Microflora of the Oral Cavity in Patients with Xerostomia

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Key words: *xerostomia; hyposalivation; microflora; age.*

Summary. *Objective. The aim of this study was to evaluate the dependence of the condition of the microflora of the oral cavity on the etiology of xerostomia, patients' sex, age, degree of hyposalivation, and duration of the sense of dryness.*

Material and Methods. A total of 64 patients with complaints of oral dryness referred to the Clinic of Oral and Dental Diseases, Hospital of Lithuanian University of Health Sciences, for consultation during the period from 2003 to 2005 were selected for the study. The etiological factors of xerostomia were as follows: radiotherapy (PRT) to the maxillofacial area, Sjögren's syndrome (SS), and xerogenic medications, tricyclic antidepressants (TCAs).

Results. There were 50 women and 14 men. Their mean age was 60.5±1.6 years. All the patients in the PRT group had high counts of Candida spp. as compared with percentages of patients in the TCA and SS groups (100% vs. 66.7% and 56.2%, P<0.05). Patients' age and sex in different etiology groups had no significant impact on the condition of their oral microflora. There were equal percentages of patients with deficient and normal salivation in the TCA group (44% in both the groups; P<0.01). All the patients in the PRT group had pronounced hyposalivation (P<0.002). A significantly greater percentage of patients with severely reduced salivation had high counts of Lactobacillus spp. (P<0.01). Significantly greater percentages of patients with the clinical duration of xerostomia of up to 6 months had high counts of Lactobacillus spp. and Candida spp. colonies.

Conclusions. In patients with xerostomia, the condition of the microflora of the oral cavity and impairment of major salivary gland function varied according to the etiology of the disease. The level of hyposalivation and the duration of xerostomia were found to have a significant impact on the microflora of the oral cavity.

Introduction

Normally functioning major and minor salivary glands excrete up to 1.5 L of saliva in 24 hours. Saliva has multiple functions: it plays a role in remineralization of teeth, maintains constant alkaline balance in the oral cavity, provides lubrication for mucous membranes, teeth, and food, regulates composition of the microflora of the oral cavity, and facilitates the functions of primary digestion, taste perception, and water balance control in the body (1, 2).

In cases of the hypofunction of the salivary glands, the harmony of the oral cavity, as conditioned by a sufficient amount of saliva and its normal chemical composition, becomes impaired. Favorable conditions appear for certain microflora to thrive, especially for streptococci, actinomycetes, and lactobacilli (3). This heightens the probability of developing intensive caries, periodontal disease, cheilitis, candidiasis, etc. In most cases, patients complain of oral dryness, itching, burning, and difficulty when speaking, which are conducive to psychosomatic disorders. The so-called syndrome of multifactorial complex xerostomia or oral dryness develops. Subjective complaints and attitudes to xerostomia and its severity will vary in patients of different age, sex, psychological condition, varying tolerance of discomfort, and tendency toward depression. Xerostomia could be more adequately defined as oral dryness or deficient salivation, which impels the patient to seek treatment by turning to a specialist because of the abovementioned problems or sensations in the oral cavity.

There is an ongoing discussion among authors in medical literature on when salivation should be considered as deficient and what level of hyposalivation is considered pathological. Attempts are made to evaluate different aspects of xerostomia course (4, 5).

A variety of tests are employed to determine reduced salivation: stimulated and unstimulated sialometry, contrast sialography, sialoscintigraphy, biopsy, and sialometry of the minor salivary glands, as well as sialoultrasonography. However, it is generally acknowledged that stimulated sialometry is the easiest and most popular method for determining the major salivary gland function. Some authors suggest that the clinically relevant level of stimulated

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salivation is 0.5 mL/min, while according to others, it ranges from 0.1 to 0.7 mL/min (6, 7). Other authors suggest that different criteria of hyposalivation should be applied to different individuals (8). In most instances, hyposalivation of up to 1 mL/min is recorded when the salivary glands are stimulated. However, most authors have the opinion that clinical expression of xerostomia is not significantly associated with the degree of hyposalivation, which varies within a certain range, but to a relative reduction of more than 50% in salivation (9). In search of a common denominator for our study, the following levels of hyposalivation were singled out: less than 1 mL/min – hyposalivation, and less than 0.5 mL/min – pronounced hyposalivation.

