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The influence of smoking on postmenopausal bone markers

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Abstract

Smoking is an important determinant of osteoporosis. There are a wide variety of mechanisms by which smoking induces bone toxic effects. Such mechanisms include alterations in calciotropic hormone metabolism and intestinal calcium absorbation, dysregulation in sex hormone production and metabolism, alterations in adrenal cortical hormone metabolism and direct cellular effects of cigarette use on bone cells. To assess the effect of smoking on vitamin D, serum parathyroid hormone (PTH) and calcium we studied 86 postmenopausal women (50-70 years), who were smokers previously or who were current smokers. Our results are compare with those of 34 women of the same age who had never smoked. Differences between the three groups were analyzed using one-way analysis of variance and Student's unpaired t-test. Postmenopausal women who were current smokers had significantly reduced levels of serum 25OHD ($P<0.01$) and PTH ($P<0.001$). There was no difference in serum calcium between never smokers, ex-smoker and current smokers ($P=0.184$). The unchanged plasma calcium among smokers in spite of lower levels of PTH and 25OHD could be a result of a decreased calcium uptake in bone.

Keywords: *Smoking, Osteoporosis, Parathyroid hormone (PTH), Vitamin D, Postmenopausal women*.

1. Introduction

Osteoporosis is a complex heterogeneous disorder characterized by an imbalance in bone remodeling which culminates in reduced BMD, deterioration of microarchitectural integrity of the bone, and increased risk of fracture. It has a major economic [1] and health impact. Osteoporotic fractures are associated with increased morbidity [2] and mortality [3].

Tobacco smoking is in most studies found to be associated with a low bone mass and an increased risk of osteoporotic fracture [4]. An increased bone loss has been registered in smokers [5].

A direct toxic effect of tobacco smoking on bone cells is also a possibility. Other hormonal systems, glucocorticoids, pituitary, and thyroid hormones, may be affected by smoking.

Parathyroid hormone (PTH) and vitamin D metabolites are crucial in the regulation of calcium homeostasis and bone metabolism. An effect of smoking on PTH or 25-hydroxyvitamin D (25OHD) levels has only been investigated in few studies [6,7,8] PTH regulates serum ionized calcium through alteration of bone resorption and renal calcium reabsorption [9] while 1,25 dihydroxyvitamin D (1,25-OH2-D) regulates intestinal calcium absorption [10, 11]. Two cross-sectional and cohort studies have demonstrated lower serum 25- hydroxyvitamin D (25-OH-D) and 1,25-OH2-D levels in current smokers compared to nonsmokers [12,13]. The mechanisms whereby smoking could decrease circulating levels of PTH and vitamin D metabolites remain to be worked out. One of the difficulties of the research area is that tobacco smoke is composed of a large number of more or less potentially toxic chemical compounds, including `tars' and nicotine, but also several heavy metals like cadmium, hydroxyquinones, thiocyanate, nitrosamines and others [14].

Reports on the effect of smoking on serum PTH have been conflicting. Few studies have shown a vitamin D dependent rise in PTH [15]. On the contrary, other studies demonstrated suppressed PTH levels despite low vitamin D levels [16]. The underlying mechanisms for this difference in serum PTH have not been fully investigated. However, confounding effects of weight, alcohol consumption, estrogen use, physical activity, sun exposure, and variability in calcium and vitamin D intake may account for the inconsistent PTH levels in published studies [17].

2. Materials and Methods

To assess the effect of smoking on vitamin D, serum parathyroid hormone (PTH) and calcium we studied 86 postmenopausal women, who were smokers previously or who were current smokers.

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Their mean age was 59 years (50-70 years). Our results are compare with those of 34 women of the same age who had never smoked.

Women with disease known to affect bone or calcium metabolism and those which are on Vitamin D supplement, were excluded from the study.

Patients taking Ca supplement were asked to stop these one week before being studied. Smoking status and fracture history was obtained by a standart questionnaire.

Serum 25-hydroxyvitamin D (25(OH)D normal range 30-60 ng/ml, PTH (10-65 pg/ml) and Ca (8-11 mg/dl) were measured on the fasting sample. We use the electrochemiluminescence assay (ECL) on Cobas 6000 from Roche Diagnostics.

Differences between the nonsmoking, smoking and exsmoking were evalueted using one-way analysis of variance.

Differences between any two groups were analysed using student's unpaired t-test. Significance limits was $P<0.05$. For the statistical analysis we used SPSS.20 programm.

