

Serum 17 β -estradiol and oral dryness feeling in menopause

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ABSTRACT

The aim of this study was to compare serum 17 β -estradiol of menopausal women with/without Oral Dryness (OD) feeling, and evaluate the relationship between serum 17 β -estradiol and severity of OD feeling. A case-control study was carried out on 70 selected menopausal women aged 40 - 77 years with or without OD feeling (35 as case, 35 as control) conducted at the Clinic of Oral Medicine, Tehran University of Medical Sciences. Xerostomia inventory (XI) score was used as an index of OD feeling severity. The serum 17 β -estradiol concentration was measured by an enzyme immunoassay kit (ELISA). Statistical analysis of Student's t-test and Spearman correlation coefficient was used. The mean serum concentration of 17 β -estradiol was significantly lower in case than control. There was a significant negative correlation between XI score and concentration of 17 β -estradiol in menopausal women ($r = -0.311$, $P = 0.004$). It seems that there is a negatively slight correlation between OD feeling severity and serum 17 β -estradiol in menopausal women.

Keywords: Menopause; Oral Dryness Feeling; 17 β -Estradiol; Serum

1. INTRODUCTION

Life expectancy for women has increased significantly during the last decade, and most women spend one third of their lives after the menopause. Menopause is a normal developmental stage in a woman's life, marking the permanent cessation of menstruation [1]. It is the result of irreversible changes in the hormonal and reproductive functions of the ovaries [2]. It is a retrospective diagnosis usually made after 12 months of amenorrhea. Menopause

is accompanied by a number of characteristic physical changes; some of which occur in the oral cavity [3].

Oral dryness feeling or xerostomia is a subjective sensation. It is associated with an unpleasant feeling in the mouth and throat [4]. 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 [5-8].

It has been suggested that changes in estrogen and progesterone play a major role in the development of some forms of gingival disease [9]. 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 [10]. 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 [11]. Our previous study has also shown that the level of stimulated salivary 17 β -estradiol concentration is lower in menopausal women with OD feeling, and there is a negative correlation between OD feeling severity and stimulated whole saliva 17 β -estradiol [5].

After complain of caries and periodontal problems, the most complain of people who referred to oral medicine department of Tehran University of Medical Sciences is dry mouth feeling. To relive their problem, consecutively studies have been designed. The purpose of this study was to evaluate whether the serum 17 β -estradiol level correlates with severity of OD feeling, and to compare serum 17 β -estradiol of menopausal women with/without OD feeling.

2. METHODS AND MATERIALS

2.1. Subjects

The Ethics Committee of Tehran University of Medi-

cal Sciences (TUMS), Iran, approved the study protocol. Informed consent was obtained from all participants.

A total of 105 menopausal women were asked to participate in a case-control study, conducted at the Clinic of Oral Medicine, TUMS. The participants were aged between 40 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 105 potential participants, 20 were excluded from the study based on these criteria (13 were eliminated owing to periodontal pocket depths more than 3 mm in multiple sites, 5 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 five answered affirmatively to at least one of the questions related to xerostomia [12,13], and formed the case group; in fact, all the participants in the case group answered affirmatively to at least 3 of the questions. Thirty-five who did not answer affirmatively to any of the questions in **Table 1** formed the control group. The remaining 15 were excluded in order to match case and control groups on the basis of age and duration of menopause. The 15 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 [14]. 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).

2.2. Sample Collection

Stimulated and unstimulated whole saliva were collected under resting conditions in a quiet room between 9 a.m. and 12 p.m. (midday), and at least 2 hours after the last intake of food or drink. Unstimulated salivary samples were obtained by expectoration in the absence of chewing movements. For pre-stimulation, the women chewed a piece of paraffin of standard size. After 60 seconds 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 over a period of about 5 minutes. Stimulated and unstimulated whole saliva were collected into a pre-weighed and dry plastic tube. By subtracting the empty tube weight from the saliva filled one, saliva sample weight was determined to calculate the salivary

Table 1. Questionnaire used for selection of subjects with xerostomia (oral dryness feeling).

Serial Number	Questions
1	Does your mouth feel dry when eating a meal?
2	Do you have difficulties 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 and no

Table 2. The xerostomia inventory (XI).

Serial Number	Questions
1	I sip liquids to help swallow food.
2	My mouth feels dry when eating a meal.
3	I get up at night to drink.
4	My mouth feels dry.
5	I have difficulty in eating dry foods.
6	I suck sweets or cough lozenges to relieve dry mouth.
7	I have difficulties swallowing certain foods.
8	The skin of my face feels dry.
9	My eyes feel dry.
10	My lips feel dry.
11	The inside of my nose feels dry.

Response options: Never (scoring 1), Hardly (2), Occasionally (3), Fairly often (4), Very often (5)

flow rate. The flow rate was calculated in grams per minute, which is almost equivalent to milliliters per minute [6].

Venous blood was collected from each participant in the morning under resting conditions in a quiet room, between 9 a.m. and 12 p.m. The specimens were obtained by venipuncture, collected in 10 ml glass vacuum tubes without additive, and allowed to clot. The blood was then centrifuged (2000 g, 10 min) and the serum were separated and stored at -70°C for later determination of 17β -estradiol concentration.