Yet, individual authors have no unified opinion on how and to what extent the etiological factor of hyposalivation is relevant to the clinical manifestation of xerostomia (5).

The aim of the present study was to evaluate the dependence of the condition of the *Streptococcus mutans* (*S. mutants*), *Lactobacillus* spp. and *Candida* spp. microflora of the oral cavity on a clear etiological factor of hyposalivation, patient's sex, age, degree of hyposalivation, and duration of the sensation of dryness.

Material and Methods

In total, 64 patients with complaints of oral dryness referred to the Clinic of Oral and Dental Diseases, Hospital of Lithuanian University of Health Sciences (HLUHS) (former Kaunas University of Medicine), for consultation during the period from 2003 to 2005 were selected for further study. All these patients had been complaining of deficient salivation or oral dryness and had agreed to participate in further study.

The etiological factors of xerostomia were as follows: radiotherapy (PRT) to maxillofacial area (radiation dosage more than 40 Gy) no sooner than 2 months after the end of the treatment (in order to allow radiation-inflicted damage to the mucous membranes to heal), in 14 subjects; Sjögren's syndrome (SS) (American-European criteria for the classification of Sjögren's syndrome, 2002), in 32 subjects; and xerogenic medications, i.e., tricyclic antidepressants (TCA), in 18 subjects (10).

There were 14 men and 50 women in our study. The mean age of the patients was 60.5±1.6 years. The patients were questioned to establish the duration (months) of the first symptoms of persistent oral dryness or lack of saliva.

A few clinical tests were conducted. Stimulated secretive function of the salivary glands was tested: saliva was collected between 9 and 11 AM, with no intake of food or drink allowed 2 hours before the test. Following the masticatory stimulation with paraffin, the initial saliva was swallowed, and then the amount of saliva secreted in 5 minutes was determined by having the subjects spit into a graded flask. The patients were divided into 3 groups according to their salivation: pronounced hyposalivation, up to 0.5 mL/min; light hyposalivation, from 0.6 to 0.9 mL/min; and normal salivation, more than 1.0 mL/min. Bacteriological tests for *S. mutans* (dentocult SM) and *Lactobacillus* spp. (dentocult LB) were conducted according to the instructions prepared by Orion Diagnostica. Fungi of *Candida* genus were cultivated on Sabouraud agar in Petri dishes after seeding 1 mL of saliva. It was kept for 5 days at 25°C in a special incubator. The colonies were counted. Upon completion of the salivation test, saliva was collected with a sterile syringe from the flask, which had served to determine the level of salivation. If more than 400 colony forming units (CFU)/mL of *Candida* were found in the saliva, the patient was considered to have candidiasis (11). For Lactobacillus and S. mutans, if classes 0, I, and II were determined, the count was considered low and not related to intensive caries.

All the clinical tests and the questionnaire survey were carried out by a single experienced and calibrated clinician. In 2003, the study was approved by the Ethics Committee for Biomedical Research at Kaunas University of Medicine.

Statistical Analysis. Quantitative and qualitative variables are given as mean ±SE. The chi-square criterion was applied for evaluation of interdependence of qualitative characteristics. For comparison of mean values, the Fisher test was used. In order to determine which of the mean values had statistically significant differences, the post hoc Bonferroni test for multiple comparisons was applied. Normality of distribution of qualitative variables was verified by means of the Kolmogorov-Smirnov test. Differences were considered significant when $P<0.05$. SPSS 13.0 statistical package was employed for data analysis.

Results

The dependence of the condition of the microflora of the oral cavity on selected criteria in cases of xerostomia is presented in Tables 1–3.

The data presented in Table 1 demonstrate that there were no significant differences in the percentages of patients with high *S. mutans* and *Lactobacillus* spp. counts comparing the groups with xerostomia of different etiology. However, the percentage of patients with high counts of *Candida* spp. was greater in the PRT group as compared with the TCA and SS groups (100% vs. 66.7% and 56.2%, respectively; $P<0.05$).

