XEROSTOMIA – an update. Part I


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The complete functioning of the salivary system depends on the proper salivary flow rate and its composition.

The secretion of saliva is critical for hard and soft tissue maintenance. This article will concentrate on the functions of saliva and how pathophysiology manifests. The etiology of xerostomia and comprehensive diagnostic procedures will be discussed. Part two of this article will evaluate the management of xerostomia.

Xerostomia is defined as "the subjective symptom of oral dryness whilst salivary gland hypofunction is an objective situation characterised by reduced salivary flow (Thomson, W. Murrray et al., 1999)." Xerostomia is frequently, but not always associated with salivary gland hypofunction (Fox PC, Eversole R., 2001).

It is estimated that 12-47% of the elderly and 10-19.3% of people in their early 30's have been suffering from dry mouth (Thomson, W. Murrray, 2005, Thomson, W. Murrray et al., 2006, Guggenheimer J, Moore PA., 2003). Xerostomia is more common in women than men.

FUNCTIONS OF SALIVA:

- Important role in mastication, swallowing and formation of a nutritional bolus which aids in digestion.
- Protects against thermal, mechanical and chemical irritants.
- Guards oral tissues against physical and microbial insults (The antimicrobial properties of saliva are due to several immune and non-immune salivary proteins that inhibit both the adherence and growth of viruses and bacteria. De Almeida, Patricia Del Vigna, et al., 2008).
- Salivary proteins and mucins lubricate and coat oral tissues.
- Maintains a neutral pH by acting as a buffer.
- Demineralisation and remineralisation balance at the biofilm/enamel interface is affected by the ion concentration in saliva.
- Provides moisture which facilitates speech and taste.
- Useful diagnostic tool as it has biomarkers which act as indicators of various physiological states in either health or disease.

PATHOPHYSIOLOGY

Saliva is produced by the parotid, submandibular and sublingual glands, as well as by many minor salivary glands situated throughout the mouth. Daily salivary output is estimated to be approximately one litre per day (Cooper JS. et al., 1995). Flow rates can vary as much as 50% with diurnal rhythms (Ghezzi EM. et al., 2000, Dawes C, 1987 and Ship J. et al., 1991). The basal secretion of saliva which occurs due to spontaneous activity of the salivary nuclei shows a circadian rhythm of high amplitude (Dawes C, 1987).

Both the parasympathetic and sympathetic nervous systems innervate the salivary glands. Parasympathetic stimulation induces more watery secretions, whereas the sympathetic system produces a sparser and more viscous flow (Dubnar R. et al., 1978). Thus, if dryness occurs, for example, during episodes of acute anxiety or stress there can be changes in salivary composition as a result of predominantly sympathetic stimulation during such periods.

Considerable loss of salivary gland function is associated with altered taste sensation called dysgeusia (Mese H, Matsuo R, 2007). Symptoms of a lack of saliva or oral dryness may be precipitated by dehydration of the oral mucosa (Ghezzi EM. et al., 2000) which occurs when output by the major and/or minor salivary glands decrease and the layer of saliva that covers the oral mucosa is reduced (Wolff M, Klineberg I, 1998, Bretz WA. et al., 2000).

CLINICAL SIGNS AND SYMPTOMS OF HYPOSALIVATION

Teeth

- Increased incidence of tooth decay (cervical and incisal)
- Loss of restorations
- Demineralisation of enamel
- Erosion and attrition of enamel
- Increased plaque accumulation
- Increased tooth sensitivity

Oral mucosa

- Reduced dilution of plaque acids and antimicrobial protection predisposing to gingivitis
- Mucositis
- Desquamation of mucosa
- Atrophy of mucosa
- Allergic or contact stomatitis
- Angular stomatitis
- Lichenoid lesions (mostly opposite metal restorations)
- Recurrent oral candidiasis
- Traumatic ulcers on the lateral border of the tongue, buccal mucosa or both
- Painful or burning mouth (cannot manage spicy, sour or salty food or drinks) which can affect quality of life and well-being.
- Non-specific gingival inflammation and generalised oral erythematous areas

Tongue

- Dryness, fissures, lobulation
- Atrophy
- Erythema
- Loss of papillae
- Scalloped borders on the tongue

Lips

- Dryness, chapping
- Peeling
- Fissuring
- Angular cheilitis

Major Salivary Glands

- Compromised salivary output
- Frothy saliva
- Reduced or absent saliva pooling
- Salivary glands are swollen or enlarged
- Recurrent sialadenitis affecting major salivary glands

