Vitamin D Receptor Gene Polymorphisms and Bone Mineral Density in Hemodialysis Patients

H.	Hisako	Yanagi ^a
S.	Shigeo	Tomura ^a
S.	Satoshi	Kurihara ^c
K.	Kei	Yamana ^a
H.	Hideo	Hamaguchi ^b
S.	Shigeru	Tsuchiya ^a

Institutes of ^aCommunity Medicine and ^bBasic Medical Sciences, University of Tsukuba, and ^cDivision of Medicine, Kasukabe-Shuwa Hospital, Kasukabe, Japan

Dr. H. Yanagi, Institute of Community Medicine, University of Tsukuba, Tsukuba 305 (Japan)

Dear Sir,

Renal osteodystrophy is one of the major complications in patients undergoing maintenance hemodialysis. Recently, common polymorphisms of vitamin D receptor (VDR) gene have been shown to be associated with bone mineral density (BMD) in healthy individuals [1]. The effects of the polymorphism of VDR gene on hemodialysis patients are, however, still unknown. We

analyzed the genotypes of VDR gene and measured BMD by dual-energy X-ray absorptiometry in 97 Japanese hemodialysis patients.

Sixty-four males and 33 females (mean age 51.5 ± 11.2 years; range 21-81 years) with a mean duration of dialytic therapy of 7.5 ± 5.0 years were evaluated. BMD at the anteroposterior view of the lumbar spine

Table 1. VDR genotype, BMD and other factors (mean $\pm$ SD) in hemodialysis (HD) patients
All patients (n = 97)

Age, years

HD duration, years

BMD at L2-L4, g/cm²

Z score at L2-L4

BMD at distal radius, g/cm²

Total calcium, mg/dl

Phosphorus, mg/dl

Alkaline phosphatase, IU/ml

Intact PTH, pg/ml

HS-PTH, pg/ml

BB

(n = 2)

59.0 ± 1.0

8.0 ± 4.0

0.918 ± 0.099
0.107 ± 0.447
0.458 ± 0.063
9.2 ± 0.2
5.2 ± 0.4
200 ± 37
127 ± 59
21,200 ± 13,300

Bb

(n=18)

49.1 ± 11.7
7.3 ± 6.6
0.905 ± 0.183
-0.299 ± 1.552
0.553 ± 0.096
9.6 ± 0.9
5.6 ± 1.4
175 ± 145
256 ± 332
25,400 ± 30,100

bb

(n=77)

51.6 ± 11.1
7.6 ± 4.9
0.939 ± 0.249
0.027 ± 1.764
0.536 ± 0.109
9.7 ± 0.8
5.8 ± 1.4
154 ± 72
215 ± 271
27,200 ± 28,900

59.0 ± 1.0
8.0 ± 4.0
0.918 ± 0.099
0.107 ± 0.447
0.458 ± 0.063
9.2 ± 0.2
5.2 ± 0.4
200 ± 37
127 ± 59
21,200 ± 13,300

CGN patients without PTx (n = 71) (n = 2)

Age, years

HD duration, years

BMD at L2-L4, g/cm²
 Z score at L2-L4
 BMD at distal radius, g/cm²
 Total calcium, mg/dl
 Phosphorus, mg/dl
 Alkaline phosphatase, IU/ml
 Intact PTH, pg/ml
 HS-PTH, pg/ml

(n=14)

49.4 ± 10.5

8.9 ± 5.2

0.874 ± 0.155

-0.565 ± 1.051

0.531 ± 0.089

9.5 ± 0.8

5.6 ± 1.5

189 ± 160

293 ± 360

28,600 ± 32,900

(n=55)

50.9 ± 10.2

7.6 ± 4.9

0.937 ± 0.226

-0.011 ± 1.816

0.524 ± 0.105

9.8 ± 0.9

5.7 ± 1.2

155 ± 76

239 ± 298

31,500 ± 31,400

HS = Highly sensitive.

KARGER

E-Mail karger@karger.ch Fax + 41 61 306 12 34 <http://www.karger.ch>

©1997 S. Karger AG, Basel 0028-2766/97/0771-0114\$12.00/0

This article is also accessible online at: <http://BioMedNet.com/karger>

Table 2. VDR genotype, intact PTH level and hemodialysis (HD) duration in HD duration

	Group PL	Group PM	Group PH	
CGN patients without PTx (n = 71)	3/4	Bb bb	BB Bb bb	BB Bb bb
< 5 years	0 16 13 8	0 0 1		
Between 5 and 10 years	0 1 8	0 1 11	0 1 4	
> 10 years	0 22 127	0 38		
Total	0 4 16 2 6 26	0 4 13		

(L2-L4) and the distal one-third portion of the right radius were measured by dual-energy X-ray absorptiometry using Norland XR-26. The Z score of BMD (average value in controls 0, SD 1) was calculated to adjust for age and sex. Japanese control data were obtained from Nisshou Med-Science Inc., Tokyo, Japan. Blood samples were taken before dialysis. Serum

calcium, phosphorus and alkaline phosphatase were measured using an auto analyzer (Hitachi 736, Hitachi, Japan). Intact parathyroid hormone (PTH) was measured by an immunoradiometric assay (IRMA-ALLEGRE technique), and highly sensitive PTH was measured by radioimmunoassay. DNA was extracted from peripheral leukocytes by the standard phenol-chloroform procedure and VDR gene allelic polymorphisms were assessed by BsmI endonuclease restriction after specific PCR amplification [1]. Genotypic polymorphism was defined as BB (absence of restriction site on both alleles), bb (presence of restriction site on both alleles) and Bb (heterozygous).

The major underlying renal disease consisted of chronic glomerulonephritis (CGN) in 76 cases, diabetic nephropathy in 14 cases, polycystic kidney disease in 3 cases and nephrosclerosis in 2 cases. Five out of 76 CGN patients had undergone parathyroidectomy (PTx). Student's t test and ANOVA were used for statistical analysis with a Stat-View version 4.11 statistical software package.

The results of VDR genotypes and study variants are shown in table 1. All of 5 patients with PTx had the bb genotype. To exclude the effects of PTx and underlying renal disease, we also indicated the data of CGN patients without PTx. There were no differences in mean age and duration of hemodialysis among the three genotype groups. Although the mean BMD and Z score at L2-L4 in the Bb genotypes were slightly lower than those in the bb genotype in both groups of all patients and CGN without PTx patients, there were no significant differences. Mean levels of BMD at the distal radius were almost the same in the Bb genotype as in the bb genotype. There were no significant differences in mean levels of total calcium or phosphorus, alkaline phosphatase, intact PTH and highly sensitive PTH between groups.

To examine the effects of VDR genotype on the PTH level, patients were divided into the following three groups: serum intact PTH levels < 60 pg/ml (L); between 60 and 360 pg/ml (M); > 360 pg/ml (H). The numbers of patients of each group and duration of hemodialysis are shown in table 2. Frequencies of genotypes were almost similar among groups, suggesting that VDR genetic polymorphisms did not influence the PTH level.

From our findings, we conclude that VDR genetic polymorphisms may not be associated with BMD at the distal radius and PTH levels in hemodialysis patients.

Reference

1 Morrison NA, Qi JC, Tokita A, et al: Prediction of bone density from vitamin D receptor alleles. *Nature* 1994;367:284-287.

VDR Genotype and BMD in HD Patients

Nephron 1997;77:114-115