Patients in the PRT group had the shortest duration of xerostomia (mean duration, 10.6 months);

Table 1. Distribution and Characterization of Subjects According to Etiological Factors

Variable	Xerostomia-causing Factor			χ^2/F, *df*, *P*
	TCA (n=18)	PRT (n=14)	SS (n=32)	
Age, mean±SE, years	65.7±1.5[a]	68.4±4.3[b]	54.1±2.0[c]	F=9.898; df=2; P<0.001 $P_{a\ vs.\ c}$=0.004 $P_{b\ vs.\ c}$=0.001
Women/men, %	77.8/22.2	71.4/28.6	81.3/18.7	NS
Salivary flow rate, %				χ^2=15.9; df=4; P=0.003
0–0.5 mL/min	44.4[a]	100[b]	68.7[c]	$P_{a\ vs.\ b}$<0.001, $P_{b\ vs.\ c}$<0.001
0.6–0.9 mL/min	11.1	0	18.8	NS
>1 mL/min	44.4[a]	0	12.5[c]	$P_{a\ vs.\ c}$<0.001
Salivary flow rate, mean±SE, mL/min	0.76±0.14[a]	0.12±0.02[b]	0.37±0.07[c]	F=9.527; df=2; P<0.001 $P_{a\ vs.\ b}$<0.001 $P_{a\ vs.\ c}$<0.01
High *S. mutans* count, %	44.4	57.1	62.5	NS
High *Lactobacillus* spp. count, %	55.6	85.7	62.5	NS
High *Candida* spp. count, %	66.7[a]	100[b]	56.2[c]	χ^2=8.72; df=2; P=0.013 $P_{a\ vs.\ b}$=0.023 $P_{b\ vs.\ c}$=0.0047
Duration of xerostomia, months	35.4±12.4	10.6±2.4	31.8±7.5	NS

TCA, tricyclic antidepressant; PRT, radiotherapy, SS, Sjögren's syndrome.

Table 2. Distribution and Characterization of Subjects According to Salivation Levels

Bacterium	Normal >1.0 mL/min n=12	Low 0.6–0.9 mL/min n=8	Very Low 0–0.5 mL/min n=44	*P* Value Chi-Square *df*
High *S. mutans* count, %	83.3	50	50	NS
High *Lactobacillus* spp. count, %	50[a]	25[b]	77.3[c]	χ^2=9.798 df=2 P=0.007 $P_{a\ vs.\ c}$=0.0689 $P_{b\ vs.\ c}$=0.0052
High *Candida* spp. count, %	50	75	72.7	NS

Table 3. Distribution and Characterization of Subjects According to Duration of Xerostomia

Variable	Duration of Xerostomia, Months		*P*
	<6 (n=28)	>6 (n=36)	
Age, mean±SE, years	57.5±2.2	62.8±2.2	NS
Women/men, % (female-to-male ratio)	71.4/28.6 (1:2.5)	83.3/16.7 (1:5)	NS
High *S. mutans* count, %	64.3	50	NS
High *Candida* spp. count, %	92.9	50	P=0.001
High *Lactobacillus* spp. count, %	78.6	55.6	P=0.054

however, no significant difference was found in comparison with other groups (P=0.2).

Evaluation of salivary flow rate by the groups with xerostomia of different etiology revealed that exceptionally all the patients in the PRT group had a very low salivary flow rate. In the TCA group, there were equal percentages of patients with highly reduced and normal salivary flow rates (44% in both the groups, P<0.01). Table 1 shows that there were no significant differences in the percentages of patients with the salivary flow rate of 0.6–0.9 mL/min comparing all 3 groups with xerostomia of different etiology. This proves that gradation of salivation is vague, inaccurate, and hard to substantiate clinically. Most patients with normal salivation (P<0.02) were found in the TCA group, while all the patients in the PRT group belonged to the group of pronounced hyposalivation (P<0.002).

Our study revealed a significant association between reduced salivation and high counts of *Lactobacillus* spp. A significantly greater percentage of patients with very low levels of salivation had a high count of *Lactobacillus* spp. (P<0.01). There were no significant associations between the level of salivation and high counts of *S. mutans* and *Candida* spp.

Table 3 presents data on the microflora of the oral cavity regarding the duration of xerostomia in patients diagnosed with hyposalivation.

Significantly higher percentages of patients with the clinical duration of xerostomia up to 6 months had high counts of *Lactobacillus* spp. and *Candida* than those with the clinical duration of xerosto-

mia of more than 6 months. More patients with the clinical duration of xerostomia up to 6 months had high counts of *S. mutans*, but the difference was not significant (64.3% vs. 50%, $P>0.05$). There were no significant age and sex differences.

