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ORIGINAL ARTICLE

Stimulated whole salivary flow rate and composition in menopausal women with oral dryness feeling

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The aim of this study was to compare stimulated whole saliva flow rate and composition of menopausal women with/without oral dryness (OD) feeling. A case-control study was carried out in 42 selected menopausal women aged 52-73 years with or without OD feeling (21 as case and 21 as control) conducted at the Clinic of Oral Medicine, Tehran University of Medical Sciences. Paraffin-stimulated saliva samples were obtained by expectoration. The stimulated whole saliva composition was measured by a spectrophotometer [magnesium (Mg⁺²), calcium (Ca^{+2}) , chloride (Cl^{-}) , inorganic phosphate (Pi) and total protein], flame-photometry [sodium (Na⁺)] and ion selective electrode (ISE) [potassium (K⁺)] methods. No significant differences were found in stimulated whole saliva flow rate, Mg⁺², Cl⁻, Pi, Na⁺, K⁺ and total protein concentrations between the two groups, but the mean calcium concentration was significantly higher in cases than in controls (P = 0.003). It seems that the level of salivary calcium concentration may be higher in menopausal women with OD feeling than in the control group. Oral Diseases (2007) 13, 320-323

Keywords: menopause; saliva composition; oral dryness feeling; flow rate

Introduction

Menopause is a physiological process typically occurring in the fifth decade of life in women, involving permanent cessation of menstruation (Frutos *et al*, 2002). 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 (Zachariasen, 1993). Major oral symptoms of menopause are xerostomia and burning mouth (Frutos *et al*, 2002).

Oral dryness (OD) 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 onethird of cases. It is associated with an unpleasant feeling in the mouth and throat (Nederfors, 2000). 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 (Narhi, 1994; Ben Aryeh et al, 1996; Greenberg and Glick, 2003). In addition, elderly people have significantly reduced salivary secretion and increased salivary components (e.g. K^+ , Cl^- , Pi, Ca^{+2} and total protein) compared with younger people (Vissink et al, 1996; Nagler and Hershkovich, 2005). It seems feasible that saliva composition (e.g. Ca⁺², Mg⁺², Na⁺, Cl⁻, Pi or total protein) may be altered in women with OD feeling.

The purpose of this study was to compare the stimulated whole saliva flow rate and components in menopausal women with or without OD feeling.

Subjects and methods

Subjects

Seventy-two menopausal women participated in a case-control study, conducted at the Clinic of Oral Medicine, Tehran University of Medical Sciences (TUMS), from November 2004 to March 2005. The participants were aged between 52 and 73 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 Sjogren's syndrome), oral candidiasis or with a bad oral health condition and periodontal breakdown were excluded. The remaining participants were asked to answer a questionnaire with a list of symptoms associated with xerostomia (Table 1). Twenty-one participants who answered affirmatively to at least one of the questions related to xerostomia formed the case group (mean \pm s.d. 58.7 \pm 4.9 years) (Torres et al, 2002) and 21 who did not answer affirmatively to any of the questions in Table 1 formed the control

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Received 12 February 2006; revised 8 April 2006; accepted 18 April 2006

 Table 1 Questionnaire used for selection of subjects with xerostomia (oral dryness feeling) and percentage of dry mouth complaints in the case group

Questions	%
1. Does your mouth feel dry when eating a meal?	42.9
2. Do you have difficulties swallowing any foods?	23.8
3. Do you need to sip liquids to aid in swallowing dry foods?	19.0
4. Does the amount of saliva in your mouth seem	47.6
to be reduced most of the time?	
5. Does your mouth feel dry at night or on awakening?	76.2
6. Does your mouth feel dry during the daytime?	42.9
7. Do you chew gum or use candy to relieve oral dryness?	14.3
8. Do you usually wake up thirsty at night?	47.6
9. Do you have problems in tasting food?	0.0
10. Does your tongue burn?	14.3

group (mean \pm s.d. 59.3 \pm 5.2 years). In fact, all the participants in the case group answered affirmatively at least three of the questions. The case and control groups were matched on age and duration of menopause.

