Xerostomia in Diabetes Mellitus

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OBJECTIVE — To determine the prevalence of xerostomia in a group of ambulatory diabetic patients and to compare the following in patients with and without xerostomia: *1*) flow rates of saliva and lacrimal fluid, *2*) the presence of other symptoms suggestive of oral and extraoral dryness, *3*) indexes of glycemic control, and *4*) noninvasive measures of cardiovagal autonomic nervous system function.

RESEARCH DESIGN AND METHODS — Forty adult diabetic patients and an equal number of age- and sex-matched healthy nondiabetic control subjects were studied. Subjects who consumed xerogenic drugs or had other significant diseases were excluded from the study. A questionnaire was administered to all patients, and the following tests were performed: resting and stimulated flow rates on whole saliva; Schirmer's test (lacrimal fluid), serum glucose and HbA_1, expiration-inspiration ratio, 30:15 ratio, Valsalva ratio, and the systolic blood pressure response to standing.

RESULTS — Forty-three percent of diabetic patients complained of xerostomia, of which 82% were women. The oral dryness was not related to age or the type and duration of diabetes. Symptoms of water loss and oropharyngeal, ocular, and vaginal dryness were much more common in the xerostomic than the nonxerostomic diabetic patients. The salivary flow rates of the diabetic subjects was consistently lower than those of healthy, nondiabetic control subjects. The mean, resting, and whole-saliva flow rate was abnormally low in the diabetic patients who complained of xerostomia; no significant differences were observed for the stimulated salivary and the lacrimal flow rates. Significant inverse relationships were shown between salivary flow and the level of HbA_1; none were shown between flow and autonomic function.

CONCLUSIONS — Dry mouth is a common complaint among ambulatory diabetic patients. It is strongly associated with objective measurements of poor salivary flow and with other oral and extraoral symptoms of desiccation. The oral dryness is not associated with cardiovagal autonomic system dysfunction but may be due to disturbances in glycemic control.

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Xerostomia is believed to be a common complaint among diabetic patients (1). To our knowledge, however, only one study has been conducted to determine the frequency of its occurrence. This study reported that 30% of the diabetic patients (n = 35) complained of dry mouth (2).

The objective of this study was to determine the prevalence of oral dryness in a group of ambulatory diabetics and to compare the following in patients with and without xerostomia: *1*) the rates of flow of whole saliva and lacrimal fluid, *2*) the presence of other symptoms suggestive of oral and extra-oral dryness, *3*) indices of glycemic control, and *4*) noninvasive measures of cardiovagal autonomic nervous system function. The term xerostomia will be used to connote the subjective feeling of oral dryness, irrespective of the presence of objective indices of oral desiccation.

RESEARCH DESIGN AND METHODS

— Consecutive adult diabetic outpatients were recruited from the Family Medicine and Diabetic Clinics at the University Hospital, Stony Brook. Patients taking xerogenic drugs or drugs known to alter autonomic function were excluded from the investigation, as were those with significant renal, hepatic, neurological, malignant, or other metabolic disorders.

The patients were required to fast overnight and not take any medications until the end of their examination; the tests were conducted between 0800 and 1000. A questionnaire was administered that elicited information about their symptoms, use of medications, and medical history. Resting and paraffin-stimulated whole saliva were collected according to the methods described by Sreebny and colleagues (3,4). These were compared to values obtained from age- and sex-matched healthy nondiabetic control subjects in a previous study (3). Flow rates are expressed as milliliter per minute. Lacrimal flow was measured by Schirmer's test: a standard strip of filter

Table 1—*Select functions of all diabetic subjects*

	Group I (N = 40)	Normal reference range
Whole saliva (ml/min)		
Resting flow rate	0.12 ± 0.14*	0.3–0.4
Stimulated flow rate	1.1 ± 0.68*	1.0–2.0
Schirmer test (mm/5 min)		
Right eye	22.5 ± 10.8	>5.0
Left eye	22.5 ± 11.5	>5.0
Fasting blood glucose (mg/dl)	172 ± 63	<115
HbA_1 (%)	9.6 ± 2.4	<8
Expiration-inspiration ratio	1.22 ± 0.18	>1.15
30:15 Ratio	1.15 ± 0.15	>1.03
Systolic blood pressure decrease in response to standing	0.47 ± 2.2	<30
Valsalva maneuver ratio	1.30 ± 0.26	>1.21