Oral Cavity

- Oral allergic or contact reactions
- Halitosis
- Difficulty talking, eating, chewing and swallowing (dysphagia)
- Plaque build-up
- Reduced oral clearance
- Altered taste sensation
- Retention of food and debris on teeth or tongue or along gingival margins

Other

- Nutritional deficiencies (dehydration, malnutrition (Zarb GA. et al., 2003), weight loss, increase in thirst, altered preferences for food and drink)
- Dry eye accompanied by dry mouth (Sjogren's Syndrome – SS)
- Extreme discomfort wearing dentures and dislodgement of dentures at rest
- Buccal mucosa, tongue and lips can stick to the denture predisposing to mucosal abrasion and ulcers.

ETIOLOGY

Causes of Xerostomia:

Medications

The use of medications is one of the most frequently reported causes of xerostomia (Napeñas JJ. et al., 2009).

The following drugs are associated with Xerostomia:

Anticholinergic Agents	
BENZOTROPINE:	
Congentin®	
IPRATROPIUM BROMIDE (short acting):	
Atrovent	
TIOTROPIUM (long acting):	
Spiriva	
Diuretics	
FUROSEMIDE:	
Lasix®	
Sedatives & Anxiolytic Agents	
BENZODIAZEPINES:	
Valium® , Mogadon®	
Muscle Relaxant Agents	
ORPHENADRINE:	
Norflex ™	
Steroids	
BUDESONIDE:	
Pulmicort ® Turbuhaler, Pulmicort® Respules	
Antihistamines	
LORATADINE:	
Claratyne	
Antiemetics	
NABILONE:	
Cesamet®	
Psychotropic Agents	
Antipsychotic agents:	
OLANZAPINE	Zyprexa®
QUETIAPINE	Seroquel®
Selective Serotonin-reuptake inhibitors:	
SERTRALINE	Zoloft®
PAROXETINE	Aropax
FLUOXETINE	Prozac, Lovan
Tricyclic antidepressants:	
NORTRIPTYLINE (high dose)	Allegron
AMITRIPTLINE (low dose)	Tryptanol
Heterocyclic antidepressants:	
AMOXAPINE	Asendin
Monamine oxidase inhibitors:	
PHENELZINE	Nardil
Atypical antidepressants:	
MIRTAZEPINE	Avanza, Axit
Antihypertensive Agents	
Angiotensin-converting enzyme inhibitors:	
VERAPAMIL	Isoptin®
Angiotensin-receptor blockers:	
ANDESARTAN	Atacand®
TELMISARTAN	Micardis®
Alpha blockers:	
PRAZOSIN	Minipress, Pressin
B-adrenergic blockers:	
METOPROLOL	Betaloc, Lopressor
PROPRANOLOL	Inderal
Analgesic Agents	
Central nervous system/ opioids;	
PROPOXYPHENE	Doloxene
Non-steroidal anti-inflammatory agents (NSAIDS):	
IBUPROFEN	Advil

Most medications do not damage the salivary glands but the chances of decreased salivary flow rates increases in the presence of many diseases and medications. Patients who take multiple xerostomic medications are more likely to have more severe dry mouth symptoms. The effects of xerostomic medications on patients can vary significantly. Some medications for example those used for overactive bladder disease, irritable bowel and Parkinson's disease are employed for their anticholinergic activity. These medicines directly inhibit saliva flow and are associated with dry mouth symptoms (Forte E. et al., 2012). Therapeutic doses of medications do not damage salivary gland anatomy and any damage is therefore reversible with discontinued use of the xerogenic drugs (Pajukoski H. et al., 2001).

Systemic Diseases

- Endocrine Disease – Diabetes Type 1 or 2, Thyroid Disease
- Viral infections – HIV, Hepatitis C, Epstein-Barr, CMV, Human T – lymphotropic virus Type 1
- Bacterial infections – Actinomycosis, Tuberculosis
- Autoimmune diseases – Rheumatoid Arthritis, Systemic Lupus Erythematosus, Primary Biliary Cirrhosis, Scleroderma
- Granulomatous Disease – Sarcoidosis, Tuberculosis
- Storage Disease – Hemochromatosis, Amyloidosis
- Primary & Secondary Sjorgen's Syndrome
- Connective Tissue Disease (Systemic Sclerosis, Mixed connective tissue disease)
- Vasculitis
- End stage renal disease – Renal dialysis
- Salivary gland agenesis (with or without ectodermal dysplasia)
- Hematopoietic stem cell transplantation and chronic graft-versus-host disease
- Parkinson's disease
- Cerebral Palsy
- Anxiety or Depression
- Post-traumatic stress disorder
- Anorexia and Bulimia
- Dehydration
- Trauma to salivary glands
- Eaten-Lambert Syndrome

Radiation therapy

Xerostomia is a common side effect of radiation therapy when used as the primary or adjunctive treatment for primary or recurrent tumours of the head and neck (Porter S. et al., 2004). The most radiosensitive gland is the parotid gland followed by the submandibular, sublingual and minor salivary gland.

