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ORIGINAL ARTICLE

The distribution of oral mucosal pH values in healthy saliva secretors

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OBJECTIVES: To establish the normal range of oral mucosal pH and to correlate these measurements to salivary flow rate in healthy individuals according to age and gender.

SUBJECTS AND METHODS: Measurements of pH levels using a flat pH meter and salivary secretion rates were established in eight mucosal sites from a total of 50 healthy individuals.

RESULTS: The mean pH (±s.d.) of all sites was 6.78 ± 0.04 with significant differences between mean pH values in the palate (7.34 ± 0.38), the floor of the mouth (6.5 ± 0.3), the buccal mucosa (6.28 ± 0.36) and the tongue (6.8 ± 0.26). A significant correlation was found between age and pH at palatal and tongue sites but no gender effects were noted.

CONCLUSIONS: This method is easy and relatively quick to manipulate, and may offer many diagnostic possibilities for oral related diseases and disorders such as oral malodour, mouth breathing, dysgeusia, acidic diet consumption and gastrointestinal disorders affecting the mouth.

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Keywords: oral pH; oral mucosa; oral diseases; saliva; diagnostic tool

Introduction

Saliva has numerous functions including lubrication, digestion and presentation of molecules to taste buds. It also acts as a medium for growth factors that promote soft and hard tissue growth and repair in the oral cavity. Saliva is essential in maintaining the ecological system in the oral cavity and acts as a carrier for immunoactive peptides. Furthermore, by maintaining the right buffer capacity saliva also aids in the enamel remineralization process (Ship, 2002; Bardow *et al*, 2004).

To maintain a non-harmful pH in the oral cavity the salivary system employs three buffer systems; bicarbonate, phosphate and protein (Lazarchik and Filler, 1997; Bardow *et al*, 2004). These systems maintain a pH of 6.0–7.5, depending strongly on the saliva secretion rate; the most alkaline fluid is secreted during stimulated flow. A drop in saliva pH below 5.5 is potentially harmful to the hard (enamel and dentin) (Bardow *et al*, 2004) and soft tissues (Robb *et al*, 1995; Markitziu and Aframian, 1997; Aframian and Markitziu, 1999). Bulimic or vomiting anorectic patients are risk groups for tooth wear mainly because of a low pH resulting from gastric acids as well as from highly acidic carbonated beverages or fruit juice consumption. In these patients extensive erosion of the palatal aspects and to a lesser extent the buccal surfaces of the upper anterior teeth is observed. Variable erosion of the occlusal and buccal surfaces of upper and lower posterior teeth also occurs, a process that can be accelerated by attrition (Little, 2002). Xerostomia, periodontal disease and atrophic mucosa are commonly seen in these patients (Aframian and Markitziu, 1999; Little, 2002). Furthermore, malnutrition affects the salivary glands manifested by gland enlargement, mainly in the parotids, and a decreased salivary secretion volume (Aframian and Markitziu, 1999; Little, 2002).

The role of mucosal pH in oral soft tissue diseases is unclear. The topographical epidemiology of diseases such as lichen planus and burning mouth syndrome suggests that local factors such as pH may be involved (Yosipovitch *et al*, 2001).

Salivary pH and buffering capacity are traditionally measured from saliva collected extra-orally, a fact that may lead to inaccuracy for the following reasons: (1) A more general pH value is produced not representing the different intra-oral micro-environments, (2) The buffering systems may alter once the saliva is taken out of the oral cavity and (3) The salivary film formation, covering the soft and hard tissues may not

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precisely correspond to secreted saliva with regard to pH levels.

The aim of this study was to quantify the mucosal pH in several sites in the oral cavity and to correlate these measurements to salivary flow rate in healthy individuals according to age and gender.

Subjects and methods

Subjects

The study included 50 volunteers, 26 males (52%) and 24 females (48%), with ages ranging between 18 and 53 years (mean 29 ± 8 years). Inclusion criteria consisted of healthy adults (>18 years) not taking any medication, with no complaint of oral or ocular dryness and no mucosal diseases. Patients with removable dentures or smokers were excluded. All the volunteers were requested not to eat, drink or brush and wash their teeth for 1 h prior to the trial. Measurements were performed between 8 and 12 AM by a single examiner.

