

Association of Oral Manifestation and Ocular Involvement in Patient of Dry Mouth: A Novel Research Approach

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ABSTRACT

Background: Dry mouth is the subjective symptom of dryness of mouth. Although dry mouth is not a disease, it may herald the onset or signal the presence of a number of serious systemic diseases and condition. The study was conducted to evaluate oral manifestations associated with dry mouth, to establish relation between salivary gland function and lacrimal gland function in individuals with dry mouth and to establish the changes in composition of saliva in patients with dry mouth.

Materials and methods: study involving a total of 30 adult individuals. The study group consisted of 15 adult individuals reporting with chief complaint of dry mouth. Control group consisted of 15 healthy age and gender matched individuals. Each group was further divided into five subgroups according to the age. A detailed case history was taken, the associated oral symptoms and clinical signs were recorded. The study population was subjected to dry mouth questionnaires to assess the severity of dry mouth. Sialometry was done to assess the salivary gland function by measuring unstimulated whole saliva, stimulated whole saliva and stimulated parotid saliva. Sialochemistry of collected saliva was done and concentration of salivary electrolytes and total protein was assessed. All the subjects were given ophthalmic examination to evaluate lacrimal gland function.

Results and conclusion: Dry mouth is a distressing symptom affecting patients' quality of life. It affects females more than males. Unstimulated whole saliva is the better indicator of salivary gland function. Salivary concentration of sodium, chloride and total protein is higher in patients with dry mouth. Multiglandular hypofunction may be phenomenon coexisting with dry mouth which often goes undiagnosed.

Keywords: Dry Mouth, Sialometry, Sialochemistry, Salivary gland hypofunction, Stimulated parotid saliva.

INTRODUCTION

Saliva is the physiological fluid of the oral cavity. As well as keeping the mouth moist and comfortable, saliva plays a vital, everyday role in protecting our general health and well-being. Reported estimates of the prevalence of dry mouth range from 12 to 39%.¹ Although dry mouth is not widely recognized, research suggests that there may be as many as one in five people suffering from the effects of dry mouth at sometime in their life. Dry mouth is the fourth most distressing symptom known. Dry

mouth is also known to be associated with other non oral symptoms like dry throat, dry eyes, dry skin, complaints of ocular dryness have been reported in 39% of xerostomic patients.² It has been recently reported that among several components, changes in sodium, chloride and phosphate concentration of whole saliva and parotid saliva have great potential in assessing salivary gland function. It is also hypothesized that multiglandular hypofunction may be phenomenon coexisting with dry mouth which often goes undiagnosed.³

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This clinical study explores the relationship between severity of dry mouth, actual salivary gland hypofunction and oral manifestation. A correlation of dry mouth is also made with lacrimal gland function and sialochemical composition in respect to electrolytes and total protein.

MATERIALS AND METHODS

The study is randomized case-control study involving a total of 30 adult individuals. The study group consisted of 15 adult individuals with complaint of dry mouth. Control group consisted of 15 healthy age and gender matched individuals. Each group was further divided into five subgroups according to the age. Patients with known cause of dry mouth like diabetes, salivary diseases, radiation therapy, chemotherapy, xerogenic medications were excluded from the study. Written informed consent was obtained from each patient after the aims and methodology of the study were explained.

A detailed case history was taken, the associated oral symptoms and clinical signs were recorded. The study population was subjected to dry mouth questionnaires to assess the severity of dry mouth. Sialometry was done to assess the salivary gland function by measuring unstimulated whole saliva (UWS), stimulated whole saliva (SWS) and stimulated parotid saliva (SPS). Sialochemical analysis of collected saliva was done and concentration of salivary electrolytes and total protein was assessed. All the subjects were given ophthalmic examination to evaluate tear flow rate and lacrimal gland function.

One way analysis of variance (one way ANOVA) was applied to determine significant difference within age groups. Mann-Whitney U-test was applied to determine nonparametric values. Pearson's correlation coefficient was applied to determine correlation between two variables. Dry mouth questionnaire by PC Fox et al⁴ and visual analog scale for dry mouth by Satishchandra Pai et al⁵ were used to assess the severity of hyposalivation and quality of life. Patients were asked for the symptoms of burning sensation, glossodynea, dysphagia, difficulty in speaking, dysguesia (altered taste sensation) and reported if present. Oral mucositis assessment scale (OMAS) (Sonis et al 1999)⁶ was adapted to report the clinical features present in the patients having dry mouth.