3. Results and Discussion

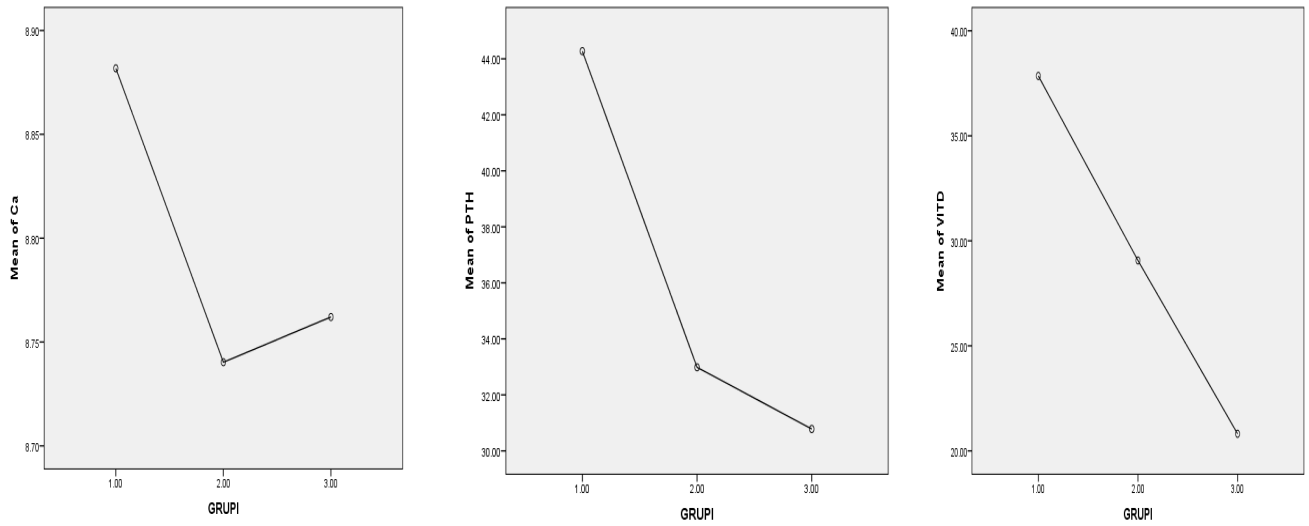
Mean level of PTH was lower in the postmenopausal women that are current smokers (30.78 pg/ml ± 9.024) compare with the nonsmokers and the exsmokers. Lower levels of 25OHD also were detected in smokers (20.08 ng/ml ± 4.232). (Table 1.).

Analysis of the variables using the one way analysis of variance (ANOVA) showed that there were significant differences in the levels of serum PTH between nonsmoker, exsmoker and current smokers with $F_s= 22.6$ and $P<0.001$.

Also significant differences we found and in the levels of 25OHD with $F_s= 50.600$ and $P<0.001$. But no defferences was found in serum calcium $F_s= 1.131$and $P=0.327$ ($P>0.05$).

Table 1. Mean and significance of differences of the parameters for the three groups

	Nonsmokers	***Exsmokers***	***Smokers***	***P***
PTH (pg/ml)	44.3± 7.8	32.99 ± 9.67	30.78 ± 9.024	0.001
25OHD (ng/ml)	37.9 ± 7.44	29.1 ± 8.55	20.08 ± 4.232	0.001
Ca (mg/dl)	8.88 ± 0.47	8.74 ± 0.44	8.76 ± 0.329	0.327^{ns}



(a) (b) (c)

Figure 1. a) Ca levels **b)** PTH levels **c)** Vitamin D levels. Differences between the three groups: **1.** Non smokers **2**. Ex smokers and **3.** Current smokers

Table 2. Paired Samples Test

		Paired Differences					*t*	*df*	*Sig. (2-tailed)*
		Mean	SD	SE Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	PTH Non smokers – PTH Smokers	13.491	6.729	1.154	11.143	15.839	11.690	33	.000
Pair 2	VITD Non smokers – VITD Smokers	17.038	8.722	1.495	13.994	20.081	11.389	33	.000
Pair 3	Ca Non smokers – Ca Smokers	.119	.514	.088	-.059	.299	1.358	33	.184

Differences between the two groups current smokers and non smokers were analysed using Student's unpaired t-test.

Postmenopausal women who were current smokers had significantly reduced levels of serum 25OHD ($P<0.01$) and PTH ($P<0.001$) compared with nonsmokers. There was no difference in serum calcium between current smokers and nonsmokers ($P=0.184$). The unchanged plasma calcium among smokers in spite of lower levels of PTH and 25OHD could be a result of a decreased calcium uptake in bone.

We can explain the lower levels of 25OHD among smokers with the fact that smoking may alter hepatic metabolism of vitamin D by influencing 25 hydroxylase (CYP2R1) in the liver and lowering serum 25-OH-D, similar to the effect of smoking on enhanced hepatic degradation of estrogen The pathophysiologic mechanism for low 1,25-OH2-D levels in smokers has not been fully explored. However, it has been hypothesized that low calcitriol levels may be due to low availability of 25-OH-D, a metabolic precursor to 1,25-OH2-D, or potentially due to suppression of PTH release [18].

The reduced serum PTH among smokers might therefore be explained by a decrease secretion or an increased degradation of the hormone. Several hypotheses have been put forward concerning the mechanisms by which smoking affects bone, the main focus being on the antiestrogenic effect. Smokers are lean [19], have an early menopause [20], and have reduced levels of circulating oestrogens due to an increased hepatic turnover [21]. All these factors contribute to a reduced exposure to estrogen, resulting in an increased early bone loss. Other lifestyle factors are regarded as more prevalent among smokers compared to nonsmokers such as less physical activity, increased alcohol intake, or associated nutritional deficiencies, all of which might play a role.

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