Discussion

The results of the present study quite clearly demonstrate the relevance of etiology of xerostomia to the condition of the microflora of the oral cavity. Essentially different data were obtained by evaluating colony counts of cariesogenic bacteria *S. mutans*, *Lactobacillus* spp., and *Candida* fungus in cases of oral dryness of different origin. The impact of hyposalivation on higher counts of *Lactobacillus* spp. was determined. The current study revealed an association between a new factor, i.e., duration of xerostomia, which had not been previously analyzed, and high counts of *Candida* spp. and *Lactobacillus* spp.

It is well known that xerostomia is more prevalent in patients with advanced age, especially in those aged more than 50 years, and that it affects women more frequently than men (1). The present study also disclosed a similar tendency: across 3 etiologic groups, the mean age varied from 54 to 68 years, and there were up to 3 times more women than men.

No statistically significant difference of the mean age in groups of different etiology, salivation, and duration of sicca symptoms was established. The mean age of our subjects was approximately 60 years. Thus, it has been assumed that determining the impact of age in xerostomia patients is a rather difficult task, since in most cases elderly patients have to be investigated, and it is not easy to differentiate them according to age groups (12). Taking into account the opinion of certain authors who state that age by itself is not significant for the prevalence of hyposalivation (13), it can be here claimed that the duration of a causal factor or disease should be considered and compared with the period of the sensation of dryness, and that severity of xerogenic disease should also be assessed. Of course, the opposite opinion, namely, that unstimulated secretion of saliva in most instances decreases with age (14, 15) and that it can substantially contribute to the severity of clinical xerostomia, cannot be dismissed.

The sensation of dryness and impaired function of the salivary glands are more common among women. In our study, there were even 81.3% of women in the SS group, while in other groups, gender distribution was more even, and the men-to-women ratio was not so dramatic (approximately 1:3). In general, women accounted for 70% of all our subjects. However, according to the chosen criteria (bacteria, hyposalivation, and duration of dryness), no significant difference was found to allow us to suspect that hyposalivation or duration of dryness could be differently determined in men and in women complaining of xerostomia – their ratio always remained the same. The higher percentage of women in our study could have resulted from hyposalivation appearing more frequently in the female population, which is influenced by the fact that women's salivary glands are smaller than those of men and hormonal imbalance due to menopause (16). It is known that men have higher pain thresholds than women, and perhaps for this reason fewer of them, and less frequently, seek professional treatment (17).

However, there are studies in medical literature upholding an opposite opinion that patients of different etiologies, especially those who have undergone radiotherapy to the head and neck area, have higher counts of cariesogenic bacteria than patients with Sjögren's syndrome. However, it can still be noted that there were 85.7% of patients with high *Lactobacillus* spp. counts in the PRT group, while in the TCA and SS groups there were only 55.6% and 62.5%, respectively. Thus, it can be stated that patients in the PRT group were at higher relative risk of developing caries, since their *Lactobacillus* spp. counts were more frequently found to be higher and since all the patients had reduced salivation. The hypothesis that there is a correlation between the microflora of the oral cavity and etiology has been confirmed by some studies carried out in the United Kingdom (18). The present study showed that the course of xerostomia was more related to the level of hyposalivation than etiologic factors.

Significantly more patients in the group of extremely reduced salivation had high *Lactobacillus* spp. counts in comparison with patients with normal or moderately reduced salivation. Evaluation of *S. mutans* counts revealed no significant difference. The present results correspond to the widely known opinion that considerably higher *Lactobacillus* spp. counts are concomitant with hyposalivation, which is not always observed in case of *S. mutans* counts. Hyposalivation creates an environment, which is more favorable for *Lactobacillus* spp. Therefore, it can be stated that patients with pronounced hyposalivation are at higher risk of developing cervical or coronal caries or regular caries on any surface (19–24). The present study cannot confirm this hypothesis, since the prevalence of caries was not investigated.

It is here considered as important that a significant difference was established among the groups when calculating *Candida* spp. counts in the saliva of patients in the groups of xerostomia caused by different etiology. Evaluation of Candida spp. colony counts revealed that all the patients in the PRT group had high Candida spp. colony counts, and the

percentages of patients with high *Candida* spp. counts in the TCA and SS groups were significantly lower as compared with the PRT group (100% vs. 66.7% and 56.2%, P=0.013). It was determined that all the PRT patients and even 66.7% in the TCA group had high *Candida* spp. counts. This demonstrates the presence of candidiasis or a considerable possibility for its development (25). However, high *Candida* spp. counts in the mouth do not always cause candidiasis or symptoms of dryness (10, 26, 27).