Caries data were expressed as decayed, missing and filled teeth (DMFT). Whole saliva (stimulated and unstimulated) was collected by using spit method. Unstimulated parotid saliva was collected by using custom-made apparatus which was fabricated by modifying the design of Carlson Crittenden. Stimulated parotid saliva was also collected directly by using gutta-percha to dilate the Stenson's duct followed by inserting needle with butterfly canula. Saliva sampling was done between 10:00 AM and 1:00 PM. Patients were forbidden any oral intake or smoking for at least 1 hour prior to saliva collection. Two percent solution of citric acid was used for stimulating the salivary glands. Saliva samples were collected in graduated cylinder and salivary flow rate was determined in milliliters per minute.

The collected saliva was given for sialo chemical analysis. Sodium, potassium and chloride in saliva were determined by using ion-selective electrode technology. Calcium and phosphates were measured by using spectrophotometry analysis. All the patients under study group were subjected to ophthalmologic test (i.e Shirmers test, Rose-Bengal test and tear film break-up time test) for evaluating the lacrimal gland function.

All the subjects were subjected to hematological examination which consists of total count, differential count, peripheral smear, hemoglobin percentage, mean corpuscular hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin concentration. Study population, were also subjected to random blood sugar and RA factor analysis to rule out any systemic disease.

RESULTS

In this study results showed that females (60%) complaining of dry mouth were two times more than that of males (40%). Patients complaining of dry mouth *per se* were relatively younger belonging to the age group 29 to 35 years (33.33%). Severity of dry mouth assessed by questionnaire study was significantly higher in study group than in controls but it did not vary significantly between gender or age group. Sialo metric results suggested that patients complaining of dry mouth had significantly lower ($p < 0.001$) salivary flow rate than that of controls. UWS and SPS were better indicators of salivary gland hypofunction than SWS. Though the mean salivary flow rate was found to be lowest

among age group (51-60 years), it did not differ significantly among the different age groups. Two individuals in study group complaining of dry mouth had normal salivary flow rate indicating toward psychiatric origin of dry mouth.

Patients with dry mouth had significantly higher associated symptoms (56.66%) (Burning sensation, glossodynia, dysphagia, difficulty in speaking, dysguesia) than that in their normal counterpart (0%). All the symptoms except difficulty in speech were higher in females than in males. These symptoms were more common in the comparatively older age group.

The patients with dry mouth have higher occurrence (66.66%) of erythema, mucositis at all the sites than that of controls (3.33%) with buccal mucosa being the most common site. Occurrence of ulceration did not differ significantly between cases and controls, although buccal mucosa ($Z = -4.858$, $p < 0.000$) was the most common site of occurrence of ulceration in the study group. Occurrence of depapillation of tongue was higher in xerostomic patients than in controls ($Z = -3.658$, $p < 0.000$). Patients with dry mouth had drier and stickier oral mucosa (83.33%) due to decreased wettability than that of the controls (3.33%). Subjects with dry mouth had caries prevalence significantly higher (DMFT average 12.2) than that in controls (DMFT average 6.9). The DMFT index did not vary significantly within gender or within age groups. Lacrimal gland function analysis suggested that individuals with dry mouth had decreased lacrimal flow rate (≤ 5 mm/min) than that of controls. Also the occurrence of dry eyes was higher in study group (16.66%) than that of controls (0%). Tear flow rate did not vary significantly with gender or with age. Sialochemistry results suggested that the mean salivary concentration of sodium ($t = 3.760$, $p < 0.00$), chloride ($t = 6.015$, $p < 0.00$) and total protein ($t = 2.441$, $p < 0.018$) were significantly higher in subjects with dry mouth than that of their normal counterparts. The mean salivary concentration of electrolytes, calcium, phosphate and total protein did not vary within gender and age groups.

The salivary pH analysis showed that saliva of individuals with dry mouth was more acidic ($p < 0.028$) than that of controls, whereas acidity of

saliva does not vary with gender or with age. The incidence of candida was found to be higher in study group (30%) than as compared to the controls (3.33%) ($Z = -3.920$, $p < 0.000$).

