

Oral Dryness & Qualitative Changes in Saliva: Impact of Menopause & Hormonal Replacement Therapy: Systematic Review

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Abstract

Oral dryness – enigma to clinicians. The emergence of oral dryness and its unrelated to salivary flow rates raised many questions over the hypothesis of oral dryness in post menopausal women. The current review focussed on qualitative changes in saliva. The parameters included calcium, Parathyroid hormone and Serum Estrogen. The effect of hormone replacement therapy in alienating the oral symptoms was also reviewed.

INTRODUCTION

Women's health undergoes physiological, pathological and psychological changes after menopause. Menopause is the consequence of hormonal changes that produce a series of general manifestations that have become increasingly important as a result of increased female life expectancy in the industrialized world. Indeed, such manifestations are observed throughout the last third of the human female lifetime.¹

The reduced level of estrogen as a result of menopause is associated with age-related factors which disproportionately increase the risk of developing cardiovascular disease, osteoporosis, Alzheimer's disease and oral diseases. Reduced estrogen levels have been implicated in the pathogenesis of osteoporosis in postmenopausal women. Estrogen is also known to affect the salivary gland functions as its reduced level affects more than 200 types of tissues of the body.²

The oral dryness is most enigmatic problem of patients when no clinical changes are seen in oral cavity, hence most difficult to diagnose and treat them comprehensively. Mostly in post-menopausal women and in old age men this problem becomes quite evident. The etiopathogenesis of oral dryness is not clear and many hypotheses have been proposed. The most

accepted is age related changes and change in hormonal level in women after menopause. Many studies have concluded that there is improvement when hormonal replacement therapy is initiated.

Painful oral symptoms have been frequently associated with reduced salivary flow rate that may be further aggravated in presence of removable partial dentures. Other potential complications of dry mouth are mandibular dysfunction, diffuse gingival atrophy or oral ulcerations, oral candidiasis, pernicious anemia, etc.^{3,4} The oral dryness in these postmenopausal women has been found to be unrelated to salivary flow. Hence it becomes quite evident to understand the underlying cause for xerostomia which might be due to qualitative changes in saliva or changes in sensitivity of buccal mucosa.

Oral dryness and Calcium Levels

Our study conducted in 2012 showed that salivary calcium concentration was significantly more in postmenopausal women with oral dryness.⁵ The previous studies have also shown that the level of estrogen status effects the saliva composition. This was reported by F Agha- Hosseini et al in 2007 and 2009,^{6,7} S Ravinder et al in 2010,⁸ I M Dizgah et al in 2010.⁹

Calcium is of much biological importance. Calcium level in turn is also regulated by level of estrogen. **Leimola-Virtanen et al in 1997** concluded that the composition of saliva in menopausal women is estrogen dependent.¹⁰ **Sewon et al in 2000** suggested that salivary calcium concentration decreased in stimulated saliva when hormone replacement therapy was initiated in menopausal women.¹¹ Ship, *et al.* in their study in the USA on 43 healthy pre-menopausal and post-menopausal females, showed that there were no alterations in the quantity of saliva, suggesting that among healthy women salivary gland function is not significantly influenced by menopause or hormone replacement therapy. **F Agha- Hosseini et al in 2010** showed that the mean cortisol concentration of saliva was significantly higher in postmenopausal women oral dryness group than in postmenopausal women without oral dryness. The study have mostly concluded that reduced level of estrogen and changes in calcium levels might play role in quality changes of saliva which may be the cause of feeling of oral dryness. Moreover the hormonal replacement therapy has reduced the severity of oral dryness and helped in improving the overall well being as stated by Volpe et al¹² in 1991 and Sewon et al in 2000.

Oral dryness with Serum Parathyroid Hormone & Serum Estrogen Levels

Parathyroid hormone, Calcitonin and Vitamin D are concerned with its regulation. Parathyroid hormone is an important hormone in calcium turnover. Its main function is maintaining the calcium level in extra cellular fluid. Secretion of parathyroid hormone is stimulated by hypocalcaemia and suppressed by hypercalcaemia. The parathyroid glands can also suffer alterations due to the lack of estrogen. Due to this, the glands occasionally become hyperactive, thereby contributing to mobilization of calcium and phosphorus deposits in osteoporosis.^{12,13}

The parathyroid hormone causes mobilization of calcium from bones and causes weakness of bones, thus making the patient prone to osteoporosis. Postmenopausal osteoporosis affects women who are postmenopausal but younger than 70 years of age. These women are said to have postmenopausal osteoporosis when the WHO BMD criteria are observed within 15–20 years after the onset of menopause.