Measurements

Unstimulated whole saliva flow (UWS) was collected for 10 min into a precalibrated tube prior to pH measurements to reduce stimulatory effect. Individuals were asked to rest for 10 min before saliva collection, sitting in an upright position and in a quiet room. During the measurement volunteers were asked not to speak or leave the room. Oral surface pH was measured with a flat, glass electrode pH meter (HI 8424; Hanna instruments, Padova, Italy). Two sets of measurements were collected from eight locations; the soft and hard palate, anterior, middle and posterior tongue, right and left buccal mucosa and the floor of mouth (Figure 1). Anatomical references to assure the exact repeated measurement in each mucosal site were established; three sites adjacent to the orifices of the major salivary glands, i.e. buccal mucosa near the orifices of Stensen's duct and one in the floor of the mouth between the sublingual carunculas. The other five locations were adjacent to minor salivary glands on the palate or to von Ebner's glands on the tongue. Each set of measurements took approximately 40 s. As the loss of carbon dioxide to the atmosphere tends to increase the pH levels with time, the first measurements in the oral cavity were established in the palate areas (hard and soft) where the saliva film coverage is thinnest and the last measurements (35–40 s later) were done in the floor of the mouth where the salivary bath is protected by the anterior portion of the tongue. Between the two measurements a 5 min break was allowed. Ethical committee approval was obtained.

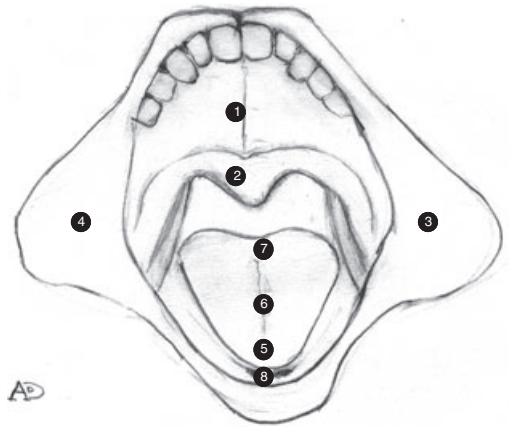

Figure 1 Diagram of eight mucosal sites examined: 1, hard palate; 2, soft palate; 3, left buccal mucosa; 4, right buccal mucosa; 5, anterior tongue; 6, middle tongue; 7, posterior tongue; 8, floor of mouth

Statistical analysis

Data were tabulated and analysed with StatView 5 software (SAS Ltd., Cary, NC, USA) with alpha for significance set at 0.05.

Following initial analysis that revealed no significant differences between areas in the same anatomical sites the data were divided into four groups for further analysis and documentation (palate, tongue, buccal, floor of mouth). The differences in pH values between the different sites were examined with a repeated measures analysis of variance (R-ANOVA) with gender as an independent variable, followed by pairwise comparisons with the Scheffe's test (Sch). The correlations between sialometry, mean site pH and age were examined separately with a simple regression analysis.

Data are presented in the text as mean ± s.d. and in the graphs as mean ± s.e.m. for clarity.

Results

Salivary flow rate

The UWS flow rate (UWSFR) ranged between 0.05 and 0. 95 ml min^{-1} with a mean of 0.37 ± 0.21 and 95% confidence interval of 0.314–0.434 ml, previously described as an adequate secretion rate (Dawes, 1987). Five individuals had <0.1 ml min^{-1} with no complaint of mouth or eye dryness and no arthralgia.

Mean site pH

The mean mucosal pH of all sites was 6.78 ± 0.04. The pH values between sites ranged from 6.24 ± 0.05 (right buccal mucosa) to 7.36 ± 0.06 (hard palate). As stated in the Subjects and methods, initial analysis revealed no significant differences between areas in the same anatomical sites. Therefore the data were divided into four groups for further analysis (palate, tongue, buccal, floor of mouth). Significant differences were noted between mean pH values in the floor of the mouth (6.5 ± 0.3), the palate (7.34 ± 0.38), the buccal mucosa (6.28 ± 0.36) and the tongue (6.8 ± 0.26) (R-ANOVA: $F_{493} = 189.1$, d.f. = 49, $P < 0.0001$: Sch for all pairwise comparisons $P \leq 0.0001$), see Figure 2. No significant effect for gender was found in the ANOVA model and this has therefore been excluded from the graph.