Values are means ± SD.
*Abnormal resting flow rate ≤0.1 ml/min; abnormal stimulated flow rate ≤0.7 ml/min.

paper (Coopervision Pharmaceuticals, San German, PR) was placed on the lower eyelid for 5 min; flow was quantified as millimeters of paper moistened/5 min. Blood was drawn from the antecubital fossa for the determination of glucose and HbA_1 by standard techniques used in the laboratories of the University Hospital. Autonomic nervous system function was evaluated by measure of the R-R interval variation (E-I [expiration-inspiration], 30:15, and Valsalva ratios) and the systolic blood pressure response to standing, as described by Ewing (5).

Data analysis

The data were examined and analyzed from subjects who were classified into the following: group 1, all diabetic subjects (n = 40); group 2, patients who did (xerostomic subjects) or did not (nonxerostomic subjects) complain of oral dryness; group 3, subjects whose resting and stimulated salivary flow rates were < or >0.1 and 0.7 ml/min, respectively; and group 4, subjects whose autonomic function tests were either normal or abnormally low. The data were examined by cross-tabulation contingency analyses, linear regressions, and comparative statistics. $P \leq 0.05$ (or $P \leq 0.01$ in Table 3) was considered statistically significant.

RESULTS— Group 1: all diabetic patients (n = 40). The mean resting flow rate was at the low end of what is commonly accepted as normal (Table 1). With the exception of the fasting blood glucose and HbA_1, all other values were within the normal reference range. A significant, positive correlation was observed between the resting flow rate (RFR) and stimulated flow rate (SFR) of saliva ($y = -0.016 + 0.13x$; $R = 0.64$; $P < 0.001$). No other function was significantly related to salivary flow.

Group 2: xerostomic versus nonxerostomic subjects. Of the 40 diabetic subjects, 43% (n = 17) stated that their mouth usually felt dry; 82% of them (n = 14) were women. By contrast, 30% of the nonxerostomic subjects were women ($P < 0.01$). No significant differences were observed between the groups for age or the type and duration of diabetes (Table 2).

Prevalence of associated oral and extra-oral symptoms

Symptoms suggestive of water loss and oropharyngeal, ocular, and vaginal dryness are present in both the xerostomic and nonxerostomic patients. However, they are more common in the subjects who complain of oral dryness (Table 3). Prominent among the oral symptoms are an increased need for water (take steps to keep mouth moist) and dryness of the throat; the prominent extra-oral symptoms are ocular burning and itching and vaginal itching.

Flow rates of saliva

The mean flow rates for resting and stimulated saliva in the xerostomic and nonxerostomic diabetic patients and the corresponding values for nondiabetic control subjects are shown in Fig. 1. The mean flow rates for the respective xerostomic and nonxerostomic diabetic patients are consistently lower than those of the nondiabetic control subjects. Indeed, the data demonstrate that the flow rates for those diabetic patients whose mouth feels wet are equal to the flows of the control subjects who complain of oral dryness. The mean RFR of the xerostomic diabetics (n = 17) was abnor-

Table 2—*Characteristics of patients with and without xerostomia*

				Sex				Type of diabetes		
				F		M				
Group II	N	%	Age (yr)	N	%	N	%	Insulin dependent	Non-insulin dependent	Duration (yr)
Xerostomic	17	43	46 ± 16	14	82	3	18	6	11	7.5 ± 8.0
Nonxerostomic	23	57	50 ± 17	7	30	16	70	9	14	13 ± 10.0

Table 3—*Group 2: prevalence of other oral and extra-oral symptoms of dryness among xerostomic and nonxerostomic subjects*