Radiation doses as low as 20Gy can result in permanent salivary flow cessation if given as a single dose. At doses above 52Gy, salivary dysfunction is severe. The treatment of oral carcinoma normally involves a dose of 60Gy – 70Gy. This can cause a rapid drop in flow during the first week of radiation and eventually a 95% reduction in the flow.

After 5 weeks of radiation, salivary flow practically ceases and rarely recovers completely (Porter S. et al., 2004). The degree of xerostomia depends on the degree of exposure of the salivary tissue to radiation.

In order to maintain as much salivary function and quality of life as possible, salivary gland exposure to radiation can be kept minimal by using intensity modulated radiation therapy (IMRT) and dose delivery techniques. As a result, radiotherapy can be directed at the lesion site in the head and neck region while sparing the surrounding salivary glands and thus preventing xerostomia. The parotid gland is the one most often spared with IMRT (Rieger JM., 2012).

A reduction in radiation-induced hyposalivation was observed by using amifostine, a radio-protective agent which confers cytoprotection to salivary glands (Guggenheimer J, Moore PA., 2003, Antonadou D. et al., 2002).

DIAGNOSIS

History and examination

Proper evaluation and patient assessment should include detailed medical and dental

history in order to diagnose salivary gland hypofunction.

The clinical examination should also include extraoral and intraoral findings. The clinician should check and palpate major salivary glands to identify masses, swelling or tenderness.

A positive response to certain questions has been linked to diminished saliva even with patients who have not expressed concerns of xerostomia.

- Does the amount of saliva in the mouth appear to be too little?
- Does the mouth feel dry when eating a meal?
- Is it necessary to sip liquids to help swallow dry food?
- Is it difficult to swallow?

Diagnostic tests

Salivary assessment:

These should be employed to measure saliva flow. Whole saliva is quite easy to collect in the clinic. Salivary flow can be defined as unstimulated or resting, and stimulated, which occurs when an exogenous factor acts on the secretory mechanisms (Dawes C, 1987).

Unstimulated whole saliva is most commonly collected by the "draining or drooling" method. The patient's head is tilted forward and pooled saliva is drooled into a sterile container.

The range of normal flow rates in unstimulated conditions is from 0.2-0.5 ml/min (Vissink A. et al., 2008). Unstimulated whole saliva flow rate of less than 0.1 ml/min suggests significant salivary gland hypofunction.

Stimulated whole saliva is collected by challenging the glands through mastication – chewing paraffin wax or by gustatory stimulation using citric acid. Then the patient expectorates into a collection tube. The normal stimulated flow rate is from 0.9-2.6 ml/min.

Stimulated whole saliva flow rates below 0.7ml/min fall within the lower range or output and suggest salivary hypofunction (Ship JA. et al., 1991).

Blood Tests

A complete blood cell count can be informative when xerostomia is thought to be associated with systemic disease. Autoantibody screening may be helpful if xerostomia is associated with xerophthalmia, a feature of Sjorgen's Syndrome. This should include blood results positive for serum antinuclear antibody, rheumatoid factor or the antibodies anti-SS-A (anti-Ro) or anti-SS-B (Anti-La) (Fox RI., Liu AY., 2006).

Biopsy

Minor salivary gland biopsy can be used to identify underlying pathological changes associated with salivary gland dysfunction. Histologic changes are one of the criteria used to diagnose Sjorgen's Syndrome. Tissue samples are graded according to the level of inflammation within the salivary gland.

Biopsy is useful to ascertain if salivary gland dysfunction is caused by other diseases such as amyloidosis, sarcoidosis or other conditions.

Conclusion

There is a significant prevalence of xerostomia and salivary hypofunction in the population. The associated factors include medications, systemic diseases and radiation therapy. Medical and dental health professionals need to work as a team to best manage the needs of the patient. ◆

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