Regression analyses of mean site pH *vs* age revealed significant correlations for the palate and the tongue (palate: $R^2 = 0.12$, $F = 6.2$, $P = 0.016$, tongue: $R^2 = 0.083$, $F = 4.33$, $P = 0.04$) but not in the buccal region or floor of the mouth, see Figure 3.

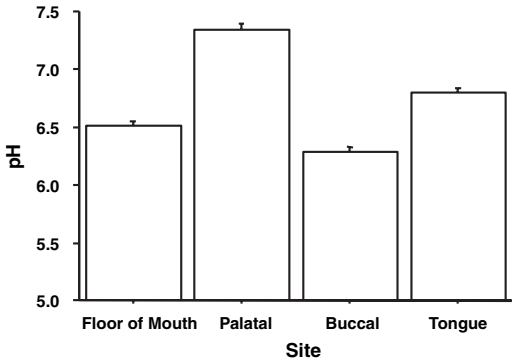

Figure 2 Mean mucosal surface pH (±s.e.m.) of four major sites examined. No significant differences between areas in the same anatomical sites (see Figure 1) were found and data were divided into four sites; floor of mouth, palatal, buccal, tongue. Significant differences were noted between mean pH values in the floor of the mouth (6.5 ± 0.3), the palate (7.34 ± 0.38), the buccal mucosa (6.28 ± 0.36) and the tongue (6.8 ± 0.26) (repeated measures ANOVA; $P < 0.0001$, all pairwise comparisons $P \leq 0.0001$)

Correlations with sialometry

No significant correlations were found between mean site pH and UWSFR, or between age and UWSFR (data not shown).

Discussion

The hydrogen ion concentration (pH) level of saliva is traditionally measured *ex vivo* and ranges between 6.0 and 7.5 (Bardow *et al*, 2004). However, oral mucosal surface pH is not well established. In order to set up ranges of oral mucosal pH in healthy individuals we used a planar electrode pH-meter that has the advantage of direct measurement on a flat surface such as skin (Dikstein and Zlotogorski, 1994) and mucosa (Yosipovitch *et al*, 2001). Using this innovative technique we offer an attractive method for the direct measurement of oral mucosal pH.

Acidity in the oral cavity may be harmful to the hard and soft tissues. The source of oral acidity may be either of extrinsic origin via (e.g. dietary: acidic beverage and fruits, industrial/environmental: battery factories) or of intrinsic nature through regurgitation of gastric contents (Little, 2002). In order to maintain adequate pH levels the salivary system is a powerful buffering system (Bardow *et al*, 2004), usually capable of maintaining a stable intraoral pH.

Salivary flow has a major effect on the buffering capacity. The mean UWSFR in the study group is in agreement with previously published studies (Dawes, 1987). However no correlation was found at any of the sites between mucosal pH and UWSFR, suggesting that at a mucosal level pH is less influenced by UWSFR. This is in contrast to the significant effects of UWSFR on salivary pH as measured *ex vivo* (Bardow *et al*, 2004).

To analyse the mucosal pH we selected eight locations representing the mucosal surfaces in the oral cavity (Figure 1). The mean mucosal pH was 6.78 ranging from a low of 6.24 in the right buccal mucosa to a high of 7.36 in the hard palate.

No mucosal pH difference was found between males and females in this study.

No significant differences were found between areas in the same anatomical sites and the data were divided into four groups (palate, tongue, buccal, floor of mouth). Between these four groups significant differences were found in mean pH values underscoring the concept that the oral cavity needs to be viewed as a collection of distinct micro-environmental compartments. Interestingly, there was a significant correlation between age and mean pH at the tongue and palate. However the clinical significance is unclear especially in light of the relatively low correlation coefficients obtained.

