Streszczenie w języku angielskim

Psoriasis is a chronic inflammatory skin disease characterized by increased epidermal proliferation and immune disorders, affecting 2-4% of the population. In the age of modern knowledge, psoriasis is perceived as a systemic disease associated with cardiovascular diseases, hypertension, diabetes, metabolic syndrome and obesity. The causes of comorbidity are considered to be a common genetic basis, as well as chronic inflammation and increased production of pro-inflammatory cytokines, which are the basis of the so-called psoriatic march, which leads to insulin resistance and the development of atherosclerosis and consequently to cardiovascular diseases.

Increased serum concentrations of the proteins such as PCSK9 (proprotein convertase subtilisin / kexin 9), ANGPTL8 (angiopoietin-like protein 8), sortilin and CETP (cholesteryl ester transfer protein) in persons with cardiometabolic diseases may indicate possible pathogenetic associations of psoriasis and its comorbidity.

The aim of the study included in this doctoral dissertation was to assess the concentration of PCSK9, ANGPTL8, sortilin and CETP proteins in patients with plaque psoriasis and to establish the relationship between them and disease activity, indicators of inflammation and metabolic disorders, and to analyze the impact of systemic therapy with methotrexate and acitretin on the concentration of evaluated proteins and the possibility of using the assessment of their concentrations in monitoring the effectiveness of treatment and assessing the risk of developing cardiometabolic complications.

The study included 35 adult patients with plaque psoriasis of varying severity requiring systemic treatment. The control group consisted of 18 healthy people, matched for sex and age. The consent for the study was granted by the Bioethics Committee of the Medical University of Bialystok (number: R-I-002/429/2017). The studies were carried out at the Department of Dermatology and Venereology of the Medical University of Bialystok in patients with plaque psoriasis during exacerbation, as well as after 3 months of treatment with two methods of systemic therapy - methotrexate at a dose of 15 mg/week orally and acitretin at a dose of 0.5 mg/kg/day. Proteins concentrations were determined by enzyme immunoassay.

In the study group, the concentration of PCSK9 was significantly higher than in the control group ($p < 0.01$). There was no correlation between the concentration of PCSK9 and the severity of psoriasis expressed by the PASI index in patients before treatment.

A statistically significant negative correlation was found between PCSK9 and total and LDL cholesterol (both p=0.048). After twelve weeks of systemic treatment, the mean concentration of PCSK9 decreased significantly, remaining significantly higher than in the control group. When analyzing the effect of individual drugs, the serum concentration of PCSK9 decreased significantly in patients treated with methotrexate ($p<0.05$), while a further significant increase in the concentration of PCSK9 was observed in patients treated with acitretin ($p<0.05$).

The mean ANGPTL8 concentration was significantly higher in the psoriasis group before treatment than in the control group ($p<0.05$). After systemic treatment, a statistically significant further increase in ANGPTL8 concentration was found in the study group. After patients were divided by drug treatment, a significant increase in ANGPTL8 concentration was observed in patients treated with acitretin ($p <0.05$). Taking into account the biochemical parameters, a significant negative correlation of the tested protein with total and LDL cholesterol was found.

Regarding the CETP protein, no statistically significant difference was found in its concentrations between the control group and the study group ($p>0.05$). A strong positive correlation was found between CETP concentration and total cholesterol (p=0.022) as well as the activity of alanine and aspartate aminotransferase (=0.022, p=0.028, respectively) in patients after treatment.

In the analysis of sortilin concentrations, no statistically significant differences were found between the control and study groups ($p>0.05$). The use of methotrexate caused a significant decrease in sortilin levels, which was lower than before the treatment. Taking into account the biochemical parameters, a strong positive correlation was found between sortilin and the parameters of inflammation.

Conclusions:

1. PCSK9 may be a new biomarker of psoriasis, but not of its severity or inflammation.

2. PCSK9 concentration determination may be helpful in choosing the treatment method in patients with psoriasis - methotrexate as the first-line drug in patients with elevated PCSK9 concentration.

3. PCSK9 may be used as an indicator of the risk of cardiometabolic diseases in psoriasis.

4. Systemic treatment with acitretin causes a significant increase in ANGPTL8 concentration, which may indicate a protective role of this protein in psoriasis.

5. High ANGPTL8 concentration may reduce the risk of developing atherogenic dyslipidaemia in patients with psoriasis.

6. Increased CETP levels may be a marker of the severity of atherogenic dyslipidemia and liver dysfunction during systemic treatment of psoriasis.

7. Sortilin may be a new marker of metabolically induced inflammation in psoriasis.