Evaluation of salivary calcium and salivary parathyroid levels in postmenopausal women with and without oral dryness

Balwinder Singh, Soheyl Sheikh, Shambulingappa Pallagatti, Kirandeep Kaur, Ravinder Sohi

Abstract

Objective: The primary objective of this study is to estimate and secondary objective is to compare the salivary calcium levels, salivary parathyroid hormone (PTH) levels in postmenopausal women with and without oral dryness (OD).

Materials and Methods: A case-control study was carried out on 80 selected postmenopausal women. Salivary calcium concentrations were assessed through Semi Autoanalyzer by Arsenazo III reaction. The salivary PTH concentration was measured by the enzyme linked immunosorbent assay. Severity of OD was assessed by a questionnaire through which the xerostomia inventory (XI) score could be measured. Statistical analysis of Student's t-test, Mann-Whitney test and Pearson's correlation was used.

Results: There was a significant difference in mean values of both salivary calcium concentration and XI score in postmenopausal women with/without OD (P < 0.001). No statistically significant difference (P > 0.05) was found in salivary parathyroid levels in postmenopausal women in both groups. A positive correlation was found between the salivary calcium concentration and XI score in both case and control groups (P < 0.05).

Conclusion: Severity of OD in postmenopausal women is associated with the high levels of salivary calcium. However, the correlation of severity of OD with PTH could not be established.

Keywords: Oral dryness, parathyroid hormone, post-menopause, salivary calcium

Introduction

Oral cavity reflects the state of systemic health more frequently than other parts of the body. In the oral cavity, the qualitative and quantitative assessment of saliva serves as an important tool for diagnosis of certain disorders and monitoring the evolution of certain pathologies even during the normal physiological functioning of the body.

Menopause is a physiological process occurring due to decrease in levels of estrogens, in the fifth decade of life in women, involving permanent cessation of menstruation. Menopause is accompanied by physiological and sensorial oral changes in select individuals. The prevalence of oral symptoms was found to be significantly greater in menopausal women (43%) than in premenopausal females (6%).[1]

Of concern to the dental professional is that menopause causes oral conditions such as oral dryness (OD) and burning mouth syndrome. OD 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.[2] 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.[3-5]

Other less common menopause-associated symptoms include bad or altered taste, viscous saliva, senile atrophic gingivitis and mucosal disorders such as lichen planus, benign mucosal pemphigoid and Sjogren's syndrome.[6] Furthermore, menopause induced osteoporosis may lead to loss of alveolar bone height.

The parathyroid hormone (PTH) and calcium plays a considerable role in the physiology of human oral cavity, functioning together in a tightly regulated system; alterations in the level of one of these chemicals have significant effects on the levels of the other. PTH is an important hormone in calcium turnover its main function being the maintenance of constant Ca²⁺ levels in extracellular fluids. It seems that oral soft-tissues are sensitive to changes in calcium and parathyroid salivary levels.[7] The parathyroid glands can also suffer alterations due to a lack of estrogen.[8]
The present study was carried out with the aim to assess and also to compare the salivary calcium and salivary PTH levels in postmenopausal women with and without OD. Further on the obtained values were correlated with the severity of OD in postmenopausal women having OD.

**Materials and Methods**

The study protocol was approved by the ethical committee of MM University, Ambala, India. The present clinical study consisted of 80 postmenopausal women aged between 45 and 75 years who reported to the Department of Oral Medicine and Radiology. Written informed consent was obtained and the participants were subjected to a detailed case history. Inclusion criterion consisted of those postmenopausal women in whom a menstrual cycle had not occurred for at least 24 months, and were not on any kind of medication at the time of the study. Patients with systemic diseases such as Sjogren’s syndrome, oral candidiasis, diabetes and patients with poor oral hygiene and periodontitis were excluded from this study. Patients with poor oral hygiene and periodontitis were eliminated by intraoral clinical examination, showing periodontal pocket depths more than 3 mm in multiple sites.

A questionnaire comprising of 10 questions was prepared with a list of symptoms related to xerostomia [Table 1]. A total of 40 patients were answered affirmatively to at least one of the questions related to xerostomia and formed the case group; in fact all the participants in the case group answered affirmatively to at least three of the questions. A total of 40 patients who did not answer affirmatively to any of these questions in Table 1 formed the control group. Each participant was then given another questionnaire so that the severity of dry mouth feeling. The scores of responses were added to provide a XI score for each individual. The minimum possible score was 11 and the maximum possible score was 55 for each individual.

**Saliva collection**

Whole stimulated saliva was collected under resting condition in a quiet room between 8 am and 11 am at least 6 h after last intake of food or drink. Patients were asked to chew a standard 1 g piece of paraffin wax. After 1 min of chewing, saliva was collected for the next 5 min. The patients were asked to expectorate whole saliva into a labeled sterile plastic container. The samples were immediately transferred to the biochemistry research laboratory and were centrifuged at 15,000 rpm for 10 min in order to remove particulate materials. The supernatants, thus obtained were stored for a maximum period of 4-6 h at -20°C, which were used for analysis of calcium.

**Biochemical analysis**

Salivary calcium levels were assessed with the method of Arsenazo III reaction. The PTH levels were assessed by the enzyme-linked immunosorbent assay (ELISA) method. Salivary calcium was estimated by using Liquix Calcium Kit (Erba) and Semi Autoanalyser (Spectra Lab, India). Estimation of salivary PTH was performed by using Parathyroid kit (Biomerica, USA) and ELISA Reader (Mind Ray).

