

Original Article

## Smoking and Hyperparathyroidism in Patients on Maintenance Hemodialysis

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### Abstract

**Background.** Smoking is a well recognized risk factor for osteoporosis in the general population but in patients with end-stage renal disease (ESRD) the association between smoking and bone turnover has never been fully investigated and clarified.

**Methods.** One hundred stable non-diabetic hemodialysis patients were included in this retrospective study. All patients underwent hemodialysis three times weekly with biocompatible filters and never used aluminum-containing phosphate binders. Hepatitis B or C positive patients were excluded. Intact parathyroid hormone (iPTH) measured by means of an immunochemiluminescence assay and alkaline phosphatase were used as markers of bone turnover. All iPTH measurements were performed before the initiation of any treatment with vitamin D or analogs. Regression analysis was used to confirm the correlations and to adjust for potential confounders.

**Results.** Sixty patients (60%) were smokers; 40% heavy smokers (>1pack/day) and 60% light smokers (<1pack/day). Heavy smokers had higher serum levels of iPTH (median: 310 pg/ml) when compared to light smokers (230 pg/ml) and non-smokers (180 pg/ml). On multivariate linear regression analysis smoking was confirmed to be an independent correlate of iPTH ( $\beta=0,27$ ,  $P=0,002$ ) and alkaline phosphatase ( $\beta=0,25$ ,  $P<0,05$ ). On univariate logistic regression analysis the risk of high iPTH was higher in heavy smokers (OR: 5,4, 95% CI: 1,7-17,  $P=0,005$ ) than in non-smokers and this risk became even stronger (OR: 10,1, 95% CI: 2,8-39,  $P<0,001$ ) after adjustment for a series of potential confounders.

**Conclusions.** In hemodialysis patients smoking is independently associated with high levels of iPTH and alkaline phosphatase. Further studies are needed to clarify whether this association is causal or not.

**Keywords:** hemodialysis; end-stage renal disease (ESRD); intact parathyroid hormone; secondary hyperparathyroidism; smoking

### Introduction

Smoking is a major health hazard and established risk factor for bone loss and fractures in the general population that appears to be independent of other risk factors such as age,

weight, sex and menopausal status [1]. Data from published studies and meta-analyses suggest that this relationship is dose-dependent and, at least partially, reversible but the mechanisms underlying smoking-associated bone loss and fracture risk remain poorly understood [2,3].

Possible explanations for the association between smoking and reduced bone density might be that smokers have a low intake of calcium and/or vitamin D, a low calcium absorption, reduced serum levels of vitamin D, a high calcium resorption from the skeleton or an excessive excretion of calcium in the urine [4,5]. This could lead to a negative calcium balance that normally would cause a compensatory increase in serum parathyroid hormone (PTH). However, both low<sup>6-9</sup> as well as high [4,10-11] PTH levels have been reported as a result of smoking.

In patients on hemodialysis and in general in chronic kidney disease, bone mineral density may be adversely affected by a number of additional factors, but many of them have not been studied extensively. Secondary hyperparathyroidism, adynamic bone disease and osteomalacia due to aluminum overload, the main bony problems in chronic renal disease, may all be responsible for a reduction in bone mineral density and result in an increased fracture risk [12].

However, in patients with chronic kidney disease the association between smoking and bone turnover has never been fully investigated and clarified. The aim of the present study is to investigate the possible interrelationships between smoking and markers of bone turnover in maintenance hemodialysis patients.

### Patients and methods

One hundred stable non-diabetic hemodialysis patients recruited from the same dialysis unit were included in this retrospective study. All patients underwent hemodialysis three times weekly with biocompatible filters and never used aluminum-containing phosphate binders. Hepatitis B or C positive patients were excluded. The patients’ characteristics are summarized in Table 1.

