Resting and stimulated whole salivary flow rates in Sjögren's syndrome patients over time: a diagnostic aid for subsidized dental care?

Lars Jorkjend, Anders Johansson, Ann-Katrin Johansson and Axel Bergenholtz

Section of Dental Pharmacology and Pharmacotherapy, University of Oslo, Norway; Department of Prosthetic Dentistry, Postgraduate Dental Education Center, Örebro, Sweden; National Resource Center for Eating Disorders (NÄT), Örebro, Sweden; Umeå University, Umeå, Sweden

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The aim of the present study was to evaluate Swedish and Norwegian criteria currently applied in the assessment of eligibility for subsidized dental care of Sjögren's syndrome (SS) patients. These criteria are partly based on a single salivary test showing a resting whole salivary secretion rate of ≤0.1 mL/min. Thirty secondary Sjögren (SSS) patients (29 F and 1 M) participated for the duration of the study, in which resting (RWS) and stimulated (SWS) whole salivary flow rates were collected in the morning and afternoon, over 3 consecutive weeks, once per week, as well as at different times over a 5-year period. Twenty patients presented levels of RWS flow rates of ≤0.1 mL/min on one or more occasions over a 3-week period, while 8 of these also exceeded, on one or more occasions, the cut-off level of 0.1 mL/min, indicating that salivary flow rates varied over time. Six patients showed consistently low secretion rates of RWS as well as of SWS, estimated as ≤0.1 mL/min and ≤0.7 mL/min, respectively. Based on the results, salivary tests that are to be used as a diagnostic aid for SS diagnosis, and thus as a basis for inclusion within the subsidy net for dental care, must be taken on several occasions in order to more accurately give information about salivary gland function. In line with this, current regulations governing the eligibility of SS patients within subsidized dental care programs should be reviewed. □ *Longitudinal studies; salivation; Sjögren's syndrome; subsidized dental care*

Anders Johansson, Department of Prosthetic Dentistry, Postgraduate Dental Education Center, Box 1126, SE-701 11 Örebro 1, Sweden. Tel. +46 19 602 40 78, fax. +46 19 602 40 85, e-mail. a.johansson@orebroll.se

The term 'xerostomia' expresses a subjective feeling of dryness in the oral cavity, and is one of the most important and common features in Sjögren's syndrome (SS) patients (1–3). 'Hyposalivation', in contrast, denotes the sign; in other words, a decreased salivary flow rate which distinguishes the two entities. There is also a third item, the 'altered salivary composition'. All three terms 'in many respects are interrelated, constituting not merely a dental but also a medical and social concern' (4).

Saliva is an important protector of tissues and organs of the oral cavity, thus greatly contributing to and maintaining oral health status. Dryness in the oral cavity is not only uncomfortable, it is also associated with progressive dental diseases. A lack of saliva may cause atypical, unusual and severe dental caries as well as different types of tooth wear, including dental erosion and cervical defects (5–7). It has been found that demineralization is rapid and aggressive in the case of caries (2).

In Norway and Sweden, SS patients are eligible for subsidized dental treatment if their dental problems can be shown to be related to the disease. In both countries, a confirmation of the diagnosis of SS is made on the basis of ophthalmological and rheumatological examinations, as well as chair-side collection and measurement of salivary flow rate. Other methods for screening hyposalivation include scintigraphy and sialography, both of which, while being sensitive tests for salivary gland function, are expensive and complicated. Collection of whole saliva as resting (RWS) and stimulated (SWS) saliva per unit time performed as a chair-side analysis in the dental office, on the other hand, is a simple and non-invasive method recommended by the Swedish Social Insurance Board. In order for the individual to obtain subsidized dental care in Sweden, the RWS flow rate should be ≤0.1 mL/min and SWS flow rate ≤0.7 mL/min.

The aim of the present study was to evaluate the criteria currently applied, namely stipulated RWS and SWS flow rates, for the identification of SS patients entitled to subsidized dental care.

Materials and methods

Of 117 patients diagnosed as having secondary Sjögren's syndrome (SSS), 36 were randomly selected and asked to participate in the investigation, of which 30 completed the whole study (29 F and 1 M). The participants ranged in age between 31 and 79 years, with a mean of 61 years ($s = 10$). Ninety-six percent of the group complained of xerostomia. The SSS patients had been diagnosed according to the European classification criteria (8), based on medical history, clinical investigation and mucous salivary gland biopsies from the lower lip region. Anatomical pathologic diagnoses were performed at the Faculty of Dentistry (Professor Hanna Kopang), University of Oslo, Norway. RWS (15 min) and SWS (5 min) saliva

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were collected in accordance with the method of Nauntofte et al. (9).

