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The effect of clinical setting on the unstimulated salivary flow rate

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ABSTRACT

Objective: Unstimulated whole saliva (UWS) sialometry uses the spitting method to assess occurrence of hyposalivation. This study compares the UWS flow rates in volunteers sitting in a laboratory or in a clinical setting, in order to evaluate the influence of environment on salivary secretion.
Design: 25 healthy volunteers were recruited and divided into two groups to perform UWS sialometry under the two different settings (T1). Eleven weeks later, the participants repeated the same test (T2). At a unique time point and under the clinical setting, 18 patients complaining of xerostomia also performed the UWS sialometry; these values were used as control to corroborate findings.
Results: Different scenarios – laboratory one vs. clinical one – did not affect measurements of mean UWS flow rates. Both intra- and inter-individual variabilities, reported as standard error of the mean (SEM) and within-subject variance (WSV), resulted below the threshold of 0.1 g/min. A significant difference was found between UWS flow rates from healthy volunteers and those from patients with xerostomia ($p < 0.05$). Test/retest reliability showed a moderate correlation of datasets collected at the two time points from healthy volunteers (T1 vs. T2, 11 weeks later): under laboratory and clinical settings, Pearson's coefficients of correlation were r = 0.62 and r = 0.32, respectively.
Conclusions: Type of environment did not influence UWS sialometry via spitting method, which appeared reliable for intra-day analysis of the salivary flow rate, although prone to physiological variations over time.

1. Introduction

While xerostomia identifies the symptom of dry mouth, hyposalivation represents the sign of oral dryness, objectively measured as a decrease in salivary flow rate (Nederfors, 2000). Hyposalivation may have harmful effects on the oral cavity, predisposing patient to oral and dental diseases (Carpenter, 2013; Cunha-Cruz et al., 2013; Kaplan, Zuk-Paz, & Wolff, 2008). Hyposalivation may also represent an important sign of underlying systemic illness, which can, directly or indirectly, affect the salivary glands (Kaplan et al., 2008; Navazesh, Brightman, & Pogoda, 1996; van den Berg, Pijpe, & Vissink, 2007).

The diagnosis of hyposalivation requires quantifying salivary secretion (Nederfors, 2000) via sialometry, the latter defined as the direct measurement of the amount of unstimulated whole saliva (UWS) per minute. UWS sialometry is the first pivotal step to assess hyposalivation related to medications, dehydration or dysfunction of salivary glands (Aliko et al., 2015; Jensen & Vissink, 2014; Löfgren, Wickström, Sonesson, Lagunas, & Christersson, 2012; Miranda-Rius, Brunet-Llobet, Lahor-Soler, & Farré, 2015; Villa et al., 2015). Spitting method is the most common technique used for UWS sialometry: saliva is allowed to accumulate in the floor of the mouth and the individual spits it out into the test tube every 60 s (Navazesh, 1993). Comparative studies of different procedures for sialometry (Kalk et al., 2002; Navazesh, 1993; Navazesh & Christensen, 1982; White, 1977), including spitting, drooling, swab and suction methods, found that the spitting one has the least degree of variability (Navazesh, 1993). This technique, however, is time-consuming and requires high levels of cooperation, thus affecting patient compliance which, in turn, decreases test reliability (Jones, Watkins, Hand, Warren, & Cowen, 2000; Madinier, Starita-Geribaldi, Berthier, Pesci-Bardon, & Brocker, 2009).

Patients can perform sialometry under resting or stimulating conditions. In resting status, the patient is quiet and ideally not

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exposed to any external stimulus, though several further factors may influence the measurement of salivary flow rate, mainly the physiological ones, such as circadian rhythms, age, sex and appetite (Dawes, 1972; Proctor, 2016; Shern, Fox, & Li, 1993). Anxiety or stressful conditions are psychological factors which can also contribute to variation (Bakke et al., 2004; Proctor, 2016). This picture even gets complicated during stimulated sialometry, where additional confounding factors, mainly related to stimulus intensity and duration and difficult to be controlled, hinder the test (Dawes, 1972, 1974, 1984; Navazesh & Christensen, 1982). UWS sialometry can be considered more appropriate than the stimulated one for the diagnosis of hyposalivation (Jensen & Vissink, 2014), although quality of evidence is currently sparse and poor (Löfgren et al., 2010; Löfgren, Wickström, Sonesson, Lagunas, & Christersson, 2012). The need of deeply investigating the reliability of such procedures is still demanding.

The effect of clinical setting, represented by the dental unit where patient usually performs UWS sialometry, is still unknown and it could represent a stressful environment potentially confounding the test. The mechanism underlining this hypothesis might be similar to that reported for blood pressure measurements: patients can show lower ("white coat" effect) or higher ("masked" effect) blood pressure values when measured at home compared to clinic, greatly affecting the correct diagnosis and management of hypertension (Bonafini & Fava, 2015; Sheppard et al., 2015). In addition, evidence is scanty on UWS flow rate variations as physiological response to the clinical scenario.

