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A simple test for salivary gland hypofunction using Oral Schirmer's test

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OBJECTIVE: The objective of this study was to develop a test for detecting salivary gland hypofunction.
STUDY DESIGN: Oral Schirmer's test was performed by placing a strip of filter paper on the floor of the mouth and measuring the wetted length after 5 min. The control group consisted of 70 healthy patients, while another group consisted of 61 patients with Sjögren's Syndrome (SS) and a third group of 31 patients who suffered from xerostomia caused by other pathologies.
RESULTS: The mean saliva flow was 40.92 ± 22.28 mm/5 min in the control group, 27.25 ± 24.11 mm/5 min in patients with SS and 36.847 ± 23.4 mm/5 min in the third group. The differences between the control group and the other two groups were statistically different ($P > 0.001$).
CONCLUSIONS: The whole saliva test was used to distinguish between healthy adults and subjects with hyposalivation.
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Keywords: hyposalivation; saliva; Sjögren's syndrome; test

Introduction

It is well known that saliva plays an important role in maintaining oral health and correct oral functioning. Salivary hypofunctioning is a relatively common disorder with a variety of causes. The most usual is related with the use of drugs (diuretics, antidepressants, neuroleptics, etc.), while other causes include diseases, mainly Sjögren's Syndrome (SS), AIDS, sarcoidosis and viral hepatitis C, chronic graft-vs.-host disease, and neck and head radiotherapy (1–4). Salivary gland hypofunction is frequently accompanied by alterations in oral functioning, including difficulty with eating, swallowing and talking, and even altered taste sensations, all of which contribute to deteriorating the quality of life of sufferers (5). Several organic manifestations may also occur, usually as a result of the accumulation of microorganisms on oral surfaces in the absence of the regulatory mechanism provided by saliva. There is a high incidence of dental demineralization, caries, periodontal and mucosal problems and a predisposition to infection, especially by *Candida albicans* (6–8).

Early recognition of decreased salivary flow will be helpful for the understanding of salivary gland dysfunction. Several techniques are currently used to determine the salivation rate: draining, in which the subject bends the head forward and allows saliva to drip off the lower lip into a container; spitting, in which the subject spits actively into a container; sucking, in which saliva is sucked from the floor of the mouth and allowed to accumulate in a vessel; and swabbing, in which preweighed, absorbent swabs are placed in the mouth (9–13). Another study uses a semi-quantitative test called the 'wafer test' to screen patients who may have hyposalivation. This test measures the time it takes to dissolve a standardized 37-mm-diameter wheat flour wafer placed on the dorsum of the tongue (14). Although these methods have been accepted by the Commission on Oral Health, Research and Epidemiology of the International Dental Federation, they are rarely used by general practitioners. Dentists are reluctant to use these methods because they may perceive them as chair time-consuming and not aesthetically pleasing (9, 15).

Schirmer's test is used routinely by ophthalmologists to measure tear film wetness as the objective ocular component of the American–European classification criteria for identifying Sjögren's syndrome (16, 17). The objective of this study was to develop a test for salivary gland hypofunction.

Material and methods

Sample selection

A total of 162 were included in the study and analysed in the Oral Medicine Unit of the University of Murcia. This project was approved by the Ethical Committee.

The control group consisted of 70 (voluntary) patients who were considered healthy and who were not taking

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drugs that might interfere with saliva flow. None had had sialometric tests previously. The criteria for taking part in the test were no systemic or nervous disease that could interfere with glandular functioning, no medicines that could interfere with saliva secretion, no symptoms of dry eyes and no oral dryness. Any patient thought to be suffering from a disease or undergoing treatment that might affect the normal functioning of the salivary gland was excluded. Group 2 consisted of 61 patients referred to the Rheumatology Service of the Morales Meseguer Hospital (Murcia) diagnosed with primary and secondary SS according to the European criteria proposed by Vitali et al. (17).

Group 3 comprised of 31 patients displaying symptoms of oral dryness from different causes: four, systemic lupus erythmatosus; one, scleroderma; five, rheumatoid arthritis, diagnosed on the basis of accepted classification criteria (18) and 21 patients with pharmacologically related xerostomia. Data were collected using the form for studying SS-related oral dryness after obtaining the consent of all participants. The statistical analyses were carried out using SPSS® version 12.0 for Windows (SPSS Inc., Chicago, IL, USA).