Although the intention was for one of the authors (LJ) to collect all salivary samples at the dental office, owing to practical circumstances and complaints by the patients over difficulties in reaching the clinic, patients were taught how to collect saliva samples in their own homes at stipulated times, and to check the amount of secreted saliva. All patients were given verbal and written instructions not to eat, drink, or smoke 2 h ahead of each salivary collection. They were also advised to start with the RWS followed by SWS. Only paraffin stimulation was used for collection of SWS. Each test-tube was graded in 0.1 mL. A summary of the samples collected follows:

1. The first saliva samples were collected between 1997 and 1999, and the second and third between November 2001 and January 2002, in both periods at 10.00 h.
2. When the decision was made to continue to estimate salivary flow rates at two given times of the day (April to May 2002), patients were asked to visit the clinic to provide a saliva sample in the morning and instructed how to perform the second collection at home in the afternoon of the same day at 16.00 h.
3. A week later, patients repeated the procedure (2), and again the following week, thus giving a total of three sets of morning and afternoon salivary collections.

Patients were also asked to answer a questionnaire concerning oral and general health symptoms, medications and on-going and past treatments.

Statistical analyses

Paired Student's *t* test was used to test differences between morning and afternoon salivary collections. All critical values were based on $P < 0.05$, and all data were analyzed in SPSS version 11.

Results

The reason for excluding six patients from the study was that they participated only in the yearly tests, and not in the weekly tests. Salivary flow rates recorded on different occasions and at different times of the day over the 5-year period are given in Table 1. Comparison between morning and afternoon samples of RWS and SWS flow rates, respectively, showed no statistically significant differences.

Twenty out of the 30 patients who completed the study showed, on one or more occasion(s), a RWS flow rate of $\leq$0.1 mL/min during the three weeks in which both morning and afternoon salivary collections were performed (Fig. 1A, B). Of 12 patients showing a consistent RWS flow rate of $\leq$0.1 mL/min, 2 had no RWS at all on each of the 6 occasions tested.

On one or more occasion(s), 12 patients exhibited a SWS flow rate of $\leq$0.7 mL/min (Fig. 2A, B), and those were all from the group who on one occasion or more presented RWS figures of $\leq$0.1 mL/min. Of these, six patients showed a consistent RWS and SWS flow rates of $\leq$0.1 mL/min and $\leq$0.7 ml/min, respectively, on each of the six occasions tested.

Of the 10 participants who consistently demonstrated $\geq$0.1 mL/min RWS flow rate during the weekly tests, 4 showed $\leq$0.1 mL/min one to three times during their yearly tests.

Reported general health problems and subjective symptoms within the sample are given in Table 2. As regards polypharmacy, 9 patients (30%) reported no medicine intake, 9 (30%) had 1, 8 patients (27%) had 2–4 medicines and 4 patients (13%) reported 5–9 medicine intake.

Discussion

SS affects women 9 times as much as it affects men, the majority of patients being above 50 years of age (3). A similar pattern was noticed in the present study, where 29 of the 30 individuals in the study sample were women and

Table 1. Volumes of resting and stimulated whole saliva secretion recorded between 1997 and 2002. *P* denotes the difference between morning and afternoon measurements

	Resting saliva mL/min					Stimulated saliva mL/min					
	n	Min.	Max.	Mean	*s*	*n*	Min.	Max.	Mean	*s*	*P*
1997–1999	30	0.00	0.57	0.19	0.17	30	0.10	3.80	1.88	0.97	
2001–2002*	29	0.00	1.13	0.14	0.27	29	0.20	3.38	1.36	0.97	
2002 day 1 a.m.*	29	0.00	0.47	0.13	0.13	29	0.08	4.26	1.66	1.24	
2002 day 2 a.m.**	30	0.00	0.60	0.14	0.16	30	0.22	3.20	1.44	1.00	NS
2002 day 2 p.m.**	30	0.00	1.00	0.19	0.22	30	0.20	3.80	1.48	0.96	
2002 day 3 a.m.**	30	0.00	0.64	0.13	0.14	30	0.10	3.50	1.41	0.96	NS
2002 day 3 p.m.**	30	0.00	0.67	0.17	0.18	30	0.20	4.30	1.55	1.05	
2002 day 4 a.m.**	30	0.00	1.10	0.16	0.22	30	0.20	3.60	1.33	1.02	NS
2002 day 4 p.m.**	30	0.00	1.00	0.19	0.23	30	0.20	3.96	1.39	0.96	

* During the period November 2001 to January 2002.
**During the period April 2002 to May 2002.

