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Abstract

Osteoporosis is characterized by reduced skeletal mass and microarchitectural deterioration of the bone tissue, leading to bone fragility and an increased risk of fractures, especially wrist, vertebrae and hip fractures. Thirty percent of 65–70-year-old women have osteoporosis, and after age of 80 its prevalence increases up to 70 %. Postmenopausal women with osteoporosis seem to be at an increased risk for cardiovascular events. Furthermore, the deterioration of oral health, as shown by attachment loss of teeth, is proportional to the severity of osteoporosis. Osteoporosis can be treated with many different medications, but the data on the efficacy and safety of estrogen treatment comes mainly from early postmenopausal women.

We randomized 90 elderly osteoporotic women between 65 and 80 years of age to receive HT (a continuous combination of 2 mg oral estradiol plus 1 mg norethisterone acetate) or 10 mg of alendronate daily or their combination for two years and compared the treatments with regard to their effects on bone mineral density and turnover, two surrogate markers of the risk of cardiovascular diseases (CVD), CRP and E-selectin, as well as oral health. The effect of HT on health-related quality of life (HRQoL) was studied in the population-based cohort of 1663 postmenopausal women, mean age 68 years, out of which 585 women were estrogen users and 1078 were non-users.

Bone mineral density (BMD) was measured with dual-energy X-ray absoprtiometry (DXA) at 0, 12 and 24 months. Urinary N-telopeptide (NTX) of type I collagen, a marker of bone resorption, and serum aminoterminal propeptide of human type I procollagen (PINP), a marker of bone formation, were measured every six months of treatment. Two surrogate markers of CVD risk, serum CRP and E-selectin, were measured at 0, 6, and 12 months. Dental, periodontal and intra- and extraoral status, saliva analyses, panoramic tomography of the jaws, buffering capacity, oral yeasts and gingival crevicular fluid (GCF) matrix metalloproteinase (MMP)-8 levels were studied to evaluate the oral health status and for the mouth symptoms a structured questionnaire was used. The HRQOL was measured with 15D questionnaire, which is a generic, comprehensive, 15-dimensional, and standardized, self-administered measurement.

Lumbar spine BMD increased similarly in all treatment groups, from 6.8% to 8.4% at 12 months and from 9.1% to 11.2% at 24 months. HT increased femoral neck BMD 4.9% and 5.8%, respectively. At the latter time point the HT group differed significantly from the other groups (+3.3% for the alendronate group at 12 months; + 2.7% for the combination group at 24 months). HT reduced bone marker levels of NTX (60.2-62.7%) somewhat less than alendronate alone (72.4-

76.1%, p=0.047) or the combination (78.1-80.4%, p<0.0001-0.0069), and the reduction for PINP 53.6-59.8%, 73.0-75.0% (p<0.001) and 67.0-71.5% (p<0.0001), respectively.

Oral HT increased serum CRP level by 76.5% at 6 months (p<0.001) and by 47.1% at 12 months (NS). The simultaneous rises in serum SHBG suggested the changes to be a sign of the unspecific stimulation of hepatic protein synthesis by HT. HT decreased serum E-selectin level by 24.3 % (p<0.001) at 6 months and 30.0 % (p<0.001) at 12 months. Alendronate did not have any effect and did not block the effect of HT on these surrogate markers of CVD risk.

Alendronate caused a decrease in the resting salivary flow rate (19 %, p< 0.05) and tended to increase GCF MMP-8 levels. Otherwise, the treatments did not have any effect on the parameters of oral health.

HT improved the HRQoL of elderly postmenopausal women significantly on the dimensions of usual activities, vitality and sexual activity, but the overall improvement in HRQoL was neither statistically significant nor clinically important.

In conclusion, in elderly postmenopausal women HT is an effective alternative to treat osteoporosis, but not to improve quality of life or oral health. HT has divergent effects on the markers of the risk of cardiovascular diseases. Given all the potential risks of CVD, thromboembolic events and cancer associated with HT, bisphonates might be the first option to start the treatment of postmenopausal osteoporosis in the old age.