

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

BALWINDER SINGH, SOHEYL SHEIKH<sup>1</sup>, SHAMBULINGAPPA PALLAGATTI<sup>1</sup>, KIRANDEEP KAUR<sup>2</sup>, RAVINDER SOHI<sup>1</sup>

## 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%).<sup>[1]</sup>

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.<sup>[2]</sup> 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.<sup>[3-5]</sup>

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.<sup>[6]</sup> 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  $Ca^{2+}$  levels in extra cellular fluids. It seems that oral soft-tissues are sensitive to changes in calcium and parathyroid salivary levels.<sup>[7]</sup> The parathyroid glands can also suffer alterations due to a lack of estrogen.<sup>[8]</sup>

Departments of Oral Medicine and Radiology, and <sup>2</sup>Oral Surgery, SGRD Institute of Dental Sciences and Research, Amritsar, Punjab, <sup>1</sup>M.M. College of Dental Sciences and Research, Mullana, Ambala, Haryana, India.

**Correspondence:** Dr. Balwinder Singh,  
Department of Oral Medicine and Radiology, SGRD Institute of  
Dental Sciences and Research, Amritsar, Punjab, India.  
E-mail: dr.balwindersingh@rediffmail.com

Access this article online	
Quick Response Code: 	Website: <a href="http://www.contempclindent.org">www.contempclindent.org</a>
	DOI: 10.4103/0976-237X.123051

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,<sup>[3]</sup> 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].<sup>[9]</sup> 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 xerostomia could be assessed [Table 2].<sup>[10]</sup> The xerostomia inventory (XI) score was determined as 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.<sup>[11]</sup> 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 (25<sup>th</sup> and 75<sup>th</sup> 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 statistical 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.<sup>[6]</sup>

**Table 1: Questionnaire used for selection of subjects with xerostomia (oral dryness feeling) Torres *et al.***

Questions	Response
Does your mouth feel dry when eating a meal?	Yes/No
Do you have difficulties swallowing any foods?	Yes/No
Do you need to sip liquids to aid in swallowing dry foods?	Yes/No
Does the amount of saliva seem to be reduced in your mouth most of the time?	Yes/No
Does your mouth feel dry at night or on awakening?	Yes/No
Does your mouth feel dry during the day time?	Yes/No
Do you use gum or candy to relieve oral dryness?	Yes/No
Do you usually wake up thirsty at night?	Yes/No
Do you have problems in tasting food?	Yes/No
Does your tongue burn?	Yes/No

**Table 2: The xerostomia inventory (Thomson *et al.*)**

Questions
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 lollies to relieve dry mouth
I have difficulties 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), very often (5); XI: Xerostomia inventory

**Table 3: Comparison of salivary calcium level, salivary PTH level and XI score in the case and control group**

Variables	Mean±SD		Significant (P value)
	Case group (n=40)	Control group (n=40)	
Salivary calcium	3.06±1.2	1.96±0.81	0.000*
Salivary PTH	10.19±14.4	8.59±11.2	0.795
XI score	22.10±4.9	12.9±2.0	0.000*

\*P<0.001 highly significant. SD: Standard deviation; PTH: Parathyroid hormone; XI: Xerostomia inventory

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.*<sup>[3,12]</sup> who reported similar findings.

**Table 4: Correlation of severity of oral dryness with salivary calcium level and PTH level in case and control group**

Group	Variables	Saliva PTH	Saliva calcium	XI score
Case	Saliva PTH			
	Pearson correlation	1	-0.192	0.065
	Significant (2-tailed)		0.236	0.692
	Saliva calcium			
	Pearson correlation	-0.192	1	0.434
	Significant (2-tailed)	0.236		0.005*
Control	XI score			
	Pearson correlation	0.065	0.434	1
	Significant (2-tailed)	0.692	0.005*	
	Saliva PTH			
	Pearson correlation	1	-0.106	-0.089
	Significant (2-tailed)		0.514	0.585
Case	Saliva calcium			
	Pearson correlation	-0.106	1	0.421
	Significant (2-tailed)	0.514		0.007*
	XI score			
	Pearson correlation	-0.089	0.421	1
	Significant (2-tailed)	0.585	0.007*	

\*P<0.05 significant. PTH: Parathyroid hormone; XI: Xerostomia inventory

Borhan-Mojabi<sup>[6]</sup> evaluated salivary flow rate and oral symptoms in menopausal women and concluded that reduced salivary flow rate and a high prevalence of oral symptoms in menopausal women may be related to the hormonal alterations that occur during this period.

The previous studies<sup>[3,6]</sup> 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.*<sup>[13]</sup> These complaints might be due to hormonal alterations taking place at menopause causing vasomotor, neurological and psychological changes

OD may be due to undetermined qualitative changes in the salivary composition, an imbalance between the various salivary glands, or changes in the mucosal sensory receptors.<sup>[14]</sup> OD not only affects the salivary flow, but also leave its impact on the composition of saliva. Our study showed that salivary calcium concentration was significantly more in postmenopausal women with OD when compared to those without OD. The previous studies<sup>[3,12,15,16]</sup> have supported these results and have also shown that the level of estrogen status effects the salivary composition. Leimola-Virtanen *et al.*<sup>[17]</sup> concluded that the composition

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.<sup>[3]</sup> Similar findings were also reported by Volpe *et al.*<sup>[18]</sup> 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.<sup>[12]</sup> Wardrop *et al.*<sup>[13]</sup> and Forabosco *et al.*<sup>[19]</sup> 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.*<sup>[20]</sup> 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.<sup>[21]</sup>

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.<sup>[22]</sup>

Agha-Hosseini *et al.*<sup>[12]</sup> 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<sup>[3,21]</sup> 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.*<sup>[12]</sup> 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.*<sup>[12]</sup>

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.