Intact parathyroid hormone (iPTH) measured by means of an immunochemiluminescence assay and alkaline phosphatase was used as a marker of bone turnover. All iPTH measurements were performed before the initiation of any treatment with vitamin D or analogs

**Table 1.** Demographics and patients' characteristics

Sex		
Men		44
Women		56
Age		
Mean		54±10
Range		25-75
Duration of hemodialysis		
Range (years)		2-10
Hours of dialysis per week		
Mean		11±4
Range		7-15
Dialysate calcium (mEq/L)		3
Serum calcium (mg/dl)		9,3±0,8
Serum phosphorus (mg/dl)		6,1±0,9
iPTH (pg/ml)		
Mean		433±294
Range		110-1150
Alkaline phosphatase (U/L)		
Mean		300±110
Range		175-580

Regression analysis was used to confirm the correlations and to adjust for potential confounders. Statistical analysis was performed with SPSS version 11.0 (SPSS Inc., Chicago, IL, USA). Statistical significance threshold was set at 0,05. Results are expressed as mean ± SD.

## Results

Sixty patients (60%) were smokers; 40% heavy smokers (>1pack/day) and 60% light smokers (<1pack/day). Heavy smokers had higher serum levels of iPTH (median: 310 pg/ml) when compared to light smokers (230 pg/ml) and non-smokers (180 pg/ml). On multivariate linear regression analysis smoking was confirmed to be an independent correlate of iPTH ( $\beta=0,27$ ,  $P=0,002$ ) and alkaline phosphatase ( $\beta=0,25$ ,  $P<0,05$ ). On univariate logistic regression analysis the risk of high iPTH was higher in heavy smokers (OR: 5,4, 95% CI: 1,7-17,  $P=0,005$ ) than in non-smokers and this risk became even stronger (OR: 10,1, 95% CI: 2,8-39,  $P<0,001$ ) after adjustment for a series of potential confounders, such as gender, age, BMI, serum calcium, etc.

## Discussion

The present study evaluated retrospectively 100 patients on maintenance hemodialysis in order to investigate possible correlations between smoking and markers of bone turnover such as iPTH and alkaline phosphatase. In summary,

smoking is independently associated with high levels of iPTH and alkaline phosphatase in hemodialysis patients. Whether this association is causal or not remains an unanswered question and further prospective randomized trials are needed to clarify this issue.

There are several previous reports on the relation between smoking and serum PTH with conflicting results, but our study is the single one referring to hemodialysis patients, a group of people suffering from a broad spectrum of bone disturbances ranging from secondary hyperparathyroidism (high PTH) to adynamic bone disease (low PTH).

Thus, Landin-Wilhelmsen *et al.* in a study on 347 men and women<sup>6</sup>, Brot *et al.* in a study on 510 women aged 45-58 years [7], Need *et al.* in a study on 405 postmenopausal women [8] and Mellström *et al.* in a case-control study on 129 men with earlier partial gastrectomy and 216 controls [9] found serum PTH to be significantly lower in smokers. On the other hand, Rapuri *et al.* in a study on 444 elderly women [4], Ortego-Centeno *et al.* in a study on 57 healthy males below the age of 45<sup>10</sup> and Szulc *et al.* in a study on 719 men aged 51-85 years<sup>11</sup> found serum PTH to be significantly higher in smokers than non-smokers.

Higher levels of iPTH in smokers than non-smokers found in our study is a plausible result if we take into consideration the negative calcium balance frequently encountered in hemodialysis patients, but unfortunately a definite explanation cannot be given.

Our study has several shortcomings. First of all, this is a retrospective study that includes a relatively small number of subjects, but the careful adjustment for potential confounders results in a conclusion that smoking is independently associated with high levels of iPTH and alkaline phosphatase. Additionally, the special population of patients on maintenance hemodialysis has not been investigated in previous studies. However, it is obvious that a prospective randomised study in the future would be necessary to confirm the results of the above work.

## Conclusions

In hemodialysis patients smoking is independently associated with high levels of iPTH and alkaline phosphatase. Further studies are needed to clarify whether this association is causal or not.

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*Conflict of interest statement.* None declared.

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