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A comparison of two clinical methods for measuring saliva in patients with Sjögren's syndrome

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Abstract

Objective. The aim of the present study was to evaluate two different ways of measuring unstimulated and stimulated whole salivary output in the dental clinic, namely by volume (mL/min) and by weight (g/min). ***Materials and methods.*** Thirty-one patients diagnosed with Secondary Sjögren's syndrome (SSS) participated in the study. ***Results.*** The results showed a large discrepancy between the measurements performed by volume and by weight ($p < 0.001$) and additionally when taking into account density calculation, especially in individuals with low salivary secretion rate. ***Conclusion.*** It is suggested that weight measurement of saliva should be more routinely implemented, especially in patients with reduced salivary secretion.

Key Words: *hyposalivation, saliva, saliva measurement, salivary secretion rate*

Introduction

Saliva is an important protector of the oral cavity, thus contributing to and maintaining oral health status [1]. Saliva comprises mostly water but also organic and inorganic components. It is well known that the composition of whole saliva differs both intra- and inter-individually [2]. Correct assessment of salivary flow rate has important diagnostic implications in both clinical and research settings. In Scandinavia the diagnosis of hyposalivation is most often established by collection of whole saliva as unstimulated and stimulated saliva measured in mL per unit time using a chair-side analysis, performed in the dental office. This is a relatively simple and non-invasive method recommended by the Swedish Social Insurance Board [3]. In other countries, different methods, for example weighting of saliva, may be more common [4].

In Norway and Sweden, some groups of patients, such as patients with Sjögren's syndrome (SS), are eligible for subsidized dental treatment if their dental problems can be shown to be related to their disease. Thus, in order for the individual to be diagnosed with hyposalivation and thus be eligible for subsidized dental care, saliva has to be collected and measured by volume. A diagnosis of hyposalivation is made on the basis of unstimulated flow rate of ≤ 0.1 ml/min and/or stimulated flow rate of ≤ 0.7 ml/min [3].

Salivary flow rates varies over time in patients with SS [5]. Since salivary tests are used as an aid for SS diagnosis and thus as a basis for inclusion within the subsidy net for dental care, it has been suggested that tests be taken on a number of occasions in order to more accurately characterize/classify salivary gland function. Thus, it has been recommended that the current regulations governing the eligibility of SS patients within subsidized dental care programs should be reviewed [5]. In this regard, it has been long accepted that standardization of the conditions for collection of saliva is very important for achieving a correct interpretation of the data [3,6,7], although the actual method for measuring the salivary flow, be it by volume or by weight, has received less attention.

Measuring the output of saliva by weight is an alternative, rather easy chair side method, but this

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Table I. Differences between unstimulated and stimulated saliva measured in milliliters and grams.

	Unstimulated saliva, 15 min (n = 28)[a]				Stimulated saliva, 5 min (n = 31)			
	Volume, mL	Weight, g	Δ, mL – g	Δ[b], %	Volume, mL	Weight, g	Δ, mL – g	Δ[b], %
$\bar{x}$ (SD)	1.31 (0.98)	1.15 (0.87)	0.16 (0.14)	18.7 (19.8)	5.82 (4.28)	5.41 (3.99)	0.41 (0.50)	9.1 (7.8)
Range	0.25–4.50	0.22–3.96	−0.11–0.54	−25.9–73.1	1.00–16.90	0.85–15.76	−0.41–2.37	−8.1–23.4
	$p < 0.001$				$p < 0.001$			

$\bar{x}$, mean; SD, Standard deviation; Δ, difference; n, number of individuals; mL, milliliters; g, grams.
[a]Three individuals had no measurable amount of unstimulated saliva.
[b]The percentage difference denotes the numerical difference (mL − g) against the weight.

technique is seldom used in the clinical situation in Scandinavia. In research, both of these methods are frequently used interchangeably. This assumption is based on the hypothesis that volume and weight measures are identical, e.g. that 1 ml of saliva corresponds to 1 mg of saliva. It seems relevant to question whether weight and volume measurements of saliva would allow the same clinical conclusion to be drawn in all situations. The method of choice may be especially crucial if the accuracy of the salivary data must be high, as for example in the diagnosis of hyposalivation or in clinical research. The aim of the present study was to examine the difference between measurements, performed by volume and by weight, of unstimulated and stimulated whole saliva in the clinical situation in Sjögren's patients. It is hypothesized that there will be disagreement between the two methods and that weighing is more accurate.

