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Bone microarchitecture in adult patients with hypophosphatasia

Introduction. Hypophosphatasia (HPP) is a rare genetic bone disease caused by low levels of tissue non-specific alkaline phosphatase (TNSALP) leading to defects in bone mineralization. Consequently HPP is characterized by stress fractures with poor healing, bone deformities and extra-skeletal manifestations. To date, no data regarding bone microstructure, one of the main components of bone strength, are available in HPP. **Materials and methods.** Twenty-one adult patients with clinical HPP were examined (9 genetically tested, 6 male, 15 female, mean age 50.7 ± 12.8 yrs). Children were excluded from the analysis. Microstructure and volumetric bone mineral density (vBMD) were assessed by HR-pQCT (SCANCO Medical) at the ultra-distal radius and tibia. Total, trabecular and cortical vBMD (mgHA/cm^3) were evaluated. Microstructure analysis included the trabecular bone volume fraction (BV/TV), trabecular number (Tb.N, 1/mm), trabecular thickness (Tb.Th, mm), cortical thickness (Ct.Th, mm) and cortical porosity (Ct. Po, %). Areal BMD (aBMD) by DXA and TBS as well as bone turnover markers (BTM) were measured. Data were compared to a healthy, age and gender-matched control group (CTRL, 15 female, 6 male, mean age 52.8 ± 14.1 years). In addition, correlations between demographic data, TNSALP, BMD and microstructure were carried out. **Results.** TNSALP was decreased in all HPP patients (mean 26.0 ±12.7 U/L), Pyridoxal phosphate was elevated (mean 478.9 ± 836.7 µ/l). A positive family history for HPP was found in 50 % of HPP patients. Bone turnover markers, Calcium and Phosphate were in normal range in all HPP patients. Vitamin D deficiency (< 30 ng/ml) was found in 19 % of HPP patients. Tb.Th was significantly lower in HPP than in CTRL. All other trabecular and cortical bone microstructure parameters as well as vBMD were comparable between HPP and CTRL at both measuring sites. High aBMD at the lumbar spine (T-score +5.6) was found in 1 patient with HPP. aBMD at the lumbar spine was similar in HPP and controls whereas aBMD values at the hip were lower in HPP by trend. TBS was above the reference range (> 1.250) in all HPP patients and comparable to CTRL. TNSALP was not correlated to parameters of bone microstructure or bone mineral density. **Conclusions.** Trabecular thinning is the most conspicuous finding in bone microstructure in HPP. Established bone turnover markers besides TNSALP P do not reflect the increased fracture risk in adult patients with HPP. A wide range of aBMD values was found in HPP, but it was seen that aBMD is lower at the hip — but not the spine — in HPP.

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Risk of development of cardiovascular pathology with different VDR genotype

The purpose of the study was to perform a comparative analysis of the frequencies of the genotypes by the alleles BsmI (B/b) (rs1544410) and FokI (F/f) (rs2228570) of the VDR gene in patients with cardiovascular pathology of Grodno region in comparison with the genotypes of ethnic Belarusians living in six regions of Belarus. **Materials and methods.** 182 patients aged from 30 to 79 years were examined, 100 of them with arterial hypertension (AH) II degree and 82 with ischemic heart disease (IHD) in combination with AH II degree. The determination of BsmI and FokI of the VDR gene was performed by polymerase chain reaction. For comparison, the results of analysis of the genotypes of 719 ethnic Belarusians, including the Western region, were used. Statistical analysis was carried out by Statistica 10.0 software. **Results.** The heterozygous genotype at both polymorphic loci of BsmI and FokI of VDR gene was found with the greatest frequency. Genotypes BB and ff were encountered with the lowest frequency ($p < 0.0001$) both among patients and in the population, including Western population. Genotype bb and allele b were more frequent ($p < 0.05$) among patients (41.2 and 63.2 %, respectively) and in the Western region (42.9 and 65.3 %, respectively) than in the general population (31.4 and 56.7 %, respectively). Homozygous genotype BBff associated with the expression of the less active form of VDR was found with the lowest frequency, both among patients and in the population, including Western populations. Genotype bbFF associated with the expression of a more active form of VDR was more common in patients with IHD 17.1% than in the entire population of Belarus — 8.8 % ($p = 0.02$) and more often than in the Western population 6.7 % ($p = 0.04$). The most common among Western region Belarusians bbFf genotype — 28.1 %, was less common among patients with AH — 16.0% ($p = 0.047$) and IHD — 13.4 % ($p = 0.017$). Genotype bbff was more common among the whole group of patients — 12.1% ($p = 0.005$) and among patients with AH — 15.0 % ($p = 0.001$) than in the entire population of Belarusians — 5.7 %. Residents of Grodno region with genotype bbff of VDR gene have an increased risk of cardiovascular pathology (OR = 2.3 (95% CI 1.32–3.93) and AH developing (OR = 2.92 (95% CI 1.55–5.496), and those with genotype bbFF of VDR gene also have an increased risk of cardiovascular pathology (OR = 1.74 (95% CI 1.06–2.83) and IHD developing (OR = 2.14 (95% CI 1.14–4.03). **Conclusions.** Significant differences in frequency distribution of genotypes BsmI and FokI of the VDR gene in patients with cardiovascular pathology of Grodno region from general population data and an increased risk of development of AH/IHD in genotypes bbff and bbFF of VDR gene have been established. ■