



Unstimulated Whole Saliva Parathyroid Hormone in Postmenopausal Women with Xerostomia

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ABSTRACT

Objective: The aim of this study was to evaluate the correlation of xerostomia severity with unstimulated saliva parathyroid hormone (PTH) and to compare unstimulated whole saliva PTH between postmenopausal women with/without xerostomia.

Methods: A case-control study was carried out in 60 (30 as case and 30 as control) selected postmenopausal women with/without xerostomia conducted at the Clinic of Oral Medicine, Tehran University of Medical Sciences. Xerostomia inventory (XI) score was also used as an index of xerostomia severity. PTH concentration was analyzed by enzyme-linked immunosorbent assay (ELISA). Statistical analysis of Student's t-test and Spearman correlation was used.

Results: The mean unstimulated saliva PTH concentration was significantly higher but flow rate was lower in the case group compared with control. XI score correlated significantly with saliva PTH ($r = 0.688$, $p = 0.001$) and flow rate ($r = -0.529$, $p = 0.001$).

Conclusion: Xerostomia severity correlated positively with unstimulated whole saliva PTH and negatively with saliva flow rate in this group of postmenopausal women. Thus, salivary flow rate and PTH levels appear associated with xerostomia and menopause.

Clinical significance: Salivary PTH level appears to be associated with xerostomia and menopause.

Keywords: Menopause, Xerostomia, PTH, Unstimulated saliva.

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INTRODUCTION

Menopause is defined as the permanent cessation of menstruation resulting from the loss of ovarian function. The age at which physiological menopause appears is between 45 and 55 years, with an average of 52.5 years.^{1,2} Menopause is accompanied by physiological and sensorial oral changes.¹ The prevalence of oral symptoms was found

to be significantly greater in postmenopausal women than in premenopausal females.^{2,3} Major oral symptoms of menopause are xerostomia and burning mouth² which can seriously damage the quality of life.⁴

Xerostomia is a common complaint in older people; it is a subjective sensation. It is associated with an unpleasant feeling in the mouth and throat.⁵ This complaint is more prevalent in postmenopausal women on medication and is quite common also in those without disease or drug usage, unrelated to lowered salivary flow rates.⁶ After caries and periodontal problems, the most common complaint of patients referred to the Oral Medicine Department of Tehran University of Medical Sciences is dry mouth feeling. We have designed a series of studies to address this complaint.

Saliva is critical to the preservation and maintenance of oral health and any changes in its amount or quality may alter oral health status.⁷ Hormonal changes may affect the composition of saliva.⁸⁻¹³ It has been shown that salivary glands may serve as target organs for parathyroid hormone action.¹⁴ Both basal and maximal PTH values were also increased in elderly women. Basal PTH values were greater in elderly than in young adults.¹⁵

It was also demonstrated that stimulated saliva and serum levels of PTH and also saliva calcium significantly were higher in postmenopausal women suffering from xerostomia.^{10,16} In addition, postmenopausal women who lose bone mineral density may experience xerostomia.¹⁷

Based on the above, and due to the high prevalence of xerostomia in postmenopausal women, the objective of this study was to determine the levels of unstimulated saliva PTH and its relationship with the xerostomia.

SUBJECTS AND METHODS

Subjects

The Ethics Committee of Tehran University of Medical Sciences (TUMS), Iran, approved the study protocol. Informed consent was obtained from all participants.

A total of 80 postmenopausal women were asked to participate in a case-control study, conducted at the Clinic of Oral Medicine, TUMS. The participants were aged between 42 and 77 years, had not had a menstruation cycle for at least 24 months, and were not taking any medication at the time of the study. Smokers, obese patients (body mass index > 30), patients with systemic diseases (including Sjogren’s syndrome), oral candidiasis or with a bad oral health condition and periodontal disease were excluded. Of the 80 potential participants, 14 were excluded from the study based on these criteria (8 were eliminated owing to periodontal pocket depths more than 3 mm in multiple sites, 4 were excluded for obesity and 2 for smoking). The remaining women were asked to answer a questionnaire with a list of symptoms associated with xerostomia (Table 1). Thirty, answered affirmatively to at least three of the questions related to xerostomia,^{11,18} formed the case group. Thirty who did not answer affirmatively to any of the questions in Table 1 formed the control group. Participants in the healthy group were selected from patients with caries but without other problems, women who accompany patients referred to the department and from dental school staff. The remaining six were excluded in order to match case and control groups on the basis of age and duration of menopause. The six, who were eliminated, were done so without knowledge of the assay data; only the demographical factors were viewed with blinding to the assay data.

Each participant also answered another questionnaire so that we could assess the severity of xerostomia (Table 2). Xerostomia inventory (XI) score was determined as the severity of dry mouth feeling.¹⁹ The scores of responses were added to provide an XI score for each individual (the minimum possible score was 11 and the maximum possible score was 55).

