	NaCMC, sorbitol, KCl, NaCl, CaCl ₂ , MgCl ₂ , K ₂ HPO ₄
Saliva Orthana* (spray)	porcine mucin, xylitol, methyl paraben, EDTA, benzalkonium chloride, NaF, KCl, NaCl, MgCl ₂ , CaCl ₂ , K ₂ HPO ₄
Saliva stimulant Salix SST (lozenge)	hydroxypropyl methylcellulose, CMC, Ca ₂ H ₂ (PO ₄) ₂ , malic acid, citric acid, hydrogenated cottonseed oil, sodium citrate, SiO ₂ , sorbitol

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