	Xerostomic (N=17)		Nonxerostomic (N=23)			
History	Yes (%)	No (%)	Yes (%)	No (%)	x^2	P
Take steps to keep mouth moist	76	24	17	83	14.7	<0.01
Get out of bed to drink	47	53	13	87	6.1	>0.01
Difficulty with swallowing	41	59	8	92	6.3	>0.01
Difficulty with speech	35	65	8	92	4.6	>0.01
Dry throat	47	53	4	96	10.7	<0.01
Dry eyes	35	65	13	87	3.0	>0.01
Eyes (burning/itching)	59	41	8	92	12.3	<0.01
Blurred vision	44	56	17	83	3.2	>0.01
Vaginal dryness	21	79	0	100	2.0	>0.1
Vaginal itching	57	43	0	100	7.2	<0.01
Vaginal candidosis	29	71	13	87	0.7	>0.1
Menopause	50	50	63	37	0.3	>0.1

$P < 0.01$ was considered clinically significant.

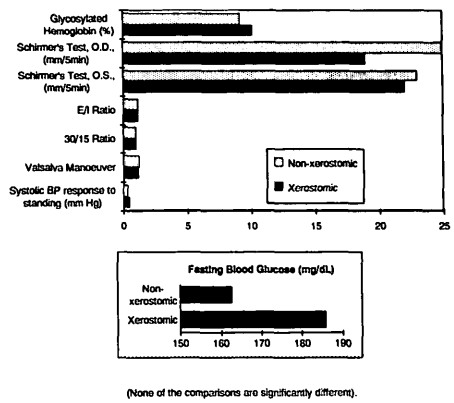

Figure 2—*Relationship of xerostomia to glycemic, lacrimal, and autonomic functions in diabetic patients.*

mally low (0.05 ml/min); 10 of them had RFRs of 0.0 ml/min. All other means were within the normal range. The effect of stimulation was 17-fold in the diabetic xerostomic patients, 7.4 in nonxerostomic diabetic patients, 7.3 in xerostomic control subjects, and 5.3 in nonxerostomic control subjects.

The distribution of the flow rates is shown in Table 4. Fifteen of 17 (88%) diabetic patients who said that their mouth felt dry had resting flow rates that were ≤0.1 ml/min; 8 of them (41%) had abnormally low stimulated flow rates ($P < 0.005$). In the aggregate, the resting flow rates of 23 of 40 diabetic patients (58%), and the stimulated flow rates of 14 of these patients (35% of the total) were abnormally low. The data for the stimulated flow rates were not significant ($P > 0.1$). Some patients demonstrated abnormal flow rates but did not complain of xerostomia; others had normal flow rates but complained of oral dryness.

The relationships between the feeling of oral dryness and the glycemic, lacrimal, and autonomic functions examined in this study are shown in Fig. 2; no significant differences were observed.

Group 3: subjects classified according to salivary flow rates. Table 5 shows the resting and stimulated flow rates of saliva treated as the independent variables while the various functions are treated as the dependent ones. Mean test results were computed for the subjects whose RFRs were ≤ or >0.1 ml/min and whose SFRs were ≤ or >0.7 ml/min. Only one statistically significant relationship was observed, the relationship between the stimulated flow rate and HbA_1. For those subjects whose SFR was <0.7 ml/min, the mean value for HbA_1 was 10.9% and 8.9% among those whose SFR was >0.7 ml/min ($P = 0.02$).

When the salivary flow rates were plotted against the various functions, significant or near-significant negative correlations were observed between flow and the levels of HbA_1. Among patients

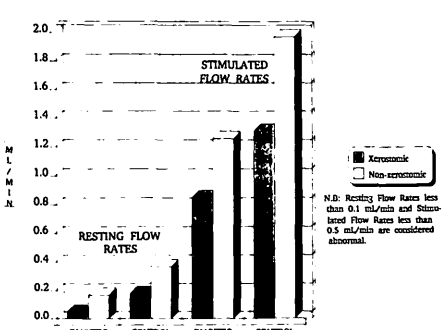

Figure 1—*Mean, flow rates, whole saliva.*

TABLE 4—*Group II—distribution, salivary flow rates of diabetic patients*

	Resting saliva			Stimulated saliva	
Flow rate (ml/min)	Xerostomic	Nonxerostomic	Flow rate (ml/min)	Xerostomic	Nonxerostomic
≤0.10	15	8	≤0.7	8	6
0.11–0.20	1	8	0.7–0.99	2	4
≥0.2	1	7	≥1.0	7	13
Total	17	23		17	23
$x^2 = 11.43$			$x^2 = 1.90$		
$P < 0.005$			$P > 0.1$		