Materials and methods

Thirty-one Sjögren's patients with expected hyposalivation (29 women and two men), mean age 41.5 years (range = 24–66, SD = 9.6), were randomly selected from a list of 170 secondary Sjögren's syndrome patients referred to a private dental specialist clinic (L.J) in Skien, Norway, and diagnosed with Secondary Sjögren's syndrome (SSS) according to the European classification criteria [8]. The clinical diagnosis was confirmed by biopsies from minor labial salivary glands. The histopathological analyses were performed at the College of Dentistry, University of Oslo, Norway.

The collection of saliva took place between 09.00 and 11.00 hrs in the morning as a chair-side analysis in the dental clinic. The patients were instructed to refrain from the use of tobacco and eating and/or drinking 2 h prior to the examination. That the patients had followed the given instructions were systematically controlled before the test. A specialist dentist (L.J.) performed all examinations during a separate visit and not in conjunction with regular recalls.

At first, collection of unstimulated saliva over a period of 15 min was performed, followed by collection of paraffin wax stimulated saliva over a period of 5 min, in 0.1 mL-graded test tubes [3]. The test tube was of a random Brand and type. Salivary flow rate was measured in mL/min (visual reading) which was obtained by dividing the volumes of collected saliva under unstimulated and stimulated conditions by 15 min and 5 min, respectively.

Secondly, salivary flow rate expressed in g/min was measured. The amount of saliva was weighted on a balance (Mettler AE 260 Delta Range scale, Mettler-Toledo International Inc., CH-8606 Greifensee, Switzerland). The balance, which indicated a variation of less than 0.001 g, was calibrated with three different volumes of artificial saliva (Saliva Orthana®); 2.0 mL, 5.0 mL and 10.0 ml for 10 consecutive registrations each, with an interval of 5 min between measurements. Salivary flow rate expressed in g/min was calculated by the formula: post-weight measure of the graduated test tube – pre-weight measure of the same tube. Three individuals had no measurable unstimulated saliva and were therefore excluded from this part of the analysis, but they all possessed the ability to secrete stimulated saliva and remained in the dataset in this aspect.

The density was calculated (D = weight/volume) and the weight of saliva in grams was assumed to be equivalent to the milliliters of saliva secreted; because the density of saliva is known to be close to 1.0 the theoretical density of saliva was assumed to be 1.0 g/ml [9].

Wilcoxon Signed Ranks Test was used for analysis of the differences between volume and weight and Mann-Whitney Test U-test for comparisons between groups.

Results

In the current study, salivary secretion rate was expressed both in milliliters (volume) and in grams (weight) per minute. The mean production of both

Table II. Mean percentage difference between total volume and weight by group-divided salivary amount based on total volume.

		Unstimulated (n = 28)[a]			Stimulated (n = 31)		
Group	Salivary secretion, mL	Δ^b, %	n	p	Δ^b, %	n	p
1	<1	27.7	12	< 0.05[c]	—	0	
2	≥1–5.0	11.9	16		10.9	16	< 0.05[d]
3	>5	—	0		7.2	15	

Δ, difference; n, number of individuals; mL, millilitres.
[a]Three individuals had no measurable amount of unstimulated saliva.
[b]The percentage difference denotes the numerical difference (mL − g) against the weight.
[c]Denotes difference between groups 1 and 2.
[d]Denotes difference between groups 2 and 3.

unstimulated and stimulated saliva (over 15 min and 5 min, respectively), measured by weight were lower than the mean level expressed by volume (Table I). The differences expressed in volume and weight represent the errors between the two different measurement methods, on the assumption that 1.0 g of saliva corresponds to 1.0 mL. In percentage, the mean difference (error) between the salivary amount expressed in volume and weight was 18.7% and 9.1% for unstimulated and stimulated condition, respectively (Table I).

Similarly, the salivary flow rate per unit time was significantly higher when expressed in mL/min compared to g/min for both unstimulated ($\bar{x}$ = 0.087 mL/min, SD 0.07 vs $\bar{x}$ = 0.076 g/min, SD = 0.06; $p < 0.001$) and stimulated saliva $\bar{x}$ = (1.16 mL/min, SD = 0.86 vs $\bar{x}$ = 1.08 g/min, SD = 0.80; $p < 0.001$), thus confirming the difference seen in Table I. Twenty-one patients were below 0.1 g/min, while 19 of those patients were below 0.1 mL/min.