Study suggested that there is positive correlation between salivary gland hypofunction and lacrimal gland hypofunction. Unstimulated whole saliva is more significantly correlated to lacrimal gland hypofunction (Fig 1). The study did not show statistically significant correlation between salivary gland hypofunction and sialo chemical changes in terms of salivary electrolytes and total protein.

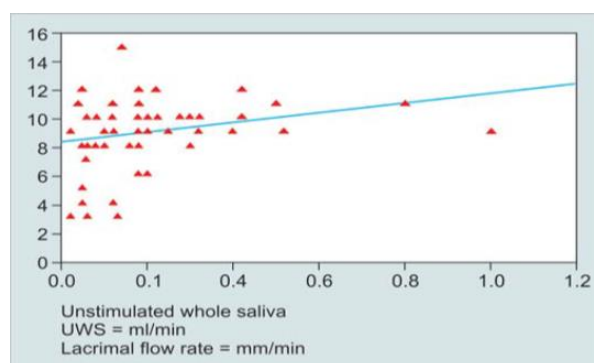


Fig 1: Correlation of salivary gland function with lacrimal gland function.

DISCUSSION

Dry mouth is the subjective sensation of dry mouth that mostly results from salivary gland hypofunction but rarely may also occur due to psychiatric causes. The study showed that more number of females suffered from dry mouth than males.⁷⁻¹⁰ Females suffer more with psychological factors, such as depression, anxiety, and stress than males and these psychological factors play an important role in subjective oral dryness. Studies have also stated that women are more susceptible to certain medical conditions known to affect salivary secretion, for example Sjogrens syndrome, rheumatoid arthritis, scleroderma, hypothyroidism, eating disorders, etc.¹¹

The study suggested that the patients complaining of dry mouth belong to relatively younger age group. This was in contrast with earlier studies.⁸⁻¹⁰ This can be due to the fact that we did not include those subjects who had dry mouth due to known cause like chronic use of medications, systemic diseases, radiation therapy, etc. (exclusion criteria).

Aging *per se* has no significant association with dry mouth.¹¹ Earlier studies have shown that dry mouth is more prevalent in the older age group, this may be explained by the fact that older people suffer more commonly with systemic diseases and are on multiple medications as compared to younger age group which may directly or indirectly cause dry mouth.¹²⁻¹⁴ Patient complaining of dry mouth, actually suffered from salivary gland hypofunction as detected by sialometric study. Unstimulated whole saliva and stimulated parotid saliva were significantly lower in xerostomic subjects. Unstimulated whole saliva was found to be better indicator of dry mouth than stimulated whole saliva.^{3,15} Unstimulated whole saliva reflects basal salivary flow rate and is present in mouth for more than 14 hours a day as compared to stimulated saliva which is in mouth for a maximum of 2 hours.^{16,17} Hence, a decrease in unstimulated saliva is more significantly associated with dry mouth than stimulated saliva. On comparing whole saliva with parotid saliva, whole saliva is better indicator of dry mouth as it contains contribution from submandibular and sublingual salivary glands secreting mucins, a family of O-linked glycoprotein which gives saliva its lubricatory properties. Parotid saliva lacks mucins, hence a decrease in parotid saliva will not affect lubricating effect of saliva and thereby may not contribute significantly to the feeling of dry mouth. However, parotid saliva analysis have an advantage over whole saliva in that it is a pure secretion from the salivary gland whereas whole saliva may have contributions from gingival crevicular fluid, sputum, food debris, etc.

Xerostomic patients were significantly associated with the symptoms of mucositis like burning sensation, glossodynia, dysphagia, difficulty in speech and dysgeusia than the controls.^{7,11,18-23} It supports the statement that burning mouth is associated with decreased salivary flow rate.¹⁸ The study also supports the role of saliva in taste sensitivity. Both transport and solubilization of gustatory stimulants are dependent on salivary flow. It may also support the mechanistic basis for the relationships between saliva and taste perception pointing to the salivary ionic environment of taste cells as being critical in gustatory signal transduction.²⁴ This may also support the hypothesis that dysgeusia, burning mouth and dry mouth with no established etiology

may be different expressions of the same oral neuropathy, merely representing a disorder of peripheral pain pathways.²⁴ Individuals with dry mouth have higher occurrence of erythema at all the sites than that of controls, buccal mucosa being the most common site. Dry mouth-induced mucositis occurs on the movable mucosae, rarely affecting the hard palate or the gingivae. The erythema can be caused due to inflammation as a result of increased friction due to decreased lubrication in salivary gland hypofunction or as a result of candidal infection.

