Influence of cigarette smoking on bone mineral density in postmenopausal women with estrogen deficiency in menstrual history

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ABSTRACT

Introduction: Estrogen deficiency leads to bone mass loss and increased risk for osteoporosis. The aim of this study was to examine influence of cigarette smoking on bone mineral density in postmenopausal women with estrogen deficiency in menstrual history.

Methods: The total of 100 postmenopausal women living in Sarajevo area, aged 50-65 years, with estrogen deficiency in menstrual history participated in this prospective study. The subjects were divided into two groups, examination and control group, based on bone mineral density values. The women in the examination group had osteoporosis while in the control group were women with osteopenia or normal bone mineral density. Bone mineral density was measured at the lumbar spine and proximal femur by Dual–Energy X-ray Absorptiometry using Hologic QDR-4000 scanner. Smoking habits were assessed for each subject.

Results: The average number of cigarettes smoked per day in women with estrogen deficiency in menstrual history was 14.86 in the examination group and 4.67 in the control group. The difference in the average number of cigarettes smoked per day between the two groups was statistically significant (p<0.01). The coefficient of linear correlation between T score and the number of cigarettes smoked per day among women with estrogen deficiency in menstrual history in the examination group was statistically significant (p<0.01). The coefficient of linear correlation between T score and the number of cigarettes smoked per day among women with estrogen deficiency in menstrual history in the control group was statistically significant (p<0.05).

Conclusion: Results of this study suggest that cigarette smoking has negative impact on bone mineral density and that healthy lifestyle (no smoking) has the potential to reduce bone loss in postmenopausal women with estrogen deficiency in menstrual history.

Keywords: osteoporosis, cigarette smoking

INTRODUCTION

Osteoporosis is a skeletal disorder characterized by compromised bone strength (bone strength primarily reflects the integration of bone density; bone
quality refers to architecture, metabolic turnover, damage accumulation and demineralization) predisposing a person to an increased risk of fracture (1). The pathogenesis of osteoporosis include: failure to achieve a skeleton of optimal strength during growth and development, excessive bone resorption resulting in loss of bone mass and disruption of architecture and failure to replace lost bone due to defects in bone formation (2). Sex steroids (estrogens and androgens) slow the rate of bone remodeling and protect against bone loss acting on osteoclastogenesis and osteoblastogenesis, osteoblast and osteocyte apoptosis (3). Estrogen deficiency increases the rate of remodeling and increases imbalance in the bone multicellular unit resulting in bone loss and structural decay after menopause (4). A premature menopause, particularly when surgically induced before age 45 years, is strong determinant of bone density and increased risk of fracture (5). Late menarche is also associated with low bone mineral density (6,7). The later the menarche and the earlier the menopause, the higher the degree of osteoporosis (7). Cigarette smoking affects the bone duo direct toxic effects on osteoblasts/osteoclasts activity of nicotine, and indirect actions on sex and adrenocortical hormones, vitamin D, intestinal calcium absorption, vessels and oxygen supply (8). Smoking affects pituitary, thyroid, adrenal, testicular and ovarian function, calcium metabolism and the action of insulin and the major salient clinical effects are the increased risk and severity of Graves’ hyperthyroidism and opthalmopathy, osteoporosis and reduced fertility (9). Some normal, estrogen-dependent physiologic processes are affected by smoking, making osteoporosis and premature menopause more common among women who smoke (10). Smoking reduces the production of estrogen by the ovaries, causing changes in hepatic estrogen metabolism, showed toxic effects on ovarian follicles and the bone cells, reduces the conversion of androgen into estrogen, the concentration of sex hormone binding globulin (SHBG), which binds circulation estrogens, is higher in women who smoke, and lower concentrations of the biologically active estrogens (9, 11, 12). The aim of this study was to examine influence of cigarette smoking on bone mineral density in postmenopausal women with estrogen deficiency in menstrual history.

METHODS

The total of 100 postmenopausal women living in Sarajevo area, aged 50-65 years, with estrogen deficiency in menstrual history participated in this prospective study. The subjects were divided in two groups, examination and control group, based on bone mineral density values. The women in the examination group (n=50) had osteoporosis. The women in the control group (n=50) had osteopenia or normal bone mineral density. Bone mineral density was measured at the lumbar spine and proximal femur by Dual–Energy X–ray Absorptiometry using Hologic QDR-4000 scanner. Smoking habits were assessed for each subject. The inclusion criteria were: postmenopausal women with estrogen deficiency in menstrual history (fewer than 30 years of menstruation, menopause before age 45 years), women aged 50-65 years, women who live in the Sarajevo area, women who do not use hormone replacement therapy, women whose finding’s of bone densitometry was at the level of osteoporosis, women whose finding’s of bone densitometry was at the level of osteopenia or normal. The exclusion criteria were: postmenopausal women without estrogen deficiency in menstrual history, women younger than 50 and older than 65 years, women who do not live in the Sarajevo area, women who are not postmenopausal, women who use hormone replacement therapy, women who have a disease that can cause osteoporosis, women who use drugs that may cause osteoporosis.

Statistical analysis

The results were statistically analyzed. Statistical significance between examination and control group in cigarette smoking was tested by Student’s t-test. The coefficient of linear correlation between cigarette smoking and bone mineral density was calculated. P < 0.05 was considered statistically significant.

RESULTS

The average age of women with estrogen deficiency in their menstrual history in the examination group was 58.48 years, and in the control group was 57.30 years. There was no statistically significant differences between these two groups, t = 1.169.
The average number of cigarettes smoked per day in women with estrogen deficiency in menstrual history stood at 14.86 in the examination group and in the control group 4.67. The difference in the average number of cigarettes smoked per day between the two groups was statistically significant, \( t = 6.009, p < 0.01 \).

