Xerostomia Diagnosis - A Narrative Review

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Xerostomia can be defined as a feeling of dryness of mouth, which may or may not be accompanied with reduced salivary secretions. Xerostomia may result in localized and systemic disturbances within the body. The overall global prevalence of xerostomia is 22% with wide variation among different countries due to difference in target population. This review presents the recent literature on the diagnostic methodologies that are present in recent times through subjective and objective corridors. The most commonly used subjective methods for the xerostomia diagnosis include: Fox questionnaire, Visual Analogue Scale (VAS), Xerostomia Inventory (XI), and Shortened Xerostomia Inventory (SXI). Objective xerostomia diagnostic tools include salivary flow rate assessment. Aside from this, there are numerous radiographical modalities that can be used especially in diagnosing salivary gland disorders or radiation exposure due to oncological treatments which can also provide the added information to diagnose or monitor xerostomia. These radiographic tools include computer tomography (CT), scintigraphy, sialography, magnetic resonance imaging (MRI), and ultrasonography. Different combination of tools gives a better xerostomia assessment, selection of which also depends on the age and health condition of the patient.

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INTRODUCTION

Whole saliva is a vital oral fluid that helps in preservation of healthy oral tissues.[1] Disturbances in the salivary flow rate may affect oral health, which can directly impact the quality of life of the individual.[2] Less saliva in oral cavity may lead to caries, frequent oral ulcers and blisters, oral malodor, periodontal problems, difficulties in swallowing and speech. One such consequence is xerostomia. Xerostomia is defined as a feeling of mouth dryness[3] which may or may not be accompanied with hyposalivation. Hence, may be classified as subjective and objective xerostomia. Xerostomia from objective hyposalivation has been termed as true xerostomia, whereas subjective oral dryness despite normal salivary function has been referred as pseudo xerostomia.[3] Additionally, the terms "xerostomia" and "salivary gland hypofunction" have been used for the same phenomenon but in reality are separate entities.[4] This solidifies the pseudo element of the condition because not all patients exhibit a pathological salivary gland dysfunction.[3] Owing to its subjective trait, xerostomia poses difficulty in better understanding of its nature. The overall global prevalence of xerostomia is 22% with wide variation among different countries due to difference in target population.[5] In developed countries such as Australia, xerostomia prevalence is reported to be 13%[6], whereas, in Iran, the prevalence is about 8%.[7] In Pakistan, limited studies have been reported on prevalence of xerostomia in general population. In a study conducted on Pakistani army soldiers with hepatitis C, the reported prevalence was 70%.[8] Xerostomia predisposition in females and especially among the geriatrics is well reported.[7]

An array of systemic diseases can be affiliated with hyposalivation. Autoimmune diseases encompassing: Sjogren syndrome, Systemic lupus erythematosus (SLE), AIDS, Parkinson's disease, rheumatoid arthritis, and hepatitis C virus (HCV) infection play a significant part in altering salivary glands functions.[3] Moreover, hormonal, psychogenic, and neurologic diseases such as anxiety, depression, schizophrenia, bipolar disorders, also have a

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brief or irretrievable impact on the salivary flow rate of the patients.[9] Xerogenic drugs or chemicals such as tricyclic antidepressants, antihistamines, diuretics, antihypertensive drugs, decongestants etc. also have a potential of lowering salivary flow or causing dry mouth in individuals.[3] Furthermore, hyposalivation is one of the most commonly reported and detrimental side effect occurring in 95% of the patients that undergo radiotherapy in the region of the head and neck.[10]

Xerostomia can cause dental caries, frequent fungal and bacterial infections, oral ulcerations and halitosis[1], taste disturbances, difficulty in eating, swallowing and speaking[9], atrophic mucosa[11], burning mouth, and difficulty in retention of dentures.[3] All of which may result in malnutrition.[12] Wide ranges of clinical features present a serious impediment in its diagnosis and treatment. To date no standard diagnostic protocol is present for xerostomia.[13]

Subjective diagnosis of xerostomia

Comprehensive history taking plays an important role in the diagnosis of a disease even before performing any physical examinations and tests.[14] Evaluation and diagnosis of xerostomia requires detailed questioning about past medical history, practice of polypharmacy, altered taste, and difficulty in any of these: eating, swallowing, chewing, and wearing dentures.[3] Multiple questionnaires are framed to identify and assess the rate of xerostomia. As xerostomia needs to be understood from patient's perspective, a patient-reported outcome measure (PROM) is essential to evaluate xerostomia.