In oral dryness patients, the elevated levels of PTH have been observed a positive correlation exists between serum parathyroid hormone levels and severity of oral dryness. This finding is in harmony with the results of the study by **F Agha Hosseini in 2009** and Singh B et al in 2016.¹⁴ F agha et al in 2011 there was a significant negative correlation between xerostomia inventory score and bone mineral density in postmenopausal women indicating that oral dryness severity was associated with decreasing bone mineral density.¹⁵

Khosla Sandeep et al in 1997 concluded that estrogen deficiency results in the increase in bone turnover in early postmenopausal women. It also indirectly results in secondary hyperparathyroidism and increase in bone turnover found in late postmenopausal women. He also concluded that increase in serum parathyroid hormone was eliminated in postmenopausal women receiving long term estrogen therapy.¹⁶

Hence the levels of calcium and parathyroid hormone seem to be affected mostly by the levels of estrogen. With estrogen deficiency causing calcium level to oscillate downwards, it also causes the Parathyroid hormone levels to go up. Also the lack of estradiol causes the glands to become occasionally hyperactive, thereby contributing to mobilization of calcium and phosphorus deposits in osteoporosis.¹⁷

Reddy et al. in 2008 found significantly higher levels in salivary calcium, phosphorus and alkaline phosphatase when osteoporotic and osteopenic women were compared with the controls. Calcium and phosphorus are present as inorganic components of saliva, which quantitatively accounts as the main mineral component of the human skeletal system. Some of the alkaline phosphatase is also secreted into the saliva and may, thus, serve as a biochemical marker for bone turnover. Hence concluding that elevated salivary calcium has role to play as indicator of osteoporosis which could be influenced by low level of estrogen in menopausal women.¹⁸

Resorption of bone may lead to diffusion of calcium into blood and further into the saliva. Increased salivary Ca can be used as a potential screening tool for assessing the risk for osteoporosis. According to Maryam Rabiei M et al, the highest salivary calcium level is 6.1 mg/dl and above which (i.e. >6.1mg/dl) can used as a screening tool to identify osteoporosis risk in postmenopausal women.¹⁹

The estrogens prevent osteoporosis by inhibiting stimulatory effects of certain cytokines on osteoclasts. Hence menopausal women have been considered at risk for periodontitis because of osteoporosis of the alveolar bone.²⁰ The occurrence of periodontitis was reported significantly greater in post-menopausal women not using HT than premenopausal women.²¹

Effect of Hormonal Replacement Therapy:

The maintenance of estrogen level may prevent oral discomfort along with other systemic problems in postmenopausal women. **Wardrop et al.** and **Forabosco et al.**²² also reported that menopausal women with oral discomfort were relieved of symptoms after systemic hormone replacement therapy.^{23,10}

As concluded by many authors, serum estrogen levels have also been maintained by hormone replacement therapy. In many studies such as those by **Robert R. Recker** in 1977, **J.C. Gallagher** in 1980, **Takashi Kameda** in 1997, **Yalcin F.** in 2005 and **Siva Reddy et al** in 2008, it was concluded that lower levels may also induce bone resorption.

Giuca et al. compared estrogens with phytotherapy in treating oral cavity symptoms in 95 menopausal women and he concluded that women on HRT had improvement in oral symptoms and estrogens were more effective than phytotherapy regarding the salivary changes.²⁴ *Elliason* in 2003 concluded that there was significant increase in the saliva flow and the complaints of dry mouth reduced on institution of HRT.²⁵ In the postmenopausal women with osteoporosis who did not receive HRT had a greater incidence of adverse dental outcomes and incurred higher dental care costs than those who received HRT as *Allen* projected in 2000.²⁶

López–Marcos et al. in a group of 190 women found no significant effect of HRT on periodontal health.²⁷ Similar results were also obtained by *Tarkkila et al.* who reached conclusion that there is no major difference in dental parameters or salivary flow rates between the groups. Also he observed that women with HRT reported more often recent dental appointments.²⁸

The unequal responses to HRT shown by different studies may be due to some local host factors or other not studied parameters.²⁹

So going by the number of positive studies, it seems that hormone replacement therapy may play a major role in alleviating oral discomfort in these women.

Conclusion:

Hence the levels of calcium and parathyroid hormone seem to be affected mostly by the levels of estrogen. So the maintenance of estrogen level may prevent oral discomfort along with other systemic problems in postmenopausal women. So it seems that hormone replacement therapy may play a major role in alleviating oral discomfort in these women. As some of studies are giving contradictory results, it leads to understand that there is need of large randomized controlled studies are needed to document significant effect of HRT and other interventions in menopausal women with oral symptoms. In patients with oral dryness, the fact that good history, and presence of signs and symptoms of oral dryness should be considered as a warning sign for possible development of osteoporosis and should be considered as a risk factor in these women. Also the scope of saliva as diagnostic cannot be ruled out in oral dryness patients.

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