The relatively high pH level measured in the palate (Figure 2) was also reported by Yosipovitch *et al* (2001) but the biological phenomenon is not well understood. One may speculate that as the hard palate has the

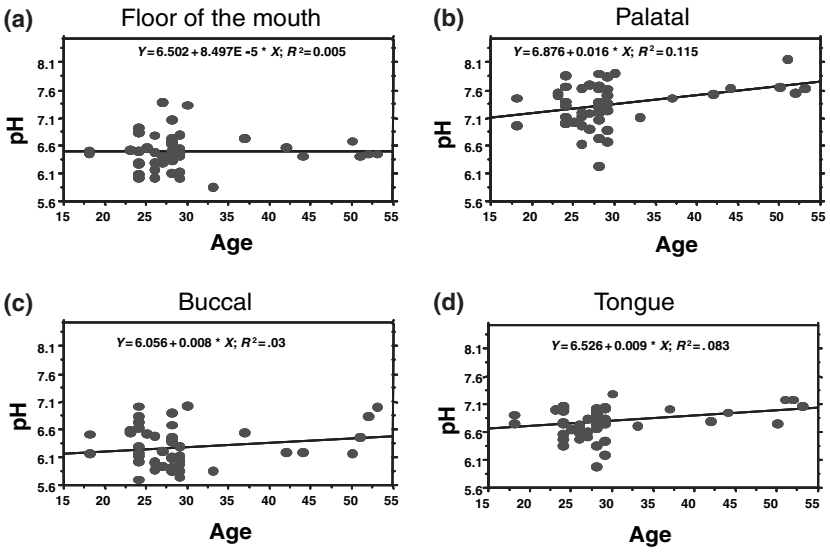

Figure 3 Regression plots between pH values in the four major sites and age. Significant correlations between age and pH were found for the palate and the tongue sites ($P = 0.016$, $P = 0.04$ respectively), albeit with low correlation coefficients. No correlation was found in the buccal area or in the floor of the mouth

thinnest saliva film (10 μm) covering the tissue (Dawes, 2004), mouth breathing induces evaporation and may rapidly decrease this thickness to zero (Disabato-Mordarski and Kleinberg, 1996; Dawes, 2004). Consequently, this process may lead to unstable pH levels. Additionally, the same mechanism may be responsible for the pH level observed in the tongue. The palate has the lowest regional blood flow in oral cavity sites in healthy controls (Heckmann *et al*, 2001). One may hypothesize that this phenomenon has a significant effect on pH buffering; however, in the same study the tongue was found to have the highest regional blood flow. Higher palatal pH levels may be attributed to the high level of carbonic anhydrase, an important enzyme which facilitates the reaction of carbon dioxide with water and is located in oral epithelial cells including those of the palate (Christie *et al*, 1995; Yosipovitch *et al*, 2001) and the tongue (Leinonen *et al*, 2001). Moreover the palate and tongue are the oral sites richest in seromucous salivary glands (Riva *et al*, 1999) and this may have some influence on local pH differences.

As breathing via the oral cavity is intimately associated with effects on the palate and dorsal surface of the tongue it will be intriguing to explore mucosal pH values in disorders accompanied with mouth breathing such as allergic rhinitis, asthma and sleep apnoea.

Secretion of saliva from minor salivary glands differs between mucosal sites (Eliasson *et al*, 1996). The palatal region was shown to contain the lowest secretion measured by the Periotron method (Eliasson *et al*, 1996) emphasizing the major role of the minor glands in maintenance of suitable microenvironment.

In conclusion the system we present herein is reliable, easy and relatively quick to manipulate and may serve as a future diagnostic tool in a number of applications. For example, in cases of gastrointestinal disorders and other related conditions (e.g. bulimia nervosa, pregnancy) that may induce a low oral pH mainly by repeated vomiting (Little, 2002). Kleinberg *et al* (2002) showed a correlation between salivary film thickness and the pH of resting whole saliva and suggested a possible role in the aetiology of oral malodour (Kleinberg *et al*, 2002). Severity of disorders associated with mouth breathing may be monitored by the value of mucosal pH.

Another venue is the use of this system to explore drug delivery and absorption via the oral mucosa (McElnay *et al*, 1995; Kurosaki and Kimura, 2000). The oral mucosal route of administration is well established for various drugs such as nitroglycerin, fentanyl, captopril and benzodiazepines. The surface area of the oral mucosa (200 cm^2) is relatively small compared with the gastrointestinal tract (350 000 cm^2). However, the oral mucosa is highly vascularized, and therefore drugs diffusing into the oral mucosa membranes have direct access to the systemic circulation via capillaries and venous drainage. Moreover, oral mucosal delivery bypasses the fate of enterically administered drugs sparing the low gastric pH and proteases as well as first-pass hepatic degradation. The data obtained regarding different mucosal pH values may aid in exploring the optimal site for specific drug delivery systems.

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