However, it is well known that hyposalivation contributes considerably to disruption of the natural barrier of the oral mucous membranes (28, 29), while immunosuppression quite frequently causes a fungal infection to flourish. Therefore, it is here assumed that the etiological factors, which have an immunosuppressive or evidently hyposalivation-causing impact, are the most dangerous ones, e.g., radiotherapy, chemotherapy, and sedative-relaxant therapy. It can sometimes be complicated to establish an exact pathogenic mechanism causing xerostomia.

The present study did not succeed in revealing a significant impact of slight or negligible hyposalivation on high *Candida* spp. counts. When evaluating xerostomia, it could be noticed that the patients were not evenly distributed into etiological groups according to the amount of secreted saliva. The proportions of the patients with slight, negligible, and normal salivation differed depending on etiology. The majority (70%) of the subjects in the group of xerostomia caused by Sjögren's syndrome had a low salivary flow rate, but around 30% of the patients with normal salivation still experienced xerostomia.

Measurements of stimulated saliva are less faulty because of variations of salivation within 24 hours, and they are more precisely indicative of the potential for the secretion of saliva. Unstimulated secretion of saliva is harder to measure, and its measurements are not accurate, but in the scientific sense, more of its correlations with subjective complaints have been uncovered. The test itself is more dependent on the tester (7, 30).

Hypofunction of the salivary glands resulting from different types of etiology can have different manifestations. Perhaps a momentary measurement of the amount of secreted saliva cannot adequately reflect the actual function of the salivary glands. While analyzing medication-induced xerostomia, it should be assumed that the most pronounced hypofunction occurs when the concentration of medication in the bloodstream reaches its peak, and as it drops, salivary gland function is gradually restored, and a wave-like function rhythm results. The degree of such dysfunction totally depends on the mechanism of effect, dosage, and duration of the use of medication.

Based on the present study, it may be assumed that hyposalivation occurs in almost 100% of cases after doses of radiation in excess of 50 Gy. Such patients should be evaluated with maximum attention. Stimulated salivary gland function may not correlate with medication-induced xerostomia (31).

However, the present study showed that there was a significant association of the initial symptoms of dryness, lasting up to 6 months, with high *Candida* spp. counts. In cases of short-term dryness (up to 6 months), most patients (up to 90%) had high *Candida* spp. counts (32). Thus, it is assumed that candidiasis appearing in the oral cavity can be erroneously likened to xerostomia and that frequently in such cases antifungal treatment is needed after all. It is quite possible that in cases of long-term xerostomia certain adaptive mechanisms develop and reduce dysbiosis.

Rapid development of xerostomia was confirmed by the fact that most patients in the PRT group had a shorter mean duration of sicca symptoms (10.6 months) than the subjects of the other groups (31.8 and 35.4 months). However, this difference was not significant, and wider studies are needed in order to establish these possibly significant differences. Patients vary in their tolerance and understanding of the problem, as well as in their reasons for seeking professional help that could be associated with their pain threshold.

To sum it up, it can be stated that in the PRT group, compared with other groups, the oral status was worse according to many aspects: high *Candida* spp. counts, short duration, extremely reduced salivation, etc. The general conclusion is that xerostomia of different etiology is of different severity. However, it is difficult to apply such conclusions to individual patients because the range of symptoms is rather wide. Every patient should be evaluated on individual basis.

Conclusions

The condition of the microflora of the oral cavity in cases of xerostomia varies in accordance with etiology of the disease. All the patients in the PRT group and the majority of the patients with SS had reduced salivation (up to 0.5 mL/min), but in the TCA group, patients with very low and normal salivation were equally distributed. Extremely reduced salivation significantly predetermines high *Lactobacillus* spp. counts, but not *S. mutans* and *Candida* spp. counts. Significantly greater percentages of patients with the duration of xerostomia of up to 6 months were found to have high counts of *Lactobacillus* spp. and *Candida* spp.

Statement of Conflict of Interest

The authors state no conflict of interest.

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