The findings may signify the lubricating, cleansing and antimicrobial properties of saliva on the oral mucosa. Ulceration is not a common clinical feature associated with dry mouth and is mostly a secondary sequela to existing mucositis. Subjects with dry mouth had significantly higher occurrence of caries than that of controls signifying that saliva has a protective role in preventing caries due to its properties of flushing action, buffering capacity, remineralization of teeth and its antibacterial action.^{7-10,15,16,19,21,23}

Saliva of subjects with dry mouth had significantly lower salivary pH (acidic saliva) when compared to controls. This can be explained by the fact that bicarbonate concentration of saliva correlates with salivary flow. A decrease in salivary flow rate decreases the bicarbonate ion concentration resulting in decreased buffering capacity of saliva accounting for decreased salivary pH.¹⁷

The detection of pseudohyphae of candida from intraoral site was significantly higher in subjects with dry mouth/ salivary gland hypofunction than that of controls, signifying that the hyphal form of *Candida* population in the oral cavity increases as the salivary flow decreases.⁷ The results also signify the protective role of saliva against *Candida*. Salivary gland hypofunction has positive correlation with lacrimal gland hypofunction.^{7,13,15} UWS was found to be more significantly correlated to lacrimal gland hypofunction than SWS and SPS. Hence, it may be suggested that basal salivary flow is associated more with lacrimal flow than the functional salivary flow. Findings may also imply the importance of unstimulated whole saliva as a better diagnostic tool than stimulated whole saliva and stimulated parotid saliva in determining the

association between salivary function and lacrimal function. These findings may suggest the possibility of multiglandular hypofunction which may be coexisting with dry mouth but remains undiagnosed. Sialochemistry results showed that the concentration of sodium, chloride and total protein was significantly higher in xerostomic patients than in controls. It suggests that even though in patients with dry mouth the salivary flow rate was low and ductal cells had more time available for absorption, the sodium and chloride were comparatively less reabsorbed indicating a possible dysregulation in the absorption mechanism in the ductal cells. The significantly higher concentration of total protein in saliva of xerostomic patients suggests possible inflammation resulting in protein leakage from the serum.

Two individuals in the study group had decreased salivary flow rate, dry eyes and significantly higher concentration of sodium and chloride and lower concentration of phosphate. Minor salivary gland biopsy of these individuals showed lymphocytic infiltration in the gland suggesting presence of subclinical Sjogrens syndrome.

These findings also support the hypothesis that in Sjogrens syndrome metaplastic epithelial cells and epimyoeplithelial cell islands (periductal lymphocytic infiltration) that replace the normal ductal cells are not capable of effectively resorbing the high sodium and chloride content of the primary secretion, despite the low flow rate.^{3,15}

Results also suggest sialochemistry as an adjunctive aid in diagnosis and assessment of degree of pathosis in Sjogrens syndrome. This is true especially in initial phase of Sjogrens syndrome however, in the advanced stage it may not be possible due to lack of saliva making sialometry highly diagnostic in such situations.¹⁵ Thus, it should be mandatory that every patient with dry mouth is subjected to dry eye test, sialometry and sialochemistry to rule out subclinical Sjogrens syndrome.

CONCLUSION

The findings of the study shows that a correlation exists between salivary gland function, lacrimal gland function and sialo chemical changes (in terms of sodium, chloride and total protein) in patients

with dry mouth *per se*. Further researches are required to be done on patients with dry mouth, so as to find the exact cause and relationship between salivary gland function, sialo chemical changes and lacrimal gland function. So more study with large number of sample size is required to get appropriate results.

CONFLICTS OF INTEREST

The authors declare they have no potential conflict of interests regarding this article.

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