Relationship of stimulated saliva 17β-estradiol and oral dryness feeling in menopause

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Objectives: The aim of this study was to compare stimulated whole saliva 17β-estradiol of menopausal women with/without oral dryness (OD) feeling, and evaluate the relationship between saliva 17β-estradiol and severity of OD feeling.

Methods: A case-control study was carried out in 76 selected menopausal women aged 41–77 years with or without OD feeling (38 as case and 38 as control) conducted at the Clinic of Oral Medicine, Tehran university of medical sciences. Paraffin-stimulated saliva samples were obtained by expectoration. Xerostomia inventory (XI) score was used as an index of OD feeling severity. The saliva 17β-estradiol concentration was measured by ELISA. Statistical analysis of Student’s t-test and Spearman correlation was used.

Results: No significant difference was found in stimulated whole saliva flow rate between the two groups, but the mean concentration and output of saliva 17β-estradiol were significantly lower in case than control. There was significant negative correlation between XI score and stimulated whole saliva concentration ($r = -0.391, P = 0.004$) and output ($r = -0.302, P = 0.002$) of 17β-estradiol in menopausal women.

Conclusions: It seems that there is a negative correlation between OD feeling severity and stimulated whole saliva 17β-estradiol in menopausal women.

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1. Introduction

Menopause is a physiological process typically occurring in the fifth decade of life in women, involving permanent cessation of menstruation [1]. It is the result of irreversible changes in the hormonal and reproductive functions of the ovaries. Menopause is accompanied by physical changes in the oral cavity [2]. Major oral symptoms of menopause are xerostomia and burning mouth [1].

Oral dryness feeling or xerostomia is a major complaint for many elderly individuals; it is a subjective sensation, and does not reflect a dry mouth in up to one third of cases. It is associated with an unpleasant feeling in the mouth and throat [3]. This complaint is more prevalent in menopausal women on medication and is quite common also in those without disease or drug usage, unrelated to lowered salivary flow rates [4–6].

Sex steroid hormones appear to play a significant role in the physiology of the human oral cavity. It seems that oral soft tissues are sensitive to changes in female sex steroid blood levels. The decrease in estrogen levels during menopause is thought to affect the oral epithelial maturation process, leading to thin and atrophic epithelium [7]. It has been shown that hormone replacement therapy can relieve oral discomfort in menopausal women, further suggesting a role for female sex hormones in the maintenance of oral tissues [8]. Previous studies have shown that ERβ is the predominant estrogen receptors subtype in the human oral epithelium and salivary glands. Estrogens may directly regulate the physiology of oral tissues by binding to the ERβ subtype [9].

The purpose of this study was to evaluate whether saliva 17β-estradiol levels correlate with severity of OD feeling, and to compare stimulated whole saliva 17β-estradiol of menopausal women with/without oral dryness (OD) feeling.

2. Subjects and methods

2.1. Subjects

The Ethics Committee of TUMS, Iran, approved the study protocol. Informed consent was obtained from all participants.

One hundred and twenty menopausal women were asked to participate in a case-control study, conducted at the Clinic of Oral Medicine, Tehran University of Medical Sciences, between 2007 and 2008. The participants were aged between 41 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 >24), patients with systemic diseases (including Sjögren’s syndrome), oral candidiasis or with a bad oral health condition and periodontal disease were excluded. Of the 120 potential participants 24 were excluded from the study, based on these criteria (16 were eliminated due to periodontal pockets more than 3 mm, 6 were excluded for obesity and 2 for smoking). The remaining numbers were asked to answer a questionnaire with a list of symptoms associated with xerostomia [10] (Table 1). Thirty-eight answered affirmatively to at least one of the questions related to xerostomia and formed the case group (mean ages ± S.D. 56.53 ± 7.27 years). In fact, all the participants in the case group answered affirmatively at least three of the questions. 38 who did not answer affirmatively to any of the questions in Table 1 formed the control group (mean ages ± S.D. 58.24 ± 6.21 years). The remaining 18 were eliminated in order to match case and control groups on the basis of age and duration of menopause.

Each participant also answered another questionnaire to assess the severity of xerostomia (Table 2). Xerostomia inventory (XI) score was determined as the severity of dry mouth feeling [11]. The score of responses to all 11 questions were added and came to a XI score for each individual. The responses to each question were marked as follows: 1 = never, 2 = hardly, 3 = occasionally, 4 = fairly often and 5 = very often. The range of XI score was 11 (11 × 1) to 55 (11 × 5).