The present study aims to address the debate on the possible confounding role of the setting in UWS sialometry, verifying, in healthy volunteers, the effect on salivary flow rate of a quiet laboratory room *versus* a stressful clinical setting represented by a dental unit.

2. Methods

2.1. Participants' recruitment

From February 2007 to July 2008, participants were recruited among dental students and patients at University of Milan, Polo San Paolo (Italy), in full accordance with ethical principles of the World Medical Association Declaration of Helsinki and under local Ethics Committee approval. Informed consent of each individual was guaranteed.

2.2. Inclusion and exclusion criteria for recruitment

As healthy volunteers, dental students, ranging from 18 to 35 years old, were consecutively enrolled, after expressing their willingness to voluntarily participate to the study. Exclusion criteria were having oral and/or systemic medical problems ongoing, having received salivary glands surgery or irradiation, taking medications, complaining of xerostomia, smoking more than one pack of cigarettes per week. Patients who complained of oral dryness and referred to General Dentistry or Oral Medicine services, at U.O Odontostomatologia A.O. San Paolo (University of Milan), were also recruited, after informed consent. In this case, the inclusion criteria consisted in being at least 18-years old and complaining of dry mouth. Patients were consecutively enrolled during their routine dental visit.

2.3. Study design

This observational and prospective clinical trial was carried out on healthy volunteers who, under standardized conditions, performed sialometry under the two environments. Group 1 was composed of healthy volunteers tested for UWS sialometry in resting condition, sitting in a quiet room of our laboratory, completely separate from the clinical scenario. Group 2 was composed of healthy volunteers tested for UWS sialometry in clinical setting, sitting in a dental unit at Oral Medicine service. Group 3 was composed of patients complaining of xerostomia, referred to General Dentistry or Oral Medicine services. Xerostomic patients performed sialometry just in the clinical setting and at a unique time point. Resulting flow rate values were considered as control to support the reliability of spitting method to detect hyposalivation and to corroborate, indirectly, the clinical meaning of our findings. They were asked to perform UWS sialometry in the same clinical setting as Group 2, thus sitting in the dental unit at Oral Medicine service.

2.4. Saliva collection

UWS sialometry was carried out via spitting method as previously reported (Navazesh, 1993) (Fig. 1), under the strict supervision of one trained dentist (V.F.). The test was performed in all cases between 12:00 noon and 1 p.m., at room temperature ($\approx$21 °C). Each individual should refrain from food, drinks and cigarettes for at least one hour before the test, resting for 5 min prior to saliva collection. Briefly, the participant was sitting upright with the head slightly tilted forward and the eyes open; he/she had a water mouthrinse to eliminate oral debris and, then, rested for three minutes, again, avoiding head movements and speaking. He/she should swallow saliva at the beginning of the three-minute collection trial and, then, spit saliva into the test tube (which weighed 1.5 g) every sixty seconds (Bretz et al., 2001; Kumar, Panchaksharappa, & Annigeri, 2014); the 3-min collection trial was repeated three times, separated by a one-minute resting period. Each of the three saliva samples was collected, immediately sealed, weighed three consecutive times and evaluated in volume, excluding the foamy phase of saliva lying on the sample surface. For each participant, mean UWS sialometry per individual was expressed in g/min flow rate. The study on healthy volunteers included a first time point of saliva collection (T1), then repeated by the participants, under the same condition (Group 1 and 2), after a period of 11 weeks (T2).

2.5. Data collection

Per each participant, demographic data were recorded, including sex and age, number of cigarettes per day, oral hygiene habit, as well as information on date and time of the collection day. Oral examination was also performed to assess the oral health status. Oral and systemic medical histories and drug medications were recorded in detail for the Group 3, composed of patients complaining of xerostomia. Xerostomia was classified according to three categories: (1) oral dryness at times = mild; (2) frequent, but tolerable oral dryness = moderate; (3) oral dryness associated with burning sensation = severe.

2.6. Statistical analysis

Statistical power of sample was calculated as 0.95, based on size effect and estimates from previous literature, reporting mean standard deviation of 0.1 (Henry, 1959; Jones et al., 2000; Navazesh, 1993). Mean values and standard deviation (SD) of UWS flow rates (g/min), related to each of the three groups, were tested for normal distribution (Kolmogorov-Smirnov normality test). They were, then, compared using a two-sample *t*-test; $p < 0.05$ was considered statistically significant. Inter-individual variability of the test within the same group was identified by standard error of the mean (SEM). SEM values $\leq$ 0.1 g/min were considered acceptable (Henry, 1959; Jones et al., 2000; Navazesh,