2.3. 17 β -Estradiol Concentration Assays

Serum 17 β -estradiol concentration was analyzed by ELISA technology using commercially available kits (DRG Instruments GmbH, Germany). Wells coated with anti-estradiol polyclonal rabbit antibody. Standards were: 0; 25; 100; 250; 500; 1000 and 2000 pg/ml. the OD was read at 450 nm with microtiterplate reader. The range of the assay was between 0 - 2000 pg/ml.

2.4. Statistical Analysis

For statistical analysis, the data are presented as a mean \pm SEM. The 2-tailed Student unpaired *t* test was used to compare serum 17 β -estradiol level between case and control groups.

The Spearman correlation analysis was used to identify any correlation between XI score and the serum 17 β -estradiol. *P* less than 0.05 was considered statistically significant.

3. RESULTS

The characteristics of case and control participants are shown in **Table 3**. There were no significant differences between two groups in BMI, age or years after menopause.

The Student's unpaired *t* test showed that there was a significant difference between the groups concerning unstimulated whole salivary flow rate. It was lower in the case (0.26 ± 0.12) than in the control (0.33 ± 0.01 ; *P* = 0.001) groups. However, No significant difference was found between the case (0.33 ± 0.02) and control (0.37 ± 0.01 ; *P* = 0.07) groups regarding stimulated saliva flow rate.

Student *t* test showed that there was a significant difference in serum concentration of 17 β -estradiol between the groups (**Figure 1**). It was significantly lower in case compared with the control (*P* = 0.01). Coefficient of variations (CV) was 0.30 for control group and 0.41 for case group.

Spearman correlations were performed to see if relationship existed between severity of OD feeling (XI score) and serum 17 β -estradiol. There was a negative significant correlation between XI score and serum 17 β -estradiol concentration ($r = -0.311$, *P* = 0.004).

4. DISCUSSIONS

Oral dryness is a major complaint for many elderly individuals, and is strongly associated with the menopause [6,15,16]. The exact mechanisms that cause sensation of OD in menopausal women have not been firmly established. However, there are reports on amelioration of these symptoms by estrogen treatment [8]. In this

Table 3. Clinical characteristics of menopausal women with/without oral dryness (OD) feeling.

Clinical characteristics (mean \pm S.D.)	Women without OD feeling	Women with OD feeling
Age (years)	56.55 \pm 6.31	55.87 \pm 6.55
Years-since-menopause	10.0 \pm 6.9	10.1 \pm 7.6
Body mass index (BMI, Kg/m ²)	24.2 \pm 2.5	24.8 \pm 2.1
Xerostomia inventory (XI) score	12.21 \pm 1.2	30.24 \pm 6.14



Figure 1. Comparison of serum concentration of 17 β -estradiol (means \pm SEM) between menopausal women with oral dryness feeling and healthy individuals as determined by unpaired student's *t*-test, **P* = 0.001.

study, the relationship between serum 17 β -estradiol level and OD in menopausal women was investigated.

Our data showed that serum 17 β -estradiol concentration is significantly lower in menopausal women suffering from oral dryness. It also appears that OD severity correlates with serum 17 β -estradiol concentration. It has been shown that the composition of saliva in menopausal women is estrogen dependent [17]. In addition, hormonal replacement therapy has been reported to reduce the complaints of dry mouth feeling resulting in improved oral wellbeing. On the other hand, oral discomfort is a common symptom of menopause, it often occurs without overt clinical signs, and it frequently resolves during appropriate hormone replacement therapy [8,15,16,18, 19]. It seems that a positive relationship exists between ovarian hormone modifications and changes in the oral mucosa, and sex hormone withdrawal might be a cause in incidence of oral dryness feeling in menopausal women [10]. Gingival tissue is known to be sensitive to changes in the hormonal balance, especially to changes in female sex steroids [9]. It has been suggested that changes in hormone levels and types (predominantly

estrogen and progesterone) play a great role in the development of some forms of gingival or periodontal disease [20]. Clinical reports of gingival enlargement concurrent with the onset of puberty and during pregnancy, or gingival atrophy and surface desquamation during menopause, have led some investigators to regard the gingiva as a secondary target organ for the direct action of female sex hormones [9]. Also, human gingiva has been showed to metabolize estrogens [21].

Consistent with our previous studies on stimulated whole salivary 17 β -estradiol [5], and serum and saliva progesterone [22] the results showed that subjects with OD had significantly lower serum 17 β -estradiol concentration in menopausal women with OD feeling compared with the control group. In addition, a negative correlation between serum 17 β -estradiol level and severity of OD in menopausal women was also observed. Therefore, it is possible that there is a relationship between serum 17 β -estradiol level and OD feeling in menopausal women.

We also found that unstimulated, but not stimulated whole saliva flow rate, was significantly lower in menopausal women with OD feeling, in comparison with women without OD feeling, which was consistent with our previous studies [5,6,22,23]. It can be concluded that menopausal women with OD feeling suffer from reduced salivary flow rate in unstimulated conditions. However, it may alleviate in a stimulated state.

Our research had not planned for day-to-day collection of serum sample, because we anticipated and experienced resistance from the study participants especially in the control group, 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.

5. CONCLUSIONS

It seems that there is a slight negative correlation between OD feeling severity and serum 17 β -estradiol in menopausal women.

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