1. Fox's questionnaire

Fox questionnaire was first introduced in 1987 and comprises 9 items pertaining to experience of oral dryness. Four of the items in the questionnaire indicates a direct correspondence to reduced salivary flow and if the patients respond positively to any one of these four questions, they are identified as xerostomic patients.[15] The purpose of this questionnaire is to identify presence of reduced saliva secretion, difficulty during swallowing, and the necessity to take sips of water with dry food.[16] For patients who are non-compliant in terms of saliva collection for salivary flow rate assessment, this questionnaire plays a vital role in the evaluation of the symptoms;[16] however, questionnaire results might not draw a parallel with the salivary flow rate effectively,[17] as xerostomia may exist in the absence of hyposalivation and vice versa.[18]

2. Xerostomia Inventory (XI)

The Xerostomia Inventory (XI) is one of the extensively used and validated PROM, introduced by Thomson et al. in 1999[19]. This consists of 11-items which are to be answered and then graded from 1 to 5: 1 being 'never' while 5 being 'very often'. The score ranges from 11 to 55, a higher score represents poor quality of life.[20] XI was introduced to better understand and record the severity of xerostomia in individuals.[19] XI covers two separate aspects one being the experience of xerostomia felt by individuals and second one involving the consequences of the disease.[19]

3. Shortened Xerostomia Inventory (SXI)

For greater convenience a shortened 5-item PROM, SXI was endorsed in 2011 by Thomson et al.[18] The need to shorten the XI was essential as some of the questions appeared to be redundant and unnecessary i.e. those associated to facial skin, nose and eyes.[21] In SXI, 5 of the 11 items used are answered by choosing one of the three response option: 1 'never', 2 'occasionally', and 3 'often'. SXI focuses on recording the experiences felt by individuals having a dry mouth while the behavioral consequences of oral dryness are not included in the questionnaire.[18] SXI is a valid and reliable instrument for assessment of xerostomia and has been widely used in epidemiological and clinical studies in conjunction with objective assessment of xerostomia.[21] The use of SXI is popular in many parts of the world and is validated in Dutch, Portuguese, English, Chinese and Japanese.[22]

4. Quality of Life Questionnaire Head and Neck (QLQ-H&N35)

The European Organization for Research and Treatment of Cancer has approved a valuable questionnaire specifically related to head and neck cancers/radiation therapy; Quality of Life Questionnaire Head and Neck (QLQ-H&N35). Related to xerostomia, this questionnaire has 4-item scales for assessing swallowing and single-item scales for presence of dryness of mouth and sticky/thick saliva. Scores may range from zero to 100.[23] This questionnaire serves as a valuable instrument for the assessment of quality of life of head and neck cancer patients before, during, and after radiation therapy.[24]

5. Visual Analogue Scale (VAS)

VAS was introduced as a reliable tool for clinical diagnosis of xerostomia and comprised of 8-items. This scale involves examination for two key aspects for salivary production: (i) Dryness of oral mucosa and (ii) functional incompetence due to dryness; and two universal components regarding the mouth dryness. Results have shown that VAS can be used in monitoring changes or improvements in salivary flow rate and can be effectively used as a continuous evaluation instrument for patients suffering from salivary

gland dysfunctions. Nearly all the components of VAS have proven to be reliable; however, when compared with objective salivary flow rate of normal individuals, they show poor to moderate validity.[25]

Objective diagnosis of xerostomia

The unstimulated salivary flow rate ranges from 0.3-0.5 ml/min and flow rate below 0.1 ml/min is considered hyposalivation[26] indicating a functional loss of salivary glands.[27] When the salivary flow rate is less than the fluid absorption and evaporation rate in the oral cavity, it is referred to as objective hyposalivation.[28] Objective salivary flow rate is best measured by collecting saliva from the three major salivary glands namely: Parotid, submandibular, and sublingual salivary glands. Different tools and techniques are used in practice for accurate collection of saliva from individual glands: Carlson-Crittenden collector or modified Lashley cup is used for collecting glandular saliva from the Stensen's duct of the parotid gland, and Wolff collector is used for collecting saliva from the ducts of submandibular and sublingual glands.[29]

