An update on xerostomia: part I

In the first of a two-part series, **Brenda Baker** and **David Reaney** discuss the function and role of the salivary system and the treatment of xerostomia

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 aetiology 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 et al, 1999). Xerostomia is frequently, but not always, associated with salivary gland hypofunction (Fox and Eversole, 2001).

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

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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 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 that facilitates speech and taste
- Useful diagnostic tool as it has biomarkers that act as indicators of various physiological states in either health or disease.

XEROSTOMIA IS MORE COMMON IN WOMEN THAN MEN

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 et al, 1995). Flow rates can vary as much as 50% with diurnal rhythms (Ghezzi, Lange and Ship, 2000; Dawes, 1987; Ship, Fox and Baum, 1991). The basal secretion of saliva, which occurs due to spontaneous activity of the salivary nuclei, shows a circadian rhythm of high amplitude (Dawes, 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, Sessle and Storey, 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 and Matsuo, 2007). Lack of saliva or oral dryness symptoms may be precipitated by dehydration of the oral mucosa (Ghezzi, Lange and Ship, 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 and Klineberg, 1998; Bretz 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.

Anticholinergic agents	
Benzotropine	Congentin
Ipratropium bromide (short acting)	Atrovent
Tiotropium (long acting)	Spiriva

Diuretics	
Furosemide	Lasix

Sedatives and 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 Quetiapine	Zyprexa Seroquel
Selective serotonin - reuptake inhibitors	Sertraline Paroxetine Fluoxetine	Zoloft Aropax Prozac, Lovan
Tricyclic antidepressants	Nortriptyline (high dose) Amitriptline (low dose)	Allegron Tryptanol
Heterocyclic antidepressants	Amoxapine Asendin	
Monamine oxidase inhibitors	Phenelzine	Nardil
Atypical antidepressants	Mirtazepine	Avanza, Axit

Antihypertensive agents		
Angiotensin - converting enzyme inhibitors	Verapamil	Isoptin

Antihypertensive agents		
Angiotensin-converting enzyme inhibitors	Verapamil	Isoptin
Angiotensin-receptor blockers	Verapamil Andesartan	Isoptin Atacand
Alpha blockers	Prazosin	Minipress, Pressin
B-adrenergic blockers	Metoprolol Propanolol	Betaloc, Lopressor Inderal

Analgesic agents		
Central nervous system/opioids	Propoxyphene	Doloxene
Non-steroidal anti-inflammatory agents (NSAIDS)	Ibuprofen	Advil

Tables 1-11: Drugs associated with xerostomia

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 and 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 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.

Aetiology

The following are the causes of xerostomia:

Medications

The use of medication is one of the most frequently reported causes of xerostomia (Napeñas, Brennan and Fox, 2009). Tables 1-11 show the drugs associated with xerostomia.

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, such as 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 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 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 – haemochromatosis, amyloidosis
- Primary and secondary Sjörgen'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)
- Haematopoietic 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 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 flow. After five weeks of radiation, salivary flow practically ceases and rarely recovers completely (Porter, Scully and Hegarty, 2004). The degree of xerostomia depends on the degree of exposure of the salivary tissue to radiation.

THERAPEUTIC DOSES OF MEDICATIONS DO NOT DAMAGE SALIVARY GLAND ANATOMY

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 and Jana, 2012).

A reduction in radiation-induced hyposalivation was observed by using amifostine, a radio-protective agent, which confers cytoprotection to salivary glands (Guggenheimer and Moore, 2003; Antonadou 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, 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, Wolff and Veerman, 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/minutes fall within the lower range or output and suggest salivary hypofunction (Ship, Fox and Baum, 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 Sjörgen'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 and Liu, 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 Sjörgen'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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