**Statistical analysis**

The data collected was first visualized to confirm their normal distribution. The resulting data was analyzed using SPSS version 10 and Epi-Info 6.04 software. Following this, descriptive statistics including the mean values and standard deviations, 95% of the confidence intervals, interquartile ranges (25th and 75th percentiles) were calculated for each variable. Two tailed Students unpaired “t”-test and Mann-Whitney test were used to determine whether a significant difference exists between means of two sets of observations (case and control group). The Pearson’s correlation was used to check whether correlation existed between XI score and the salivary components. P < 0.05 was considered to be statistically significant.

**Results**

In the present study, the mean age for case group was 60.4 years and for the control group was 57.9 years with no statistically significant difference between the two (P > 0.05).

The mean value of calcium in saliva was calculated to be 3.06 mg/dl in the case group and 1.96 mg/dl in the control group with a highly significant difference (P < 0.001) between the two groups [Table 3]. The mean value of XI scores in case group was 22.10 and in the control group was 12.90, which showed a highly significant difference (P < 0.001) [Table 3]. Furthermore, there was a positive and significant (P < 0.05) correlation between XI score and salivary calcium levels in both groups [Table 4]. Thus, it showed that XI score and salivary calcium are dependent variables, where increase in one shows subsequent increase in other.

The mean salivary PTH level estimated in the case group was 10.19 pg/ml and in the control group was 8.59 pg/ml, with no statistically significant difference (P > 0.05) [Table 3]. Furthermore, no significant correlation (P > 0.05) was found between the XI score and salivary parathyroid levels in both groups [Table 4].

**Discussion**

OD and burning mouth is an increasingly common problem in the aging population and has remained an enigma for the treating clinician, because visible pathologic lesions or processes are usually not evident. An increased incidence of dry mouth (xerostomia), burning mouth syndrome, disorders such as lichen planus, benign pemphigoid and as well as a debated rise in the prevalence of periodontal disease is noticed as an oral manifestation of menopause. [9]
Singh, et al.: Oral dryness with salivary parathyroid hormone and salivary calcium

In our study, the severity of OD (XI score) was more in postmenopausal women of the case group, when compared with the control group ($P < 0.001$). These findings were in concordance with studies done by Agha-Hosseini et al.\cite{3,12} who reported similar findings.

The previous studies\cite{3,6} and the high XI score in postmenopausal women with OD in the current study points toward the possible variation in quantitative changes in saliva, which may lead to the high prevalence of oral symptoms.

The high prevalence of oral discomfort in women at menopause was also reported by Wardrop et al.\cite{13}. These complaints might be due to hormonal alterations taking place at menopause causing vasomotor, neurological and psychological changes.

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of saliva in menopausal women is estrogen dependent. In their study, they found that the concentration of calcium was low during ovulation when estrogen level was high and appeared to be lower during the pregnancy than in labor. They also stated that hormone replacement therapy reduced OD resulting in improved oral well-being. Similar findings were also reported by Volpe et al. who in their study reported improvement of oral symptoms in menopausal women with estradiol-based treatment.

The possible mechanism is that low level of estrogen in postmenopausal women reduces calcium absorption in intestine, leading to decreased serum calcium level resulting in increased serum PTH hormone level. The increased serum PTH level removes calcium from bones by its resorption and increases its level in the serum. However, calcium level is regulated by many factors, which prevents the serum calcium level from increasing significantly, therefore it is possible that elevated calcium is excreted in saliva or urine. Wardrop et al. and Forabosco et al. also reported that menopausal women with oral discomfort were relieved of symptoms after systemic hormone replacement therapy, supporting the fact that there is a correlation between oral discomfort and level of hormones in menopausal women.

In a longitudinal study, Sewón et al. suggested that salivary calcium concentration decreases in stimulated saliva when hormone replacement therapy was initiated in menopausal women. They concluded that this may indicate that individual salivary calcium concentration is modified and/or regulated by factors other than salivary flow.

With estrogen deficiency causing calcium level to oscillate downwards, it also causes the PTH levels to go up. As PTH rises in response to hypocalcemia, it will tend to restore eucalcemia by reduced renal calcium excretion and by its stimulation of renal conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D. It also increases intestinal calcium absorption.

The PTH causes mobilization of calcium from bones and causes weakness of bones, thus making the patient prone to osteoporosis. Furthermore, the lack of estradiol causes the glands to become occasionally hyperactive, wherefore contributing to mobilization of calcium and phosphorus deposits in osteoporosis.

Agha-Hosseini et al. in his study found a significant increase in salivary PTH levels between the case and control group. Even in the present study, the patients with OD had increased levels of salivary PTH levels when compared to the control group, although not statistically significant.

Though previous studies have shown that to compensate for a reduced serum calcium level in menopausal women a corresponding increase in serum PTH level has been noted. In the present study, increase levels of salivary PTH was found in the case group than the control group. However, there was no statistically significant increase in salivary PTH level in menopausal women, which may be due to the fact that salivary PTH was not selectively increased in saliva stressing the need for further evaluation.

In the present study, the severity of OD was also correlated with salivary calcium and PTH levels. A positive correlation ($P < 0.05$) was seen between salivary calcium and XI score which was in agreement with the study done by Agha-Hosseini et al. No correlation was found between the severity of OD and salivary PTH levels, which is in contrast to the findings by Agha-Hosseini et al.

This study highlights the emergence of OD feeling in postmenopausal women in the present scenario as a possible indicator for levels of salivary calcium, salivary PTH and their possible role in maintaining the overall well-being of an individual. Hence, a larger sample size and a long-term assessment in the form of longitudinal studies are needed to further corroborate the findings of the present study. Since the composition of saliva is dependent on estrogen level, further studies are required to ascertain the role of estrogen by comparing calcium and PTH levels and their relationship with OD.

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