Saliva samples

Saliva flow was measured between 09:00 and 12:00 hours and the patients were not allowed to eat, smoke or brush their teeth 2 h prior to the measurement. Prior to the test, the patients were encouraged to adopt a restful position and told to swallow the saliva. An unstimulated sialometric test using the drainage method described by Navazesh and Christensen (12) was carried out for 15 min. Saliva in excess of 1.5 ml every 15 min was considered normal.

An unstimulated sialometric test using oral Schirmer's test (WST) was also carried out, as described previously (10). This is a variation of Schirmer's eye test and uses a calibrated Whatman 41 filter paper (1 cm wide, 17 cm long) in a polyethylene bag. The strip is placed on the floor of the mouth and, as the saliva accumulates on the tongue vallecula, it is absorbed by the filter paper. After 5 min, the strip is extracted and the wetted length (mm) is recorded (Figs 1 and 2). The rate of saliva secretion is expressed as mm/5 min. The test was applied twice to the control group. To carry out the stimulated saliva test, citric acid (4%) was applied dropwise to the dorsum of the tongue. The patient was asked to swallow

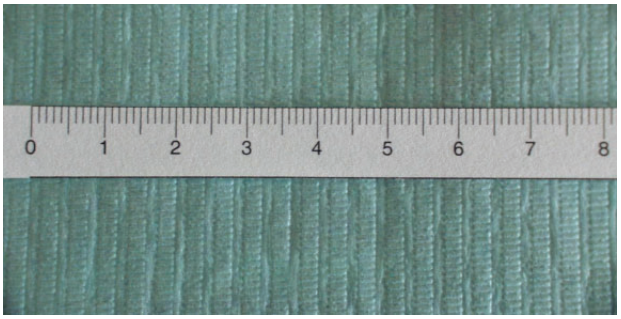

Figure 1 Filter paper used for oral Schirmer's test.

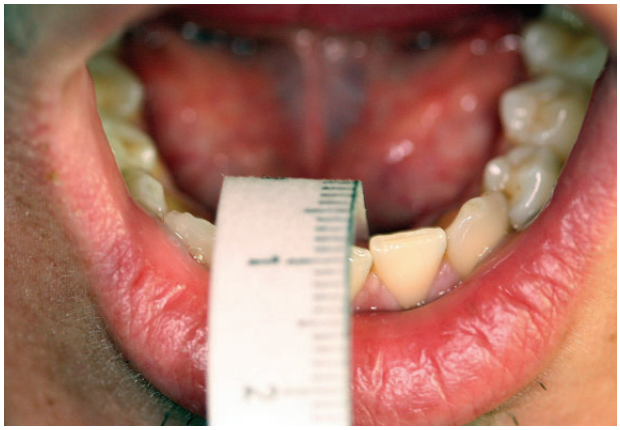

Figure 2 Application of WST.

his/her saliva and Schirmer's test was applied as described.

Sialometric tests were always performed on the same day in the following order: drainage test (15 min) according to European criteria followed by 20 min of rest; unstimulated WST (5 min) and, after another resting period, acid-stimulated WST (5 min).

Statistical analysis

Descriptive statistics were used to define the characteristics of each group. Categorical variables were compared using the chi-squared-test or Fischer's exact test. Continuous variables were analysed by one-way analysis of variance and the Bonferroni *t*-method for multiple comparisons. Values were considered statistically significant at $P \leq 0.05$. So as to define the WST value that best identified individuals with salivary gland hypofunction, 2×2 tables and receiver operating curves (ROC) were used at different cut-off points. Sensitivity, specificity, positive predictive value and negative predictive value were calculated.

Results

The mean age of the control group was 40.53 years, with a standard deviation (SD) of 15.22 years (50% male and 50% female). The mean age of the SS patients was 57.08 years with a standard deviation of 12.48 years (11 male, 18.04%, and 50 female, 81.96%). The mean age for the third group was 52.52 years, comprising two males (6.45%) and 29 females (93.55%) (Table 1).

The unstimulated WST showed lower values in the SS patients than in the patients of the other two groups, the difference with the healthy group being significant ($P = 0.003$), but not with group 3 ($P = 0.202$). Analysis of the ROC-curves suggests that a cut-off value of ≤30 mm/5 min provides high sensitivity (67.9%) and specificity (62.8%) (Table 2).

