Streszczenie w języku angielskim

Chronic kidney disease (CKD) and its main complication, called mineral and bone disorders (CKD-MBD), are leading health problems. Impaired mineralization, abnormalities in bone microarchitecture, and reduce bone strength, results in increased risk of fractures in patients with CKD. Disturbed bone quality and quantity negatively affect patient's life, and treatment, especially in advanced stages of CKD.

The aim of this doctoral dissertation was comprehensive assessment of the endogenous vitamin K (VK) metabolism by measuring the concentrations of vitamin K1 (phylloquinone), MK-4 and MK-7 (menaquinones) in the serum of healthy and 5/6 nephrectomy-induced CKD animals. Similarly, the concentrations of VK-dependent proteins (VKDP), such as osteocalcin (OC), non-carboxylated form (Glu-OC), and non-carboxylated matrix Gla protein (ucMGP) were assessed in serum. Additionally, both forms of OC: carboxylated (Gla-OC) and Glu-OC were evaluated at the bone level. To assess VK recycling, the expression of VKORC1, GGCX, and UBIAD1 genes in the bone tissue was determined. In order to assess the relationships between VKDP and bone mineral status, the obtained results were compared with densitometric measurements.

The analysis of vitamin K metabolism showed simultaneous decrease of VK1 levels and increase MK-4 and MK-7 concentrations in CKD rats. This may results from increased VK1 conversion to menaquinones. Progressive loss of kidney function results in increased concentration of total OC, which is associated with accumulation of this protein in the blood of uremic rats. On the other hand, the enhanced Glu-OC levels may be related to stimulatory effect of PTH. Despite the fact that bone tissue has required set of enzymes that enables VK recycling and its conversion to menaquinones, the production of sufficient amounts of active form of osteocalcin is impaired. In a consequence, in the course of CKD occur disturbed bone mineralization process. The analysis of the relationships between the parameters of bone mineral status, the VK cycle enzymes and VKDPs expression, showed that the above mentioned disorders may be associated with hyperparathyroidism and accelerated process of osteoblastogenesis stimulated by PTH. As a result, immature osteoblasts are unable to produce an adequate amount of active form of OC. The practical, and clinical significance of this research is that the measurement of the serum concentrations of total OC and Glu-OC, which are commonly used markers of VK deficiency, appear to have a limited importance in the course of CKD, especially in the presence of hyperparathyroidism.