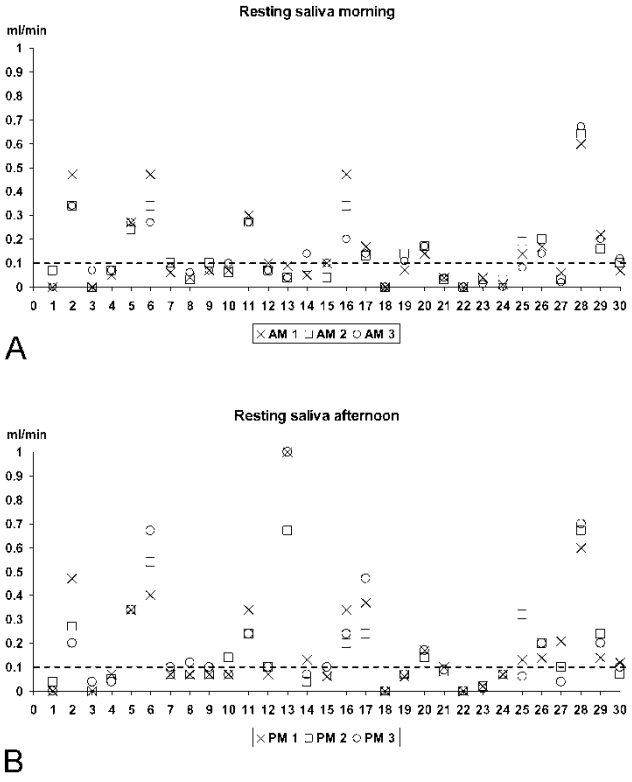

Fig. 1. Morning (A) and afternoon (B) resting whole saliva collection on 3 occasions (a.m. and p.m. over 3 weeks, 1, 2, 3), with 1 week between each set of a.m./p.m. measurements in 30 individuals.

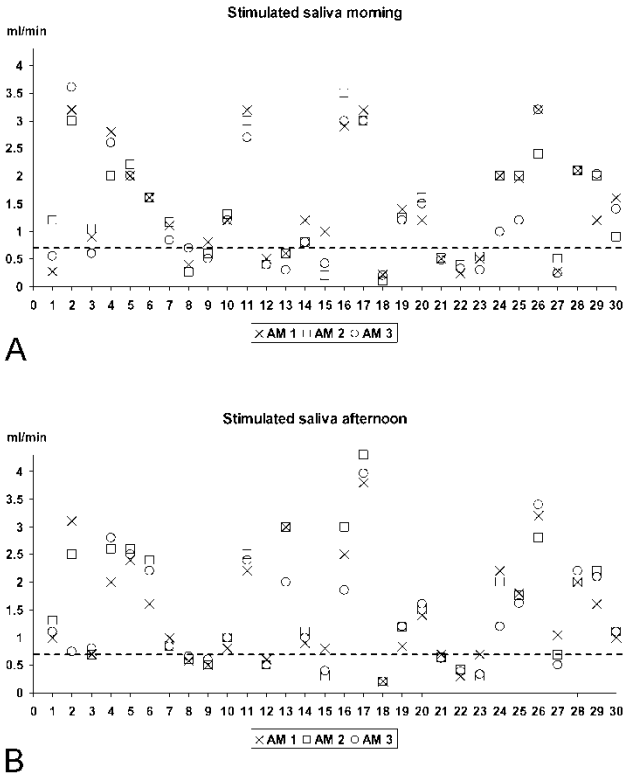

Fig. 2. Morning (A) and afternoon (B) stimulated whole saliva collection on 3 occasions (a.m. and p.m. over 3 weeks, 1, 2, 3) with 1 week between each set of a.m./p.m. measurements in 30 individuals.

26 were above 50 years of age. Indeed, of the total group of 117 patients, only 4 were men. General complaints of patients suffering from SS include oral, ocular, vaginal, skin and nasal complaints, which is in agreement with results in the present study (Table 2) (4).

As regards the compliance of patients following the procedures for saliva sampling at home, it is important to mention that all had participated in several similar saliva tests earlier. When questioned about how they had adhered to the timetable and instructions for saliva sampling, all responded that they had performed the procedures properly.

The diagnosis of SS followed the new European classification criteria, which include both signs and symptoms—subjective feeling of dry mouth, measurement of RWS and evaluation of a lower lip salivary gland biopsy. RWS of $\leq$0.1 mL/min are the stipulated criteria for subsidized dental care as regards SS patients in both Norway (12) and Sweden (13). The Swedish regulations require in addition that the SWS should present levels of $\leq$0.7 mL/min.