The drainage test results were higher in the healthy patients, and significant differences were obtained with both the other groups. However, despite the low saliva values of the SS patients, the differences between groups 2 and 3 were not significant.

Table 1 Mean values of different tests in the three groups studied

	Age, mean ± SD (years)	*Male/female*	*Unstimulated WST (mm/5 min)*		*Stimulated WST (ml/5 min)*		*Draining (ml/15 min)*	
			Mean ± SD	*ANOVA*	*Mean ± SD*	*ANOVA*	*Mean ± SD*	*ANOVA*
Group 1	40.53 ± 15.22	50/50	40.92 ± 22.28	Between groups 1 and 2: $P = 0.003$	107.41 ± 58.23	Between groups 1 and 2: $P = 0.000$	2.7 ± 3.2	Between groups 1 and 2: $P = 0.000$
Group 2	57.08 ± 12.48	11/50	27.25 ± 24.11	Between groups 1 and 3: $P = 1.000$	56.7 ± 25.9	Between groups 1 and 3: $P = 0.000$	0.83 ± 1.1	Between groups 1 and 3: $P = 0.000$
Group 3	51.51 ± 12.49	2/29	36.847 ± 23.4	Between groups 2 and 3: $P = 0.202$	62.3 ± 28.7	Between groups 2 and 3: $P = 1.000$	1.36 ± 1.04	Between groups 2 and 3: $P = 1.000$

P-values were considered statistically significant at $P \leq 0.05$.

Table 2 Overall saliva at rest. Different cut-off values in mm/5 minutes as predictors of salivary gland hypofunction

Unstimulated WST (mm/5 min)	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*	*NPV (%)*	*ROC (%)*
WST1 ≤ 30	67.9	62.8	56.6	26.7	65.2
WST1 ≤ 40	64.1	58.6	48.7	27.2	61.2
WST1 ≤ 50	63.5	57.3	44.6	25.5	58.3
WST1 ≤ 60	63.6	56.6	41.6	23.8	54.6

PPV, positive predictive value; NPV, negative predictive value.

Table 3 Stimulated saliva with 4% citric acid; sensitivity, specificity, PPV and NPV values. Different cut-off values in mm/5 min as predictors of salivary gland hypofunction

Stimulated WST (mm/5 min)	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*	*NPV (%)*	*ROC (%)*
WST2 ≤ 50	62.2	59.1	53.1	32.3	59.6
WST2 ≤ 60	69.1	63.05	56.06	25	66.2
WST2 ≤ 70	74.6	64.9	56.4	19.1	69.5
WST2 ≤ 80	87.6	67.5	55.7	7.8	72.9

PPV, positive predictive value; NPV, negative predictive value.

The stimulated saliva test (WST) showed significant differences between groups 1 and 2 ($P = 0.000$) and between groups 1 and 3 ($P = 0.000$) but not between groups 2 and 3 ($P = 1.000$). The best balance between sensitivity and specificity was seen with a cut-off value of ≤80 mm/5 min (Table 3).

The unstimulated WST was performed twice on the control group. Although the first test provided lower values than the second, the differences were not significant ($P > 0.05$). The correlation coefficient (made with a Kappa statistic) was 0.66.

Discussion

The study described in this paper suggests that an unstimulated oral Schirmer's test is a good indicator of the function of the salivary gland and can be used as a simple, objective test to diagnose salivary gland hypofunction.

Ideally, a test should have both high sensitivity and specificity. The choice of the cut-off value, among other factors, depends on the relative consequences of having too many false-positives or too many false-negatives. In the case of saliva, high sensitivity (few false-negatives) is desirable, as failure to detect severe hyposalivation may have devastating consequences in the oral cavity. Additionally, although subjective assessments or complaining of oral dryness may not reflect actual salivary gland capabilities, there are certain questions for patients that have shown significant predictive value concerning salivary performance. Based on current data, the authors suggest a cut-off of ≤30 mm/5 min (a sensitivity of 67.9% and a specificity of 62.8%). However, in patients with a positive result, salivary gland functioning should be evaluated more exhaustively

because of the potential harmful consequences of saliva hyposecretion (18, 19).