## References

1. Frutos R, Rodríguez S, Miralles-Jorda L, Machuca G. Oral manifestations and dental treatment in menopause. *Med Oral* 2002;7:26-30, 31.
2. Nederfors T. Xerostomia and hyposalivation. *Adv Dent Res* 2000;14:48-56.
3. Agha-Hosseini F, Mirzaei-Dizgah I, Moghaddam PP, Akrad ZT. Stimulated whole salivary flow rate and composition in menopausal women with oral dryness feeling. *Oral Dis* 2007;13:320-3.
4. Ben Aryeh H, Gottlieb I, Ish-Shalom S, David A, Szargel H, Laufer D. Oral complaints related to menopause. *Maturitas* 1996;24:185-9.
5. Tarkkila L, Linna M, Tiitinen A, Lindqvist C, Meurman JH. Oral symptoms at menopause – The role of hormone replacement therapy. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001;92:276-80.
6. Borhan-Mojabi K, Esfahani M, Jahani HH. Evaluation of unstimulated salivary flow rate and oral symptoms in menopausal women. *J Dent* 2007;4:103-6.
7. Karen F. The effects and interactions of vitamin D deficiency calcium and parathyroid hormone on physical concerns in the elderly: A review. *J Geriatr Phys Ther* 2004;27:30-4.
8. Pérez-López FR. Vitamin D and its implications for musculoskeletal health in women: An update. *Maturitas* 2007;58:117-37.
9. Torres SR, Peixoto CB, Caldas DM, Silva EB, Akiti T, Nucci M, *et al.* Relationship between salivary flow rates and Candida counts in subjects with xerostomia. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002;93:149-54.
10. Thomson WM, Williams SM. Further testing of the xerostomia inventory. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;89:46-50.
11. Bauer PJ. Affinity and stoichiometry of calcium binding by arsenazo III. *Anal Biochem* 1981;110:61-72.
12. Agha-Hosseini F, Mirzaei-Dizgah I, Mansourian A, Zabihi-Akhtechi G.

- Serum and stimulated whole saliva parathyroid hormone in menopausal women with oral dry feeling. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009;107:806-10.
13. Wardrop RW, Hailes J, Burger H, Reade PC. Oral discomfort at menopause. *Oral Surg Oral Med Oral Pathol* 1989;67:535-40.
  14. Bhat S, Hegde S, Sujatha D. A study on evaluation of the effect of menopause on saliva and dental health. *J Adv Dent Res* 2010;1:33-6.
  15. Singh R, Pallagatti S, Sheikh S, Singh B, Arora G, Aggarwal A. Correlation of serum oestrogen with salivary calcium in post-menopausal women with and without oral dryness feeling. *Gerodontology* 2012;29:125-9.
  16. Mirzaii-Dizgah I, Agha-Hosseini F. Stimulated and unstimulated saliva progesterone in menopausal women with oral dryness feeling. *Clin Oral Investig* 2011;15:859-62.
  17. Leimola-Virtanen R, Helenius H, Laine M. Hormone replacement therapy and some salivary antimicrobial factors in post- and perimenopausal women. *Maturitas* 1997;27:145-51.
  18. Volpe A, Lucenti V, Forabosco A, Boselli F, Latessa AM, Pozzo P, *et al.* Oral discomfort and hormone replacement therapy in the post-menopause. *Maturitas* 1991;13:1-5.
  19. Forabosco A, Criscuolo M, Coukos G, Uccelli E, Weinstein R, Spinato S, *et al.* Efficacy of hormone replacement therapy in postmenopausal women with oral discomfort. *Oral Surg Oral Med Oral Pathol* 1992;73:570-4.
  20. Sewón L, Laine M, Karjalainen S, Leimola-Virtanen R, Hiidenkari T, Helenius H. The effect of hormone replacement therapy on salivary calcium concentrations in menopausal women. *Arch Oral Biol* 2000;45:201-6.
  21. Sneve M, Emaus N, Joakimsen RM, Jorde R. The association between serum parathyroid hormone and bone mineral density, and the impact of smoking: The Tromso Study. *Eur J Endocrinol* 2008;158:401-9.
  22. Slavkin HC. Building a better mousetrap: Toward an understanding of osteoporosis. *J Am Dent Assoc* 1999;130:1632-6.

**How to cite this article:** Singh B, Sheikh S, Pallagatti S, Kaur K, Sohi R. Evaluation of salivary calcium and salivary parathyroid levels in postmenopausal women with and without oral dryness. *Contemp Clin Dent* 2013;4:488-92.

**Source of Support:** Nil. **Conflict of Interest:** None declared.

#### Announcement

#### iPhone App



Download  
iPhone, iPad  
application

FREE

A free application to browse and search the journal's content is now available for iPhone/iPad. The application provides "Table of Contents" of the latest issues, which are stored on the device for future offline browsing. Internet connection is required to access the back issues and search facility. The application is Compatible with iPhone, iPod touch, and iPad and Requires iOS 3.1 or later. The application can be downloaded from <http://itunes.apple.com/us/app/medknow-journals/id458064375?ls=1&mt=8>. For suggestions and comments do write back to us.