Speight et al. (14) suggested that RWS flow of $\leq$0.1 mL/ min was highly specific for hyposalivation, and that it would therefore be reasonable and suitable for use as an objective test in clinical situations for screening patients for subsidized dental care. Haga et al. (3) concluded that salivary flow rates may 'show alterations but over a year it is highly reproducible and stable', 'when performed twice with one year interval'—a finding which is at variance with the results obtained in the present study. While RWS flow rates varied among patients intra-individually at the cut-off level of secretion, viz. $\leq$0.1 mL/ min, they were fairly stable. However, of the 20 patients with RWS flow rates of $\leq$0.1 mL/min, 8 exceeded the cut-off point on one or more occasions. As regards the 12 individuals who presented $\leq$0.7 mL/min of SWS, 6 exceeded the cut-off point on one or more occasions.

Table 2. Percentage distribution of reported general health problems within the sample

Health problem	%	Subjective symptom	%
Heart problems	28	Dry mouth	96
Allergy	36	Dry eyes	86
Rheumatoid arthritis	74	Dry nose	78
Stomach problems	57	Dry skin	73
Medication intake	77	Dry vagina	65
Under medical care	82	Easily freezing	71
Smoking habit	29	White fingers	48
Bad state of health	17	Tired the whole day	89
Less bad state of health	57		
Good state of health	26		

From the foregoing, the conclusion can be drawn that 40–50% of individuals with reduced salivary secretion, as defined, viz. ≤0.1 mL min (RWS) and ≤0.7 mL/min (SWS), may at one or more times present false positive or negative results, which calls into question both the sensitivity and the specificity of the subsidy criteria currently applied.

Wang et al. (15) found that a symptom of mild dry mouth is correlated with a decreased RWS flow rate, while greater severity of dry mouth is correlated with both decreased RWS and SWS flow rates. Nederfors et al. (16) concluded that fasting RWS is the diagnostic salivary secretion of choice and that xerostomia predicts hyposalivation on a group level, but not on an individual level. In this study, low SWS flow rates correlated well with low RWS flow rates, although no separate analysis of their correlation with symptoms of dry mouth was conducted despite that almost all of the individuals reported dry mouth.

Consecutive investigations of salivary flow rates among SS patients over time are not common in the literature. Healthy persons show a large variability of flow rates for both RWS and SWS salivary secretions, with ranges of between 0.08 and 1.8 mL/min and 0.2 and 5.7 mL/min, respectively (17). Using anticholinergic agents to influence salivary flow, Dawes (18) observed that patients experienced the sensation of dry mouth with a 50% reduction of the normal flow rate of RWS, but not with a 40% reduction. On this basis, Sreebny et al. (17) suggested that a rate of 0.1 mL/min of RWS and <0.5 mL/min for SWS should be suspect. If these limits had been used in our study, only two patients demonstrated a RWS flow rate of ≤0.1 mL/min and a SWS flow rate of <0.5 mL/min on all 6 occasions. Among those who on one or more occasion(s) presented ≤0.1 mL/min RWS flow rates, 10 were below 0.5 mL/min and 12 ≤ 0.7 ml/min for SWS flow rates. Only 6 of the 12 patients with ≤0.7 mL/mL SWS flow rate obtained this level on all 6 occasions.

According to Skopouli et al. (19) salivary flow rate measurement should be abandoned as a diagnostic tool of xerostomia, while Sreebny (20) believes that measurement of both RWS and SWS flow rates should be used to confirm salivary gland hypofunction. Arising from the results obtained in this study, it is difficult to assess the status of a patient's salivary gland function from a single measurement of flow rate. 'It is more likely that changes in salivary flow over time are a reliable indicator of a patient's oral health' (17). Therefore, it is suggested that estimation of an individual's salivary flow rate should be based on samples of both RWS and SWS taken on three weekly occasions. By including the SWS flow rate test at the same time, the salivary gland secretory potential could be more properly evaluated. It is, however, important to state the time and the procedure for sampling (fasting salivary collection) as well as to include a questionnaire containing the patient's medication, drugs, diseases, ongoing and performed treatments, etc.

SS is a condition which affects patients physically, emotionally and socially, irrespective of the fact that salivary flow rates may be above or below 0.1 mL/min. With regard to dental care, whether subsidized or not, it is the clinician's role to support and explain to the affected individual that even if decreased salivary flow rate might be irreversible, dental caries and other oral health problems can be prevented (2).

Based on the present results, salivary tests to be used as a diagnostic aid for SS diagnosis must be conducted several times if they are to provide more accurate information about salivary gland function. It may be suggested that at least two of three tests have to be equal or less than the stipulated values for RWS (≤0.1 mL/min) and SWS (≤0.7 mL/min) if hyposalivation is to be validated. In conclusion, the regulations for inclusion of a SS patient for subsidized dental care should be reviewed.

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