VII. Streszczenie w języku angielskim

Vitamin D is a fat-soluble derivative of cholesterol and the main source of vitamin D3 for humans is its endogenous synthesis under the influence of sunlight. Vitamin D deficiency has been the subject of much research and in recent years the systemic role and pleiotropic effects of vitamin D, including its relationship to the cardiovascular system, diabetes, chronic kidney disease and other chronic diseases have received increasing attention. Vitamin D binding protein (VDBP) is a glycoprotein produced mainly in the liver, but also in the kidneys, lungs and brain. It is responsible for transporting about 85% of vitamin D metabolites. Research on VDBP is being conducted to discover new therapeutic possibilities. The association of VDBP with cardiovascular disease and diabetes has been documented. The gene encoding VDR is located on chromosome 12, with exons encoding, among other things, transcription factor and ligand-binding domains and the so-called zinc fingers of DNA-binding proteins and non-translational regions, and polymorphism of these regions has been linked to the occurrence of many diseases. VDR has been shown to be present in many tissues of the human body.

The aim of the present study was to evaluate the levels of vitamin D, vitamin D binding protein and vitamin D receptor in the general Primary Care population, to evaluate their levels in a group of patients with comorbidities such as hypertension, diabetes, chronic kidney disease and in a group of patients with other selected chronic diseases in the Primary Care population.

Included in the analysis were 252 adult patients aged 19-65 years under the care of the Academic Family Medicine Practice in Bialystok in 2019. Blood samples for the study of 25(OH)D3, 1α,25(OH)2D3, VDBP and VDR concentrations were collected in the winter-spring period of 2019. According to the diseases present, the group was divided into a reference group, comprising 56 patients without chronic diseases, and a study group, comprising 196 patients with chronic diseases. The study group was divided according to the presence of hypertension, diabetes, chronic kidney disease, lipid disorders, heart failure and hypothyroidism. The median age of patients in the study group was 58 years (minimum=32 years, maximum=65 years). Women accounted for 76.1% of patients, while men accounted for 23.9%. The most common chronic diseases were hypertension (63.8%), dyslipidemia (49.5%) and diabetes or pre-diabetes (26.5%). Vitamin D was supplemented by 39% of patients, with an additional 14.2% of patients supplementing vitamin D and vitamin K together. We analyzed the prevalence of vitamin D deficiency and vitamin D binding protein and vitamin D receptor levels in the general population and in selected disease entities.

Comorbidities, medications used chronically, and vitamin D supplementation were analyzed. Analysis of laboratory parameters in addition to the evaluation of concentrations of metabolites of vitamin D, its binding protein and receptor included assessment of morphotic elements of peripheral blood, selected biochemical parameters and lipidogram.

In our study population, vitamin D deficiency in the form of reduced 25(OH)D3 concentrations affected 43.9% of patients (86 subjects). In the study group, the median concentrations were: 25(OH)D3 - 21.85 ng/ml, 1α,25(OH)2D3 - 74.26 pg/ml, VDBP - 267.8 μg/ml, and VDR - 30.73 pg/ml. These values were not statistically significantly different compared to the reference group ($p>0.05$). When the study group was divided by gender, a statistically significant higher concentration of 1,25-dihydroxyvitamin D3 was observed in women compared to men (Me=82.85pg/ml vs. Me=58.99pg/ml, $p=0.001$). In the entire study group, a statistically significant decrease in vitamin D Vit D 25(OH) total was observed with an increase in triglycerides ($R=-0.16$, $p=0.036$) and with an increase in fasting glucose ($R=-0.17$, $p=0.028$). Vitamin D supplementing patients in the study group had statistically significant higher 25-hydroxyvitamin levels compared to non-supplementing vitamin D patients (Me=25.06ng/ml vs Me=18.84ng/ml, $p=0.000$) and vitamin K supplementers had statistically significantly higher 25-hydroxyvitamin D3 concentrations compared to non-supplemented vitamin K patients (Me=30.53ng/ml vs Me=20.26ng/ml, $p=0.000$) and higher VDBP concentrations than non-supplemented vitamin K patients (Me=287.55μg/ml vs Me=267.45μg/ml, $p=0.0237$).

Among patients with hypertension, diabetes, chronic kidney disease, dyslipidemia, heart failure and hypothyroidism, the values of 25(OH)D3, 1α,25(OH)2D3, VDBP and VDR concentrations were not statistically significantly different compared to the reference group ($p>0.05$). Patients with diabetes had statistically significantly higher levels of VDR compared to patients without diabetes in the study group (Me=38.78pg/ml vs Me=29.105pg/ml, $p=0.022$). In turn, statistically significant correlations of vitamin D metabolites, VDBP and VDR occurred in detailed analysis according to variables such as, gender, weight, BMI, blood pressure values, cardiac function, concentrations of biochemical parameters and coexistence of other diseases. Examining the effect of chronic medications in the study group, patients taking ACEIs had statistically significant lower concentrations of 1α,25-hydroxyvitamin D3 compared to patients not taking this group of medications (Me=70, 76pg/ml vs Me=80.45pg/ml, $p=0.045$), while those using diuretics had statistically significant higher

25(OH)D3 concentrations compared to patients not taking diuretics (Me=24.13ng/ml vs Me=21.37ng/ml, p=0.0247).

Based on the study, the following conclusions were drawn:

1. The phenomenon of vitamin D deficiency is common in the Primary Care patient population.

2. The lack of differences in the concentrations of total 25-hydroxyvitamin D3, 1α,25-dihydroxyvitamin D3, VDBP and VDR compared to the reference group may be due to the insufficient size of the study group and the use of vitamin D supplementation by some patients of the study group.

3. The presence of chronic diseases did not affect the difference in 25-hydroxyvitamin D3, 1α,25-dihydroxyvitamin D3, VDBP and VDR concentrations in the study group compared to the reference group.

4. Significant correlations of 25(OH)D3, 1α,25(OH)2D3, VDBP and VDR were present in the detailed analysis of chronic diseases according to variables such as, gender, weight, BMI, blood pressure values, cardiac function, concentrations of biochemical parameters, and coexistence of other diseases and nicotinism.

5. Vitamin D supplementation along with vitamin K increased 25-hydroxyvitamin D3 and VDBP levels.

6. Statins, angiotensin-converting enzyme inhibitors and diuretics affect the concentrations of vitamin D metabolites, while VDBP steadiness is affected by smoking tobacco products.

7. There is a need to revise the norms of vitamin D concentrations depending on the presence of chronic disease, especially hypertension, diabetes mellitus or chronic kidney disease, and coexisting chronic diseases.

8. Due to the limitations of the presented study, the effect of vitamin D supplementation on cardiovascular disease was not studied prospectively, but such studies are planned for the future.