Sample Collection

Unstimulated whole saliva was collected under resting conditions in a quiet room, between 9 AM and 11 AM, at least 2 hours after the last intake of food or drink. At the

Table 1: Questionnaire used for selection of subjects with xerostomia (oral dryness feeling)
1. Does your mouth feel dry when eating a meal?
2. Do you have difficulty swallowing any foods?
3. Do you need to sip liquids to aid in swallowing dry foods?
4. Does the amount of saliva in your mouth seem to be reduced most of the time?
5. Does your mouth feel dry at night or on waking?
6. Does your mouth feel dry during the daytime?
7. Do you chew gum or use candy to relieve oral dryness?
8. Do you usually wake up thirsty at night?
9. Do you have problems in tasting food?
10. Does your tongue burn?
Response options: Yes/No

Table 2: The xerostomia inventory (XI)
<ul style="list-style-type: none"> • I sip liquids to help swallow food • My mouth feels dry when eating a meal • I get up at night to drink • My mouth feels dry • I have difficulty in eating dry foods • I suck sweets or cough lozenges to relieve dry mouth • I have difficulty swallowing certain foods • The skin of my face feels dry • My eyes feel dry • My lips feel dry • The inside of my nose feels dry
Response options: Never (scoring 1), hardly (2), occasionally (3), fairly often (4) and very often (5).

Table 3: Clinical characteristics of menopausal women		
Clinical characteristics (mean ± SD)	Women without xerostomia	Women with xerostomia
Age (years)	58.00 ± 6.11	57.41 ± 7.71
Years-since-menopause	9.0 ± 6.9	9.1 ± 7.3
Body mass index (BMI, kg/m ²)	23.2 ± 2.5	23.8 ± 2.1

beginning and end of saliva collection, the time was recorded. The participants were asked to swallow the saliva present in the mouth. Thereafter, whole saliva was collected in about 5 minutes into a preweighed, dry, deionized and sterilized plastic tube. The saliva-filled tubes were weighed and the weight of the tubes subtracted. The flow rate was calculated in g/min, which is almost equivalent to mL/min. The saliva was then centrifuged (2000 gm, 10 min) and the supernatants were separated. Immediately, the specimens were stored at -70°C for later determination of PTH concentration.

PTH Assays

PTH was measured utilizing a two-site enzyme-linked immunosorbent assay (ELISA) specific for the biologically intact 84 amino acid chain of PTH. A kit from Biosource, Nivelles, Belgium was utilized in the analysis. In the assay, color development was stopped with the addition of acid as specified by the manufacturer and the ELISA assay microplate then read at 450 nm and also at 590 nm as a background control. Plots of concentration vs absorbance for standards were prepared using a 4 parameter fit and concentrations of unknown samples extrapolated from the standard curve.

Statistical Analysis

For statistical analysis, the data are presented as a mean ± SEM. The 2-tailed Student unpaired t-test was used to compare unstimulated saliva flow rate and PTH levels between case and control groups. The Spearman correlation analysis was used to identify any correlation between XI score and the salivary components. p less than 0.05 was considered statistically significant (Table 3).

RESULTS

Student's unpaired t-test showed that there was a significant difference between the case and control groups concerning unstimulated whole salivary flow rate (ml/min). It was lower in the case than in the control group ($p = 0.001$) (Fig. 1A).

The mean unstimulated whole saliva concentration of PTH has been shown in Fig. 1B. There was a significant difference in saliva PTH concentration between the groups. It was higher in the case group than in the control group ($p = 0.001$).

Spearman correlation coefficient was also performed to see if any relationship existed between severity of xerostomia (XI score) and salivary flow rate or concentration of PTH. XI score correlated significantly with saliva PTH ($r = 0.688$; $p = 0.001$) and flow rate ($r = -0.529$; $p = 0.001$).

DISCUSSION

Xerostomia is a major complaint for many elderly individuals and is strongly associated with the menopause,²⁰ but the exact mechanisms that mediate the sensation in these women have not been firmly established. In this study, the

relationships between xerostomia and unstimulated saliva PTH and also flow rate levels in postmenopausal women were investigated, and we found that concentration of unstimulated whole saliva PTH in women with xerostomia and saliva flow rate in healthy individuals were significantly higher. Our data also indicated that severity of xerostomia significantly correlates with concentration of unstimulated saliva PTH level (positively) and with flow rate (negatively) in postmenopausal women.