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

Saliva collection

Saliva was collected under resting conditions in a quiet room, between 9 AM and 12 PM, at least 2 h after the last intake of food or drink. The patients were asked to chew a standard piece (1 g) of paraffin wax. Collection was started after 1 min of chewing and initial swallowing, after which the final 5-min collection was started. The patients were asked to expectorate whole saliva into a preweighed, 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 (Navazesh, 1993).

The samples were immediately stored at -70° C for later determination of total protein and electrolytes.

Saliva analysis

Whole saliva was assessed colorimetrically by a spectrophotometer and using affiliated kits (ZiestChem Diagnostics, Tehran, Iran) for analysis of whole saliva Pi, Ca⁺², Mg⁺² and Cl⁻. The total protein concentration was measured by the biuret method (Rosenthal and Cundiff, 1956), using bovine serum albumin as standard; inorganic phosphate by photometrical measurement of the blue colour formed after adding ammonium molybdate and stannous chloride (Bodansky, 1932; Daly and Erthinghdusen, 1972); calcium by Arsenazo reaction ([Bauer, 1981); magnesium by the xylidyl blue complex (Barbour and Davidson, 1988) and chloride by the thiocyanate red complex (Tietz, 1976).

Potassium and sodium concentrations of whole saliva were measured by ISE and flame-photometry methods respectively.

Electrolyte and total protein output were calculated as concentration \times flow rate.

Statistical analysis

The two-tailed Student's unpaired *t*-test and the Mann–Whitney *U*-test were used to compare the salivary components between case and control groups. P < 0.05 was considered statistically significant.

Results

The mean and median stimulated whole saliva flow rate, concentrations of electrolytes and total protein are shown in Table 2.

No significant difference was found between case and control groups regarding salivary flow rate. Moreover, no significant differences were observed between case and control groups with respect to salivary chloride, sodium, potassium, magnesium, phosphate and total protein concentrations, although the potassium, phosphate and total protein concentrations in the case group, and sodium and magnesium concentrations in the control group showed a slight increase.

The calcium concentration was higher in the case group than in the control group (P = 0.003) (Figure 1).

Discussion

Our data indicated that there was no significant difference in stimulated whole saliva flow rate between menopausal women, either with or without oral dryness feeling. This is consistent with studies of other investigators (Narhi, 1994; Ben Aryeh *et al*, 1996; Greenberg and Glick, 2003). It seems that OD feeling may be unrelated to lowered salivary flow rates.

Significant differences in other ions, namely sodium, potassium, chloride, phosphate and magnesium were not observed. Our data also indicated that there were no significant differences in stimulated whole saliva total protein concentration between the two groups. It also seems that OD feeling is unrelated to stimulated whole saliva total protein and alterations in those ions.

Oral dryness feeling is a major complaint for many elderly individuals (Ben-Aryeh *et al*, 1985; Wardrop *et al*, 1989; Vissink *et al*, 1996; Narhi *et al*, 1999; Nederfors, 2000; Ship *et al*, 2002; Asplund and Aberg, 2005). In addition, it has been shown that elderly people

 Table 2 Stimulated whole saliva flow rate, electrolyte and total protein levels in case (xerostomia) and control groups