Several screening instruments have been proposed so as to identify subjects with xerostomía or sicca syndrome, including questionnaires (7, 20), specific tests (13, 14), devices (6) and physical signs on physical examination (1, 10). However, none of them is widely used, in part because they have not been validated and require special equipment or are invasive. Questionnaires are the most commonly used screening instruments. However, although symptomatic xerostomia is positively correlated with a decrease in salivary flow, the subjective complaint of oral dryness is highly individual and some subjects do not demonstrate a reduced flow rate. In addition, subjective complaints of oral dryness may not be reliable indicators of early salivary gland dysfunction either, because salivary flow must be approximately 50% as before and individual becomes symptomatic (21).

There are several methods for measuring the quantity of saliva that a human being produces per unit of time, both in resting conditions and after stimulating the secretion. In the case of parotid saliva, intra-oral cannulation in the duct and Lashley cups (or their modifications) can be used, while Schneyer's device can be used to measure submandibular and sublingual saliva. Techniques for the measurement of whole saliva are usually based on draining into a recipient, the collection by aspiration or the difference in weight of an absorbent material that is chewed or placed in the mouth. Although used in research, these methods are not normally used by doctors or dentists in their daily practice as they require trained personnel and experience in the study of xerostomia (10).

Filter paper strips of a predetermined size can be used to blot secretions from minor glands over a fixed time, measuring moisture levels with a calibrated Periotron (Harco Electronics Winnipeg MB, Canada), which is a device that measures small volumes of fluids (22, 23). Some authors have used filter papers that incorporate the iodo-starch reaction.

Previous studies have measured saliva secretion using paper strips in a manner similar to Schirmer's test. One such study by Davis and Marks (24) used Schirmer's test strip placed between two tongue-depressors, with a protruding 3-mm end placed against the patient's parotid papilla for 5 min. The slower wetting rate observed by these authors can be attributed to the fact that they took saliva measurements from the flow of a single parotid duct and not the whole saliva as in our study.

Fontana et al. (25) studied unstimulated secretion of the saliva using modified Schirmer's test with 90 patients aged from 9 to 90 years. They obtained values of 25 mm/3 min with a sensitivity of 77% and a positive predictive value of 71%, concluding that the test was a viable diagnostic tool for hyposalivation.

Chen et al. (26), using the same procedure as ours, a 4-cm long strip of filter paper impregnated with blue colourant and two groups (a control group and another with xerostomia), obtained mean values of 29.5 mm and 6.9/3 min respectively.

Saliva flow varies widely and so it is not sufficient to compare the results of a patient with slight glandular hypofunction with a mean value for the general population (5). It is more advisable to determine changes in saliva secretion in the same individual on several occasions in a longitudinal study (9, 14). We, therefore, suggest that sialometry should be used as a matter of routine, preferably using simple procedures that take little time to perform. According to the results of our study the WST has the following advantages: it is inexpensive and can be readily sterilized; it also enjoys a high degree of patient acceptability. The use of catheters and suction devices in some sialometric tests may cause local irritation of tissues that are already inflamed as a result of hyposalivation. The WST may be of use for the routine testing of patients who complain of salivary gland hypofunction.

Although xerostomia is a common problem, it has received little attention. The absence of a recognized test may have contributed to the underestimation of its importance as a public health problem, even when associated with SS, one of whose principle characteristics is, precisely, xerostomia. In clinical practice, only subjects with definitive symptoms or keratoconjunctivitis sicca (inflammation of the conjunctiva and of the cornea associated with lacrimal deficiency) are investigated for SS; patients with symptomatic xerostomia alone are investigated only if the symptoms are extreme (14). Paradoxically, in subjects with sicca symptoms who later develop SS, oral symptoms are found more frequently than ocular symptoms (27).

The parallelism between Schirmer's test and the WST is evident: the material (Whatman paper no. 41), principle (the paper strip is soaked by absorption of the fluid), time taken (5 min) and the measurement (mm) are the same. However, our test has some slight advantages compared with normal Schirmer's test. First, the resting test causes less stimulation. The stimulus produced when the oral mucosa contacts the strip and the bag is minimal, as these materials are soft and flavourless (10). The results suggest that the whole saliva test may have application in routine screening of patients who complain of xerostomia, but further studies are required.

An abnormal test result may be indicative of saliva hyposecretion because of any cause, but does not provide information about the structural and functional defects in the salivary glands, nor is it specific for any disease. The clinician should decide whether additional diagnostic evaluation is justified.

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