Our results showed that unstimulated salivary flow rate was significantly lower in postmenopausal women with xerostomia in comparison with the women without xerostomia, which was in agreement with other studies.^{12,13,21} There was also a significant negative correlation between unstimulated saliva flow rate and xerostomia in postmenopausal women. It has been indicated that a reduced unstimulated salivary flow and subjective oral dryness are associated with age and the female gender.²² As flow rate lower than 0.1 ml/min for unstimulated whole saliva is considered hyposalivation or true oral dryness,²³ the measurements were higher than the lower limit of normal flow rate and could not be considered as true hyposalivation. In addition, xerostomia can occur in spite of the existence of correct glandular function and normal salivary flow rates²⁴ and the mean onset of xerostomia occurs when the total salivary flow rate is reduced to just less than 50% of normal.²⁵ It can be concluded that postmenopausal women with dry mouth feeling suffer from reduced salivary flow rate in unstimulated conditions.

Our data showed that patients with sensation of xerostomia had significantly more concentration of unstimulated whole saliva PTH. There was also a significant positive correlation between unstimulated saliva PTH levels and xerostomia in postmenopausal women. That is consistent with our previous study about serum and stimulated saliva PTH in postmenopausal women.¹⁰ It has been shown that serum level of PTH increases with ageing and is greater in elderly than in young adults.^{15,26} In addition, salivary glands serve as target organs for parathyroid hormone action.¹⁵ Therefore, it is possible that PTH may also be a cause in incidence of xerostomia in postmenopausal women.

It has been demonstrated that serum and saliva 17β -estradiol and progesterone levels are significantly lower in patients with xerostomia, compared with control individuals in postmenopausal women.^{9,13} Furthermore, it has been shown that the composition of saliva in postmenopausal women is estrogen-dependent.²⁷ In addition, the concentration of saliva calcium is higher and bone mineral density is lower in these patients.^{10,16,17} A decrease in female hormones, especially 17β -estradiol, suppresses intestinal absorption of calcium, which leads to elevated concentrations of serum PTH and enhanced bone

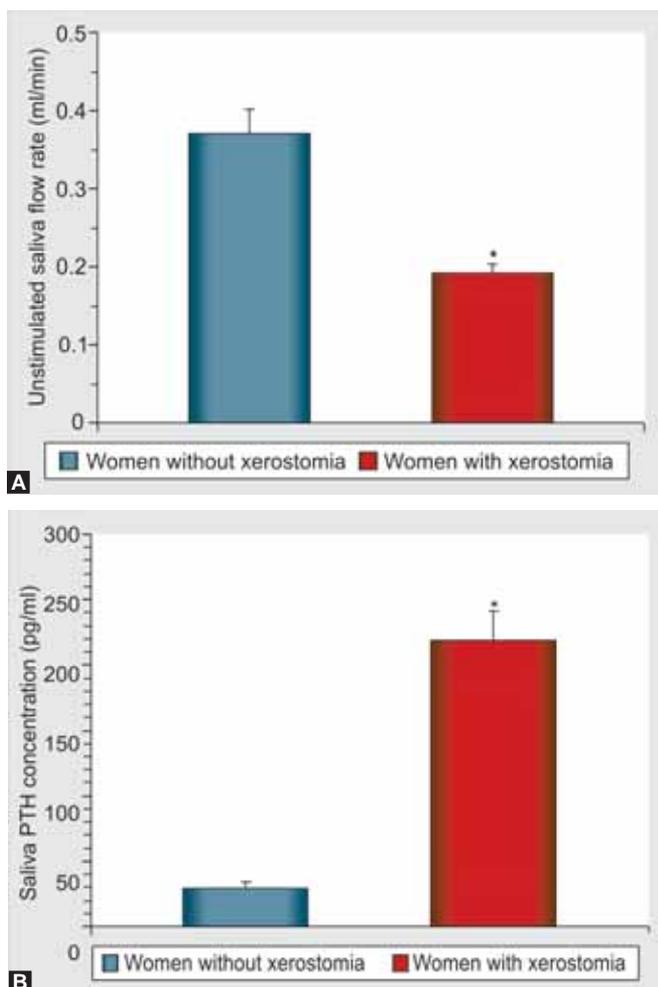


Fig. 1: Unstimulated whole saliva (A) flow rate and (B) concentration of parathyroid hormone (PTH) in postmenopausal women. Data are expressed as mean \pm SEM (* $p < 0.05$)

resorption²⁸ and may increase saliva PTH level. Therefore, postmenopausal women with xerostomia have been considered at risk of osteoporosis.¹⁷

Our research had not planned for day-to-day collection of saliva sample, because we anticipated and experienced resistance from the study participants, so we took only one sample. There were other limitations to this study, e.g. this was a cross-sectional study and longitudinal studies may find similar or different results.

CONCLUSION

Xerostomia severity correlated positively with unstimulated whole saliva PTH in postmenopausal women. Thus, salivary PTH level appears associated with xerostomia and menopause.

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