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PLENARY ABSTRACT

Xerostomia: prevalence, assessment, differential diagnosis and implications for quality of life

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Prevalence of symptoms of xerostomia

There are few population-based studies although a systematic review suggested that 6 to 13% of males, and 20 to 40% of females over 65 years of age may have symptoms of xerostomia. These numbers climb to above 60% in groups of institutionalised elderly persons (van der Putten *et al*., 2010). The frequency of symptoms may be higher than that of objective evidence of xerostomia as a strong correlation between the two has not always been observed. Nevertheless patients reporting xerostomia (but not having objective salivary gland dysfunction) often experience allied symptoms including difficulty in eating foods (particularly dry agents), labial dryness and difficulty in swallowing foods (van der Putten *et al*., 2010). It would be expected that the numbers of individuals experiencing xersotomia will continue to rise as longevity increases, the number and range of drugs that may cause salivary dysfunction rises and as infections such as Hepatitis C Virus (HCV) continue to spread across the globe.

Aetiological aspects

A wide range of disorders can give rise to xerostomia although drug therapy and Sjogren's syndrome are possibly the most commonly recognised causes.

Drug-induced xerostomia is usually due to anticholinergic or sympathomimetic actions. The agents most commonly implicated in xerostomia include tricyclic antidepressants, antipsychotics, benzodiazepines, atropinics, beta-blockers and antihistamines, although a wide range of other drugs can give rise to oral dryness, including some chemotherapeutic agents. Depending upon the dose, Conventional Radiotherapy (CRT) that involves the salivary glands may cause rapid-onset xerostomia in up to 100% of patients. Newer techniques such as Intensity Modulated Radiotherapy (IMRT) can still cause xerostomia although this may be less longlasting than that caused by CRT (Jensen *et al*., 2010). Radioactive iodine used for treating thyroid disease can also sometimes cause long-standing salivary damage.

Sjogren's syndrome is the second most common autoimmune connective tissue disorder and thus is a common cause of xerostomia. Aside from having the oral features of long-standing xerostomia, patients with secondary Sjogren's syndrome may have oral manifestations of the accompanying connective tissue disease such as ulceration (e.g. Systemic Lupus Erythematosis (SLE) and dermatomyostitis, Mixed Connective Tissue Disease (MCTD)), microstomia (scleroderma), white patches (SLE), telangiectasia (primary biliary cirrhosis and scleroderma), trigeminal neuropathy (scleroderma) and rarely temporomandibualr joint involvement (rheumatoid arthritis). Xerostomia is a common feature of Chronic Graft Versus Host Disease (cGVHD) (Fall-Dickson *et al*., 2010).

Infections that may give rise to xerostomia include HIV and HCV. Other viruses such as Epstein-Barr virus have been implicated in causing xerostomia. A link with xerostomia and HTLV-1 infection has also been suggested (Martins *et al*., 2010).

Sarcoidosis may give rise to dry mouth and xerostomia can rarely be a feature of cystic fibrosis, diabetes mellitus, salivary gland agenesis with or without ectodermal dysplasia, triple A syndrome, amyloidosis, haemochromatosis and dyskeratosis congenital (Porter *et al*., 2004).

Diagnosis and investigation

The clinical diagnosis of recent onset xerostomia can be challenging as unless the patient has an identifiable cause (e.g. the introduction of xerostomic drug therapy) there may be no clinically detectable signs, and salivary flow rates (regardless of the method employed) may be normal. In the early stages of xerostomia the saliva can take on a "stringy" quality, saliva may be sparse or when present can be frothy and localised to the posterior floor of the mouth and lower buccal vestibules. Patients may gradually experience dysguesia and oral mucosal soreness as well as dysphagia and dysarthria.

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In contrast, the clinical signs of longstanding xerostomia are simple to identify, particularly as the mucosa is dry, and adheres easily to any clinical instruments. The mucosa of the dorsum of the tongue will become flattened and corrugated.

Bacterial and fungal infections may be evident. Food and oral debris may easily adhere to the teeth and gums and together with the possible loss of any innate or acquired immunity provided by saliva increases the risk of cervical, root and recurrent dental caries. Patients are also at risk of increased gingivitis and possibly periodontitis. Acute suppurative sialadenitis (bacterial sialadenitis) can arise. This usually affects a parotid gland and manifests as painful glandular enlargement and the symptom of dysgeusia (due to a purulent discharge from the ductual opening). Rarely the swelling can become extreme, the overlying skin being tender and red.

Patients with xerostomia may be at increased risk of oral candidosis – usually pseudomembranous candidosis, angular stomatitis (cheilitis), chronic atrophic candidosis (denture-associated stomatitis) and median rhomboid glossitis.