	Case group	Control group	P-value
Flow rate (ml min ⁻¹)	$1.38 \pm 0.02 (1.47)$	$1.37 \pm 0.03 (1.44)$	0.837
Chloride (mmol l ⁻¹)	$26.4 \pm 2.1 (24.3)$	$28.1 \pm 3.3 (24.1)$	0.664
Sodium (mmol l ⁻¹)	$16.1 \pm 1.2 (15.0)$	$19.7 \pm 1.9 (19.0)$	0.120
Potassium (mmol l^{-1})	87.7 ± 7.0 (74.9)	75.5 ± 4.4 (73.0)	0.145
Phosphate (mmol l^{-1})	$4.97 \pm 0.41 \ (4.58)$	$4.55 \pm 0.26 (4.73)$	0.389
Calcium ($\mu g m l^{-1}$)	$108.3 \pm 6.0 (108.2)$	81.9 ± 5.3 (83.7)	0.003*
Magnesium($\mu g m l^{-1}$)	$11.6 \pm 1.8 (8.9)$	$12.4 \pm 1.3 (12.8)$	0.690
Total protein	8.82 ± 0.60 (7.94)	$8.17 \pm 0.57 (7.78)$	0.440
$(mg ml^{-1})$			

Data are expressed as mean \pm s.e.m. and median values in parentheses. *P < 0.05 was considered statistically significant.



Figure 1 The stimulated whole saliva calcium level in case (xerostomia) and control groups. Data are expressed as mean \pm s.e.m. *P < 0.05 was considered statistically significant

have significantly increased salivary calcium compared with younger people (Ben Aryeh *et al*, 1996; Nagler and Hershkovich, 2005). Data from the present study show that the mean concentration of stimulated whole saliva calcium is significantly higher in patients with OD feeling compared with the control group. Therefore, it is possible that there is a relationship between saliva calcium level and OD feeling in menopausal women.

The composition of saliva in menopausal women is oestrogen dependent (Leimola-Virtanen *et al*, 1997). The concentration of calcium in submandibular saliva is low during ovulation (Puskulian, 1972) – when the oestrogen level is high – and appears to be lower during pregnancy than in labour (Guidozzi *et al*, 1992). In a longitudinal study Sewon *et al* (2000) suggested that salivary calcium concentration decreased in stimulated saliva with hormone replacement therapy (increased oestrogen level) in healthy menopausal women. They also reported that the concentrations of calcium did not correlate with the flow rate.

Hormonal replacement therapy (HRT) has been reported to reduce OD resulting in improved oral wellbeing (Leimola-Virtanen *et al*, 1997). None of the patients participating in our study were under hormone replacement therapy. A decrease in female hormones, especially oestradiol, suppresses intestinal absorption of calcium, which leads to elevated concentrations of serum parathyroid hormone and enhanced bone resorption (Tohme *et al*, 1990). Furthermore, menopausal women have been considered at risk of periodontitis because of osteoporosis of the alveolar bone (Sewon *et al*, 2000; Chohayeb, 2004). Patients who have salivary calcium concentrations over the mean have more gingivitis than those with values lower than the mean (Sewon *et al*, 1998).

All of the above suggest that an increase in oestrogen (ovulation, pregnancy, HRT) is associated with a decrease in saliva calcium concentration. It seems that low levels of oestrogen in menopausal women affect general calcium turnover and its salivary concentration. Further studies need to evaluate the correlation of serum oestrogen level and salivary calcium concentrations in menopausal women with and without OD feeling to approve this hypothesis.

Conclusion

It seems that the level of salivary calcium concentration and output may be higher in menopausal women with OD feeling than in controls.

