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Association of polymorphisms of VDR and CASR with clinical and laboratory manifestations of primary hyperparathyroidism (PHPT)

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OBJECTIVES

Clinical manifestations and severity PHPT patients vary significantly. Some studies show that changes in the clinical manifestations PHPT may be due to genetic factors, in particular the VDR polymorphisms and CASR.

The objective of this study was to evaluate the influence of VDR gene polymorphism and CASR on the performance of calcium-phosphorus metabolism and condition of bone density in patients with PHPT.

METHODS

The study included 187 patients with PHPT (54 [49; 64] years,160W/27M). Exclusion criteria were genetically confirmed by multiple endocrine neoplasia syndrome type I or II, suspicion of MEN syndrome based on the identification of patients younger than 40 years PHPT two or more adenomas (hyperplasia) of the parathyroid glands, and / or entities pituitary, adrenal, pancreas, neuroendocrine tumors of the gastrointestinal tract), normocalcemic PHPT, severe chronic renal failure, hepatic failure, congenital anomalies of the kidney and urinary tract diseases, cancer and severe somatic diseases. All patients were examined: biochemical blood analysis (total and ionized calcium, phosphorus, creatinine to estimate GFR, alkaline phosphatase), the definition of a daily urinary calcium excretion, hormonal analysis of PTH, 25 OH (D). All patients were analyzed polymorphisms CASR. In 166 patients (139W/27M) were analyzed polymorphisms VDR- ApaI, BsmI, FokI, Cdx2, TaqI. The distribution of genotypes consistent with the condition of Hardy-Weinberg.

RESULTS

VDR polymorphism analysis showed that the polymorphisms FokI and BSMI influence the clinical manifestations PNPT. Carriers FF genotype polymorphism FokI level 25OH D is significantly higher than in the presence of a genotype ff and Ff (p = 0,014).
PTH levels tended to a higher level in the group genotype FF and Ff but the differences were not statistically significant (p = 0,07).
Carriers genotype bb polymorphism Bsml level b-cross laps and osteocalcin was lower than in the combined genotype BB + Bb (p = 0,036 and p = 0,041). The relationship with the levels of calcium in the blood, urine calcium or PTH has been received.
According to the results determined by densitometry higher BMD values in all parts of the skeleton, but significant differences were only in the spine (p = 0,038). There was no association with indicators CASR polymorphisms metabolism of calcium and phosphorus, PTH, bone turnover markers, BMD in patients with PHPT.

Tab.1. Indicators of calcium-phosphorus metabolism, bone turnover markers in genotype polymorphism FokI

Parameters	FokI				p
	FF	Ff	ff	FF+Ff	
PTH, pg/ml	672,7 [103,5;815,4]	424,8 [130,9; 475,3]	380,7 [126;507]	466,5 [126,6;475,2]	NS
OK,ng/ml	112,7 [30,3;300]	97,7 [37,7;120]	84,2 [32,9;106,7]	91,9 [35,9;111,6]	NS
CTX,ng/ml	1,61 [0,529;2,23]	1,53 [0,66;1,78]	1,26 [0,62;1,56]	1,42 [0,65;1,67]	NS
25OHD, ng/ml	14,8[1,2,3] [11,2;18,0]	10,69 [6,95;13,5]	11,9 [7,8;15,2]	11,2 [7;14,4]	P<0,05
Ca, mmol/l	2,92 [2,75;3,06]	2,98 [2,73;3,23]	2,92 [2,71;3,07]	2,96 [2,71;3,13]	NS
Ca++, mmol/l	1,39 [1,29;1,4]	1,39 [1,27;1,5]	1,42 [1,28;1,47]	1,4 [1,27;1,49]	NS
alkaline phosphatase, Ed/l	236,5 [93;246]	207,7 [84;282,1]	261,4 [84;274]	252,6 [84;258]	NS
Ca, mmol/day	7,41 [4,07;10,08]	9,17 [5,48;12,05]	8,16 [4,76;10,5]	8,7 [5,27;11,4]	NS

[1] BB vs bb, [2] BB+Bb vs bb, [3] BB+Bb vs bb

Tab.2 Indicators of calcium-phosphorus metabolism, bone turnover markers in genotype polymorphism Bsml

Parameters	Bsml				p
	BB	Bb	bb	BB+Bb	
PTH, pg/ml	450,2 [125,5;489,9]	518,2 [130,8;542]	458,8 [114,3;570,0]	456,8 [125,9;475,5]	NS
OK,ng/ml	91,4 [37,9;94,4]	101,69 [35,9;129,5]	68,2[3] [25,5;108,9]	93,15 [34,5;115,5]	P<0,05
CTX,ng/ml	1,45 [0,626;1,78]	1,51 [0,67;1,67]	1,093[1,2] [0,428;1,31]	1,43 [0,633;1,7]	P<0,05
25OHD, ng/ml	11,7 [7,39;15,8]	11,5 [2,48;15,1]	13,4 [7.8;15,5]	11,8 [7,7;15,5]	NS
Ca, mmol/l	2,92 [2,7;3,06]	2,96 [2,76;3,13]	2,95 [2,68;3,08]	2,94 [2,71;3,09]	NS
Ca++, mmol/l	1,4 [1,28;1,44]	1,38 [1,28;1,47]	1,42 [1,24;1,59]	1,39 [1,28;1,47]	NS
alkaline phosphatase, Ed/l	267,7 [67;300,05]	256,1 [86;267]	215,9 [55;237,9]	256,2 [79;266,8]	NS
Ca, mmol/day	8,51 [5,8;10,5]	8,7 [4,2;11,4]	7,76 [4,8;10,5]	8,51 [5,2;10,5]	NS

[1]ff vs FF, [2] Ff vs FF, [3] ff+Ff vs FF

Tab.3 Indicators of bone mineral density (BMDg / cm2) in genotype polymorphism Bcml

Parameters	Bsml				p
	BB	Bb	bb	BB+Bb	
L1-L4	0,96 [0,821;1,136]	0,881 [1,2] [0,744;0,994]	0,979 [0,869;1,117]	0,924 [0,774;1,096]	P<0,05
Total Hip	0,821 [0,718;0,954]	0,789 [0,678;0,905]	0,84 [0,714;0,923]	0,808 [0,714;0,923]	NS
Neck	0,749 [0,666;0,867]	0,738 [0,634;0,841]	0,784 [0,719;0,864]	0,748 [0,649;0,861]	NS
Radius total	0,429 [0,379;0,501]	0,432 [0,366;0,503]	0,489 [0,380;0,594]	0,427 [0,371;0,505]	NS
Radius 33%	0,507 [0,429;0,574]	0,508 [0,425;0,601]	0,579 [0,459;0,667]	0,504 [0,429;0,598]	NS

[1]bb vs Bb, [2] bb vs Bb

CONCLUSIONS

The polymorphisms FokI and BsmI VDR may affect clinic PGPT, which is of interest, given the high prevalence in the population PGPT. This result requires further study.

References

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