Salivary gland enlargement can be an accompanying feature of xerostomia. The swelling may be a consequence of mild ductal obstruction by thickened saliva (e.g. in Sjogren's syndrome), or the effects of local glandular inflammation (e.g. in Sjogren's syndrome, HIV and HCV disease, sarcoidosis and radioactive iodine therapy). Of great significance, patients with Sjogren's syndrome are at increased risk of non-Hodgkin's lymphoma (mucosa-associated lymphoid tumour (MALT)) of a major salivary gland. This tumour usually affects a single parotid gland and manifests as a diffuse non-tender swelling.

The lack of saliva may cause a loss of retention of the upper denture. The increased movement of the denture (together with the lack of mucosal salivary lubrication) may give rise to traumatic oral mucosal ulceration.

A summary of the possible clinical features of longstanding xerostomia is provided in Table 1 (Porter, Habbab and Fedele, 2010).

Objective investigation of xerostomia centres around a series of clinical, radiological and laboratory-based tests. A detailed review of the investigations is provided elsewhere (Porter *et al*., 2004). The radiological investigation of xerostomia is reviewed in an accompanying article (Brown, 2010).

Implications on quality of life

Despite the absence of a strong correlation between symptoms of xerostomia and objective salivary gland dysfunction, and the many different scoring methods for both xerostomia and quality of life, there is consistent evidence that longstanding oral dryness impacts adversely upon the lifestyle of affected individuals (Jensen *et al*., 2010). Almost regardless of the cause of xerostomia patients reporting, or having, oral dryness have poorer quality of life measures. In patients with primary or secondary Sjogren's syndrome some of the adverse effects upon quality of life may reflect non-oral features (e.g. associated lethargy). However, individuals with symptoms of xerostomia, but without objective salivary gland dysfunction, can also

Table 1 Oral manifestations of longstanding xerostomia

Symptoms
Dysphagia
Dysarthria
Dysgeusia
"Sticky" saliva
Oral mucosal and/or labial dryness and soreness
Signs
Oral mucosal dryness and lingual mucosal change
Liability to caries and gingivitis
Liability to candidal infection(s)
Liability to acute suppurative sialadenitis*

*Other causes of salivary gland enlargement that accompanies xerostomia include: Sjogren's syndrome, diffuse infiltrative lymphoocytosis syndrome of HIV salivary gland disease, HCV-related sialadenitis, Sarcoidosis and MALT lymphoma secondary to Sjogren's syndrome

have reduced health-related quality of life measures (Rostrom *et al*., 2002). Oral health-related quality of life (OHRQOL) measures may also be reduced in patients with xerostomia associated with primary or secondary Sjogren's syndrome (McMillan *et al*., 2004), these reflecting difficulties in eating and speaking, as well as problems such as sticky saliva, coughing and impaired taste (Kamel *et al*., 2009). Xerostomia secondary to conventional radiotherapy for head and neck malignancy adversely impacts upon various quality of life measures (Porter, Habbab and Fedele, 2010) while Intensity Modulated Radiotherapy (IMRT), although perhaps having no significant impact in the first 6 months post-therapy, does lessen the fall in quality of life measures between 6 and 24 months post-treatment (reviewed by Jensen *et al*., 2010). The xerostomia of cGHVD can lessen quality of life (Fall-Dickson *et al*., 2010) and it would be expected that many instances of drug-related xerostomia lessen quality of life measures, independent of any associated systemic disease.

A further concern for patients, and indeed clinicians, is that there remains no means of reversing the salivary gland dysfunction of common disorders such as Sjogren's syndrome and radiotherapy associated xerostomia (reviewed in the accompanying article by Moutsopoulos, 2010). Similarly it may not be possible to modify the drug therapy of patients with drug-induced xerostomia to provide a less xerostomic agent as often there is a commonality of adverse side-effects within groups of drugs.

The future

In general the clinical management of patients with longstanding xerostomia is likely to be lifelong and will be principally aimed at lessening the local consequences of oral dryness, the use of salivary substitutes and/or sialogogues. However in the near future it may be possible to reduce the likelihood of xerostomia arising in some groups of patients. For example the wider application of IMRT and radioprotectants may reduce the numbers of individuals who develop radiotherapy-associated xerostomia, the wider use of systemic sialogogues may aid patients with drug-induced, or radiotherapy-associated xerostomia or those with Sjogren's syndrome. The global introduction of anti-retroviral therapy (ART) may lessen the prevalence of HIV-related salivary gland disease, although it may not reduce xerostomia as protease inhibitors can cause dry mouth (Navazesh *et al*., 2009). However improved health care measures may lessen the risk of iatrogenic acquisition of HCV. Gene therapy (e.g. human aquaporin), stem cell transfer and other tissue regenerative procedures may offer the potential that the longstanding xerostomia of many individuals can ultimately be lessened or resolved.

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