### 2.2. Saliva collection

Stimulated whole saliva was collected under resting conditions in a quiet room, between 9 a.m. and 12 p.m., at least 2 h after the last intake of food or drink. At the beginning and the end of saliva collection, the time was recorded. For pre-stimulation, the women chewed a piece of paraffin of standard size. After 60 s of pre-stimulation, the participants were asked to swallow the saliva present in the mouth. Thereafter, whole saliva, stimulated by the same piece of paraffin, was collected for about 5 min into a pre-weighed, dry, de-ionized 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⁻¹, which is almost equivalent to ml min⁻¹ [12]. 17β-Estradiol output was calculated as its saliva concentration (pg ml⁻¹) multiplied by saliva flow rate (ml min⁻¹).

The samples were clarified by centrifugation (2000 g, 10 min) and immediately stored at −70 °C for later determination of 17β-estradiol concentration.

### 2.3. Analysis of saliva

17β-Estradiol concentration was analyzed by ELISA technology using commercially available kits (DRG Instruments GmbH, Germany).

### 2.4. Statistical analysis

For statistical analysis, the data are presented as a mean ± S.E.M. The two-tailed Student’s unpaired t-test was used to compare saliva flow rate, and saliva concentration and output of 17β-estradiol between case and control groups.

The Spearman correlation analysis was used to identify any correlation between XI score and the salivary components. P < 0.05 was considered statistically significant.

### 3. Results

The mean stimulated whole saliva flow rate and mean concentrations and output of 17β-estradiol in saliva are shown in Fig. 1. No significant difference was found between case (0.37 ± 0.03) and control (0.35 ± 0.03) groups regarding salivary flow rate. Student’s t-test showed that there were significant differences in stimulated whole saliva 17β-estradiol concentration and output between the groups. The 17β-estradiol concentration (pg ml⁻¹) was lower in the case group (17.60 ± 1.54) than in the control group (21.64 ± 1.12), P = 0.036. The individuals in the case group also showed a lower 17β-estradiol output (pg min⁻¹) (5.98 ± 0.67) than the individuals in control group (8.56 ± 0.95, P = 0.031).

Spearman correlations were performed to see if any relationship existed between severity of oral dry feeling (XI score) and salivary flow rate, saliva concentration or output of 17β-estradiol (Fig. 1). There was a significant negative correlation between XI score and concentration (r = −0.391, P = 0.004; Fig. 1a) or output (r = −0.302, P = 0.002; Fig. 1b) of stimulated whole saliva 17β-estradiol, no significant correlation with flow rate (r = −0.073; P = 0.54).

### 4. Discussion

Menopause is the consequence of hormonal changes that produce a series of general manifestations that have become increasingly important as a result of the increased female life expectancy in the industrialized world; indeed, such manifestations are observed throughout the last third of the female lifetime. Oral discomforts like dryness have been reported to be strongly associated with the menopause [3,13–16]. In this study, relationship between saliva 17β-estradiol and OD feeling in menopausal women was investigated.

Our data indicated that there was no significant difference in stimulated whole saliva flow rate between menopausal women, either with or without OD feeling. This is consistent with studies by other investigators [4–6,17]. Our results further showed that there was no significant correlation between stimulated flow rate and severity of oral dryness feeling in menopausal women. Therefore,
Fig. 1. Relationship of oral dry feeling severity (XI score) and concentrations (a), or output (b) of stimulated whole saliva 17β-estradiol (E2) in menopausal women as determined by Spearman correlation coefficient. *P < 0.05.

the sensation of dry mouth may not be clearly associated with stimulated whole salivary flow rate.

The female hormone estrogen influences many physiological and psychological functions. The composition of saliva in menopausal women is estrogen dependent [18] and hormonal changes may affect the composition of saliva. Hormonal replacement therapy has been reported to reduce the complaints of dry mouth feeling resulting in improved oral wellbeing [7,8,16–18]. Some evidence suggests a positive relationship between ovarian hormone modifications and changes in the oral mucosa [7]. It seems that steroid hormone withdrawal might be a cause in incidence of OD feeling in menopausal women. The results of this study support the observation by many authors of an association between oral discomfort and symptoms of estrogen deficiency seen in menopausal women.

Our data showed that there were significant differences in stimulated whole saliva 17β-estradiol concentration and output between case and control groups. Data from the present study show that the mean concentration and output of stimulated whole saliva 17β-estradiol are significantly lower in patients with OD feeling compared with the control group. Our data also indicated that there were significant negative correlations between saliva 17β-estradiol concentration or output and severity of oral dryness feeling. Therefore, it is possible that there is a relationship between saliva 17β-estradiol level and OD feeling in menopausal women. This study, to our knowledge, is the first to show an association between a subjective complaint of dry mouth and a decrease in stimulated saliva 17β-estradiol of menopausal women.

5. Conclusion

It seems that the level of salivary 17β-estradiol concentration and output may be lower in menopausal women with OD feeling than in controls and there is a negative correlation between OD feeling severity and stimulated whole saliva 17β-estradiol.

References