Table 5—*Group III—the relationship of the resting and stimulated salivary flow rates to glycemic, autonomic, and lacrimal functions*

Function	Resting flow rate (ml/min)		Stimulated flow rate (ml/min)	
	≤0.1 (N=23)	>0.1 (N=17)	≤0.7 (N=14)	>0.7 (N=26)
Resting flow rate (ml/min)	0.04 ± 0.04	0.23 ± 0.14*	0.06 ±0.06	0.16 ± 0.15*
Stimulated flow rate (ml/min)	0.82 ± 0.46	1.45 ± 0.78*	0.52 ± 0.12	1.39 ± 0.67*
Fasting blood glucose (mg/dl)	176 ± 64	168 ±64	191 ± 69	163 ± 60
HbA_1 (%)	9.91 ± 2.5	9.17 ± 2.3	10.9 ± 2.6	8.9 ± 2.0*
Schirmer test				
Right eye	20.8 ± 9.6	24.8 ± 12.3	20.6 ± 10.9	23.5 ± 10.9
Left eye	21.9 ± 11.3	23.2 ± 12.2	22.3 ± 11.8	22.6 ± 11.8
Expiratory-inspiratory ratio	1.24 ± 0.19	1.20 ±0.18	1.26 ± 0.19	1.20 ± 0.18
30:15 Ratio	1.14 ± 0.14	1.17 ± 0.17	1.14 ± 0.12	1.16 ± 0.16
Valsalva maneuver ratio	1.31 ± 0.27	1.30 ± 0.24	1.24 ± 0.26	1.33 ± 0.26
Systolic blood pressure response to standing	0.37 ± 2.1	0.62 ± 2.4	−0.08 ± 0.13	0.77 ± 2.7

Values are means ± SD.
*P = 0.02.

whose resting flow rate was ≤0.1 ml/min, the relationship was: $y = 0.11 - 0.007x$; $R = -0.44$; $P = 0.06$; for those whose stimulated flow was ≤0.7 ml/min, the relationship was $y = 0.83 - 0.03x$; $R = -0.56$; $P = 0.05$. None of the other functions were significantly related to the flow rate of saliva.

Group 4: salivary flow and autonomic function. When patients were categorized according to their autonomic function, the following salivary flow rates were obtained (Fig. 3). In five of six comparisons, the subjects whose autonomic function tests were abnormal had higher salivary flow rates than those whose ratios were within normal limits. However, none of the differences were statistically significant.

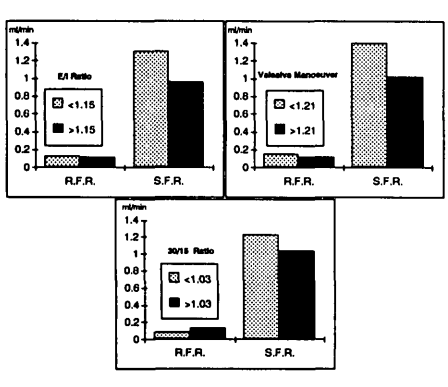

Figure 3—*Resting and stimulated salivary flow rates for subjects with normal or low autonomic function tests. RFR, resting flow rate; SFR, stimulated flow rate.*

CONCLUSIONS— Our studies showed that the mean flow rates of whole saliva among the diabetic patients, selected only for the absence of xerogenic drugs and no other serious disorders, were significantly lower than that of nondiabetic control subjects. Similar findings were observed by Kjellman (6) and Ben-Aryeh et al. (2). However, whereas the mean resting flow in our patients (0.12 ml/min) was at the interface between the normal and the abnormal flow rates (0.1 ml/min), the flow rates reported by the others were well within the normal range. In our studies, the saliva was collected after an overnight fast. It is not known whether this accounts for this difference. The SFRs among the diabetic patients, were also lower than those observed in healthy nondiabetic control subjects. However, they were within the normal reference range for this secretion. Studies conducted on stimulated parotid saliva among diabetic patients have shown that flow may be low, normal, or increased (1,7–9).