The mean difference between salivary volume and weight was larger when the total salivary amount was low. For example, at levels of <1 mL of unstimulated saliva, the volume difference was 27.7% greater than the measurement in grams. For stimulated saliva the difference was only 7.2%, if the amount was >5 mL (Table II). Consequently, the measurement difference between volume and weight becomes greater the smaller the measured amount of saliva. The calculated densities of unstimulated and stimulated saliva, measured in grams and millilitres, showed large differences compared to the theoretical density (1 g/mL) (Table III).

Discussion

More than 99% of the composition of whole healthy saliva is water; different dissolved organic and inorganic constituents, including debris and other cells not originated from the salivary glands, make up the remaining 1% [2]. The density (or specific weight) of saliva, expressed in grams per milliliter, is normally very close to 1. However, saliva contains bubbles of carbon-dioxide, oxygen and/or nitrogen and the presence of gas reduces the density of saliva. The calculated salivary density in this study based on actual volumes and weights measured showed a relatively large deviation from the theoretical salivary density of 1 g/mL. Thus, the presence of gas may add to the volume of saliva, whereas an accurate measurement of the volume of saliva depends on correct visual reading of the volume. Despite such inherent errors in volume estimation, the common practice in the Scandinavian countries is to express saliva secretion in milliliters/minute and not as grams/minute. One could, of course, argue the significance of such an error in the clinical situation. In this study 21 patients were below 0.1 g/min, while 19 of those patients were below 0.1 mL/min. Consequently, two (~ 10%) patients would have been misdiagnosed if volume, and not weight, was considered the correct basis for estimating secretion rate. These patients would consequently not qualify for receiving subsidized dental

Table III. Differences in calculated mean density and theoretical density (1 g/mL) of unstimulated and stimulated whole saliva.

	Unstimulated (n = 28)		Stimulated (n = 31)	
	D	Δ^a, %	D	Δ^a, %
$\bar{x}$ (SD)	0.86 (0.14)	−13.6 (14.2)	0.92 (0.07)	−7.9 (6.8)
Range	0.578–1.35		0.81–1.09	

D, Density; $\bar{x}$, mean; SD, Standard deviation; Δ, difference; n, number of individuals.
[a]If assumed theoretical density = 1.

care. In addition and as previously mentioned, serial measurements need to be performed due to variation of salivary secretory capacity over time in order to detect patients with hyposalivation [5].

Thus, an accurate estimation of salivary secretion, based on its volume (expressed in ml), is difficult due to reading errors, e.g. gas bubbles and the operator's visual capacity, while weighing of saliva seems to be more correct on condition that the scale used has a high accuracy. Another possible problem relates to the manufacturing process of the test tube which could have resulted in an incorrect grading of the scale on the tube. This could be tested by an incremental addition of 0.1 mL of water into the tube followed by weighing which would evaluate the accuracy of the grading of the tube. Other methods for assessing salivary secretion could also be used in order to increase the accuracy such as the sample sponge technique or the use of compresses/gelatin-based gel and weighing [10–12]. The results from this study clearly show that the lower the saliva secretion rate, the greater the error recorded if we choose to express saliva secretion in milliliters. From a clinical standpoint, volume measurement overestimates saliva flow, especially at low secretion rates. This may have a negative impact for specific patients as a flow rate of <0.1 ml unstimulated saliva is the cut-off for receiving subsidized dental care in countries such as Norway and Sweden. Our results are in contrast to a recent study of Alves et al. [4] where it is suggested that volume measurement of saliva in graduated syringes is comparable to that of weight measurement. It is noteworthy that the aforementioned study comprised healthy individuals; medically compromised patients were excluded which could explain the divergent results. In this regard, our study included medically compromised patients and the relatively large difference between the methods was found especially in patients with hyposalivation.

Consequently, it is suggested that weight measurement in addition to serial examinations of saliva should be more widely implemented than is practiced today, and especially so in patients with substantial reduction of salivary secretion. The hypotheses that there is a disagreement between the two methods (weighing in g and measuring in mL) and that weighing is more accurate was fulfilled.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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