The coefficient of linear correlation between T scores and the number of cigarettes smoked per day among women with estrogen deficiency in menstrual history in the examination group was statistically significant, \( r = -0.671; \) \( p < 0.01 \). The coefficient of linear correlation between T scores and the number of cigarettes smoked per day among women with estrogen deficiency in menstrual history in the control group was statistically significant, \( r = -0.350; \) \( p < 0.05 \).

**DISCUSSION**

Estrogen deficiency leads to bone mass loss and increased risk for osteoporosis. Late menarche and early menopause are associated with bone loss. The objective of the study of Parker et al. was to investigate the association between age at menarche, age at menopause, and years of menstruation with incidence of osteoporosis and assess the impact of prenatal exposure to diethylstilbestrol (DES), a synthetic estrogen, on such associations. The results support the hypothesis that lifetime cumulative exposure to estrogens is protective against osteoporosis (6). The results of the study of Li et al. showed significant increase in osteoporosis of lumbar spine in women with the age of menarche \( \geq 17 \) compared with women with age of menarche \( \leq 13 \). Among all women aged between 55 − 65, there was significant increase in osteoporosis in women with the menopause age \( \leq 48 \), compared with the menopause age \( > 54 \) (7). In our previous study we evaluated the influence of menstrual factors (years between menarche and menopause, years since menopause) on bone mass loss in Bosnian postmenopausal women. Average years between menarche and menopause in women with osteoporosis was significant lower than in women in control group (osteopenia or normal mineral bone density values). Average years since menopause was significant higher...
in women with osteoporosis than in women with osteopenia or normal bone mineral density values (13). Meta-analyses on the effects of smoking on the bone revealed that current smokers sustained decreased bone mass and increased fracture risk at age 50 years and older (14). Numerous studies point to the negative effects of smoking on bone tissue. Giampietro et al. assessed the relative impact of cigarette smoking, statin use, genetic polymorphisms, and one-way interaction of these factors on development of osteoporosis in postmenopausal women. The results suggested a role for genetic variation in the interleukin 6 (IL6) and the lipoprotein receptor-related protein 5 (LRP5) in conferring risk for osteoporosis in Caucasian women, with the latter manifest only in smokers (15). Ward and Klesges studied cross-sectional and prospective human studies that provided a quantitative measure of bone mass (X-ray, absorptiometry, or computed tomography) as a function of cigarette smoking exposure. Smokers had significantly reduced bone mass compared with nonsmokers (never and former smokers) at all bone sites. Overall, effects were greatest in men and in the elderly, and were dose-dependent. In prospective studies, smokers had greater rates of bone loss over time compared with nonsmokers. Absolute effect sizes at most bone sites were greatest for current smokers compared with never smokers, intermediate for current smokers compared with former smokers, and lowest for former smokers compared with never smokers, suggesting that smoking cessation may have a positive influence on bone mass (16). Brook et al. assessed how different trajectories of women’s smoking, covering the ages 40 to 48 years, relate to osteoporosis at age 65. The chronic/heavy smokers were significantly more likely than the non-smokers to report having osteoporosis. Quitters and moderate smokers did not differ significantly from non-smokers on the osteoporosis measure (17). The association between secondhand smoke exposure and lumbar and femoral neck osteoporosis was assessed in postmenopausal never-smoking Korean women in the study of Kim et al. The finding of the study was that in postmenopausal never-smoking Korean women, exposure to secondhand smoke was positively associated with osteoporosis (18). Jenkins and Denison found that former and current smoking increased the risk of hip fracture in population of postmenopausal women living in rural and urban areas of Northwest Texas (19). In the study of Cummins et al. showed that although hereditary factors strongly contribute to bone health, behavioural factors can modulate the genetically determined pattern of skeletal modelling and remodelling. Smoking was the strongest behavioural predictor of lumbar and femoral bone mineral density in pre- and postmenopausal adult Irish women (20). The aim of the present study was to examine influence of cigarette smoking on bone mineral density in postmenopausal women, aged 50-65 years living in Sarajevo area with estrogen deficiency in their menstrual history. The results showed that smoking has a negative effect on bone mineral density in postmenopausal women, aged 50-65 years living in Sarajevo area with estrogen deficiency in their menstrual history. The average number of cigarettes smoked per day in women with estrogen deficiency in menstrual history stood at 14.86 in the group of women with osteoporosis and in the group of women without osteoporosis 4.67. The difference in the average number of cigarettes smoked per day between the two groups was statistically significant (p < 0.01). The coefficient of linear correlation between T scores and the number of cigarettes smoked per day among women with estrogen deficiency in menstrual history was statistically significant in the group of women with osteoporosis (p < 0.01) and in the group of women without osteoporosis (p < 0.05). It was shown that the negative effects of smoking on bone mineral density are dose-dependent. The deficit of estrogen is associated with a decrease in bone mass, but healthy lifestyle (no smoking) has the potential to preserve bone mass in postmenopausal women with estrogen deficiency in their menstrual history. Encouragement of lifestyle alterations, including smoking cessation, should be a major component of any bone therapeutic programme (21).

CONCLUSION

The results of this study suggest that cigarette smoking has influence on bone mineral density and increases bone loss in postmenopausal women, aged 50-65 years living in Sarajevo area, with estrogen deficiency in their menstrual history. Further healthy lifestyle (no smoking) has positive impact on bone
in postmenopausal women with estrogen deficiency in their menstrual history.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

REFERENCES