The lacrimal flow was studied to determine if the lacrimal glands, like their salivary counterparts, demonstrated objective signs of hypofunction. No differences in the flow rates of lacrimal fluid were observed between the xerostomic and nonxerostomic subjects.

Almost half of our diabetic subjects complained of xerostomia at the time of examination. This compares with a value of 31% in a study reported by Ben-Aryeh et al. (2). These observations support the widely held belief that xerostomia is a common complaint among diabetic patients.

An analysis of the data revealed that the female:male ratio among the dry-mouth patients was 8:2; for the nonxerostomic subjects, it was 3:7. In general, more women complained of xerostomia than men. No significant differences were observed with respect to age or type or duration of diabetes.

Because xerostomia is usually, although not invariably, associated with salivary gland hypofunction, it is odd that most studies have been unable to demonstrate reduced, let alone abnormally low, flow rates in diabetic subjects. Our results suggest that this discrepancy

can be resolved if the diabetic patients are classified according to symptoms. The mean RFR of the 17 subjects who said that their mouth felt dry was 0.05 ml/min. Fifteen of 17 (88%) demonstrated flow rates that were <0.1 ml/min, the generally accepted cutoff value. Only 2 xerostomic patients (12%) had normal resting flow rates. Thus, the likelihood is great that diabetic patients who complain of oral dryness will demonstrate objective signs of salivary gland hypofunction. Most of the subjects (65%) who do not complain of oral dryness have normal resting flow rates. The data with regard to stimulated saliva are less convincing but, on the whole, the SFR also tends to be lower than that observed in age- and sex-matched nondiabetic control subjects. In general, therefore, diabetic patients can be categorized as those who feel dry and generally demonstrate severely impaired RFRs and those who do not complain of oral dryness and whose RFRs are generally normal, or nearly so. The fact that the feeling of oral dryness does not always correlate with the objective measurement of salivary flow indicates that confirmatory sialometric tests should always be conducted on patients.

The findings also show that diabetic patients who complain of xerostomia more frequently complain of other oral and extra-oral symptoms of desiccation.

The depressed salivary flow in diabetic patients could be due to autonomic dysfunction, damage to the gland parenchyma or alterations in the microcirculation to the salivary glands. Lamey et al. (9) investigated the effects of diabetes and autonomic neuropathy on the rate of flow of parotid saliva. They observed that patients with autonomic dysfunction exhibited an increase, not a decrease, in the rate of flow of stimulated parotid saliva. The whole-saliva flow rates in our patients with autonomic dysfunction was also higher than the flow rates of those whose autonomic function was within normal limits. However, the differences were not significant. Neither Lamey et al.'s findings nor ours support the belief that the oral dryness observed in diabetic patients is associated with a decrease in cardiovagal dysfunction. Indeed, it suggests that tests of cardiovagal activity may not be a valid indicator of the autonomic control of the salivary glands. Alterations of parotid basement membrane have been described (10) but no in vivo functional correlations are available. When stimulated with paraffin wax, the flow of saliva in the xerostomic diabetic patients is 17 times greater than their resting flow rate. As a result, the SFRs are within the normal range. These findings suggest that even if there are anatomical defects in the salivary glands of the diabetic patients, they can still be stimulated to function normally.

An inverse relationship was observed between the flow rates of both resting and stimulated saliva and the blood level of HbA_1. In the case of resting saliva, this was of borderline significance ($P = 0.06$); for the SFR, it was significant ($P = 0.05$). To the extent that these correlations are valid, they indicate that salivary gland hypofunction may be an indicator of chronic hyperglycemia and therefore polyuria and mild dehydration.

This study establishes that dry mouth is a common complaint in the ambulatory diabetic population and that the subjective symptom of oral dryness is strongly associated with objective measurements of poor salivary flow and with other oral and nonoral symptoms of desiccation. The oral dryness is not associated with cardiovagal autonomic nervous system function but may be due to disturbances in glycemic control.

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