The term resting or unstimulated saliva is used when any stimulus either external or pharmacological are not used for the collection of saliva. Methods such as spitting and passive drooling are commonly used for the collection of unstimulated saliva. When a stimulus, in the form of a mechanical or gustatory such as chewing gum or citrus, are used for saliva acceleration and collection, it is termed as stimulated saliva.[30] Rate for both the stimulated and unstimulated saliva can be assessed; pH value of the saliva is lower in the unstimulated than in the stimulated saliva.[31] Significant differences are observed for both stimulated and unstimulated salivary flow rates during the day time and evening.[32]

Radiographically diagnosing xerostomia

Radiographic methods can also be of aid when it comes to diagnosing xerostomia i.e. sialography, scintigraphy, ultrasound (US), MRI, CT, and (18) F-FDG positron emission tomography (PET);[33] which may be useful in situations in which salivary glands function are affected by some underlying disease or radiation therapy.

1. Sialography

Sialography is considered as a valuable and reliable exam, centred on cannulation of main salivary ducts and injecting an iodinated contrast medium, which henceforth allows radiographic imaging of the entire anatomy of the main salivary glands. The shortcoming of this method is its invasiveness and exposure to the radiation.[34] It detects changes in the course of salivary gland ducts and thus is helpful in diagnosing patients with a chief complaint of mouth dryness.[35] Sialography is a non-aggressive procedure and can be a painless method if handled accurately;[36] however, breach in ductal arrangement, hostile reactions to contrast agent, and instigation of some clinically dormant infections might pose as a complication.[33] Sialography serves as an effective diagnostic tool to check for the severity of xerostomia.[37]

2. Ultrasonography

Recently, sialography has been replaced by high-resolution ultrasound for the detection of salivary stones, also known as sialolithiasis.[33] Ultrasound is widely gaining acceptance as a diagnostic tool for the evaluation of salivary glands in diseases such as xerostomia. Some of the advantages of this technique are that it is a noninvasive procedure, cost-effective, and safe without exposure to ionizing radiation.[38]

Ultrasound is a simple and reliable method, but has its limitations when exploring mild parenchymal variations, and can only detect obvious variations.[39] Moreover, American-European Consensus Group (AECG) guidelines have declined to include ultrasound as an accepted imaging modality in the diagnosis of xerostomia associated with Sjögrens syndrome.[40] For this imaging technique to come under authentication, it still needs further multicentric studies.[38]

3. Scintigraphy

Scintigraphy is one of the most frequently used methods for the evaluation of salivary gland function in various diseases: Sjögren's syndrome, xerostomia, and radiation therapy for head and neck cancers.[41] This technique not only aids in the interpretation of both salivary accumulation and release but is also used for the quantitative analysis.[42]

99m Technetium pertechnetate are radionuclides that are intravenously injected and are taken up by the salivary glands and eventually secreted. Extent of functional acinar tissue depends on the degree of uptake and secretion into the oral cavity.[43] Scintigraphy is a reliable and an effective method to study the progression and severity of xerostomia and salivary gland functions.[44]

Scintigraphy results are based on Schall's classification, which is widely considered the standard method of evaluation, showing salivary gland function that is categorized into four grades corresponding to the uptake and activity of the gland after injecting the radionuclide (Grade 1 being normal and grade 4 showing a total lack of function or uptake).[45] A drawback of this technique is chances of any errors due to the misinterpretation by the evaluator as it is an observer dependent process.[46]

4. MRI

MRI detects any salivary gland anomaly due to its ability to visualize and detect water-containing structures.[43] These masses result in the obstruction of salivary flow. MRI reveals the minor details of the anatomy of glands, which aids in
better understanding of xerostomia diagnosis.[47]

5. [^{18}F] fluorodeoxyglucose-labelled positron emission tomography-CT (FDG-PET-CT) biomarkers

FDG-PET-CT imaging delivers efficient evidence about the metabolic activity of tissue especially in head and neck cancer patients. Xerostomia caused by radiation exposure is a subsequent side effect of head and neck cancer which can best be diagnosed using PET biomarkers.[48] 11C-methionine PET-CT unveils the metabolic clearance of 11C-methionine whenever there is an augmented amount of radiation dose; hence, this serves as an important biomarker that correlates with salivary flow rate.[49]

CONCLUSION

There are numerous methods used to identify and monitor xerostomia, largely depending on the underlying medical condition. These methods may be used alone or in combination, such as using both subjective and objective tools, which may help the clinician to approach xerostomia holistically. Different combination of tools gives a better xerostomia assessment, selection of which also depends on the age and health condition of the patient.

CONFLICT OF INTEREST

None declared

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