References

- Asplund R, Aberg HE (2005). Oral dryness, nocturia and the menopause. *Maturitas* **50**: 86–90.
- Barbour HM, Davidson W (1988). Studies on measurement of plasma magnesium: application of the Magon dye method to the 'Monarch' centrifugal analyzer. *Clin Chem* **34**: 2103–2105.
- Bauer PJ (1981). Affinity and stoichiometry of calcium binding by arsenazo III. *Anal Biochem* **110:** 61–72.
- Ben Aryeh H, Gottlieb I, Ish-Shalom S, David A, Szargel H, Laufer D (1996). Oral complaints related to menopause. *Maturitas* 24: 185–189.
- Ben-Aryeh H, Miron D, Berdicevsky I, Szargel R, Gutman D (1985). Xerostomia in the old: prevalence, diagnosis, complications and treatment. *Gerodontology* **4**: 77–82.
- Bodansky A (1932). Phosphatese studies I. Determination of inorganic phosphate. Beer's law and interfering substances in the Kuttner-Lichtenstein method. *J Biol Chem* **99**: 197–206.
- Chohayeb AA (2004). Influence of osteoporosis on the oral health of menopausal women. *Gen Dent* **52**: 258–261.
- Daly JA, Erthinghdusen G (1972). Direct method for determining inorganic phosphate in serum with 'centrifiChem'. *Clin Chem* 18: 263–265.
- Frutos R, Rodriguez S, Miralles L, Machuca G (2002). Oral manifestations and dental treatment in menopause. *Med Oral* **7:** 31–35.
- Greenberg M, Glick M (2003). *Burket's oral medicine*, 10th edn. DC Decker Inc.: Hamilton, Ontario, Canada, pp. 235–236.
- Guidozzi F, Maclennan M, Graham KM, Jooste CP (1992). Salivary calcium, magnesium, phosphate, chloride, sodium and potassium in pregnancy and labour. *S Afr Med J* 81: 152–154.
- Leimola-Virtanen R, Helenius H, Laine M (1997). Hormone replacement therapy and some salivary antimicrobial factors in post- and perimenopausal women. *Maturitas* **27**: 145–151.
- Nagler RM, Hershkovich O (2005). Relationships between age, drugs, oral sensorial complaints and salivary profile. *Arch Oral Biol* **50**: 7–16.
- Narhi TO (1994). Prevalence of subjective feelings of dry mouth in the elderly. J Dent Res 73: 20–25.
- Narhi TO, Meurman JH, Ainamo A (1999). Xerostomia and hyposalivation: causes, consequences and treatment in the elderly. *Drugs Aging* **15**: 103–116.
- Navazesh M (1993). Methods for collecting saliva. Ann N Y Acad Sci 694: 72–77.
- Nederfors T (2000). Xerostomia and hyposalivation. *Adv Dent Res* **14:** 48–56.
- Puskulian L (1972). Salivary electrolyte changes during the normal menstrual cycle. *J Dent Res* **51** (Suppl. 5): 1212–1216.
- Rosenthal HL, Cundiff HF (1956). New biuret reagent for the determination of proteins in cerebrospinal fluid. *Clin Chem* 2: 394–400.
- Sewon LA, Karjalainen SM, Soderling E, Lapinleimu H, Simell O (1998). Associations between salivary calcium and oral health. *J Clin Periodontol* **25**: 915–919.
- Sewon L, Laine M, Karjalainen S, Leimola-Virtanen R, Hiidenkari T, Helenius H (2000). The effect of hormone replacement therapy on salivary calcium concentrations in menopausal women. *Arch Oral Biol* **45**: 201–206.

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- Ship JA, Pillemer SR, Baum BJ (2002). Xerostomia and the geriatric patient. J Am Geriatr Soc 50: 535–543.
- Tietz NW (1976). *Fundamentals of clinical chemistry*, 1st edn. W.B. Saunders: Philadelphia, PA, 897 pp.
- Tohme JF, Bilezikian JP, Clemens TL, Silverberg SJ, Shane E, Lindsay R (1990). Suppression of parathyroid hormone secretion with oral calcium in normal subjects and patients with primary hyperparathyroidism. *J Clin Endocrinol Metab* **70**: 951–956.
- Torres SR, Peixoto CB, Caldas DM *et al* (2002). Relationship between salivary flow rates and Candida counts in subjects with xerostomia. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* **93**: 149–154.
- Vissink A, Spijkervet FK, Van Nieuw Amerongen A (1996). Aging and saliva: a review of the literature. *Spec Care Dent* **16**: 95–103.
- Wardrop RW, Hailes J, Burger H, Reade PC (1989). Oral discomfort at menopause. Oral Surg Oral Med Oral Pathol 67: 535–540.
- Zachariasen RD (1993). Oral manifestations of menopause. *Compendium* 14: 1586–1591.

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