3. Streszczenie w języku angielskim

Biomarkers in the prediction of perinatal complications in twin gestation.

Multifetal gestations carry a high risk of developing serious pregnancy complications with the most common one being premature delivery. According to the literature, the percentage of premature deliveries reaches about 60% in twin gestations. Therefore, the reduction of the percentage of premature deliveries and development of the effective methods of their prediction in the population of multifetal pregnancies is one of the most important aims of perinatology.

The dissertation aimed at the assessment of three biomarkers: pregnancy-associated plasma protein A, elafin and secretory leukocyte peptidase inhibitor in the prediction of perinatal complications in twin pregnancy.

Research hypotheses:

- the risk of twin pregnancy complications depends on the concentrations of pregnancy-associated plasma protein A in the first trimester of pregnancy;
- low (below the 10^{th} percentile for gestational age) and high (above the 90^{th} percentile for gestational age) concentrations of pregnancy-associated plasma protein A are the predictive factors of pregnancy complications, such as premature delivery, preterm premature rupture of membranes, cervical insufficiency, gestational diabetes, gestational hypertension, preeclampsia, intrauterine fetal demise, low birth weight of a newborn, or intertwin birth weight discordance;
- the presence of elafin or SLPI in the cervicovaginal fluid of asymptomatic women between 20 and 24 weeks of twin gestation is a predictive factor of premature delivery before 37 or 34 weeks of gestation.

The dissertation includes two original papers. The paper entitled „**Cervical expression of elafin and secretory leukocyte peptidase inhibitor does not predict preterm delivery in twin pregnancy – results from a pilot study**" presented the effectiveness of the assessment of the presence of elafin and secretory leukocyte peptidase inhibitor in the cervicovaginal fluid in the prediction of premature delivery in twin gestations. The mRNA of elafin and secretory leukocyte peptidase inhibitor was measured in the samples of the fluid collected between 20 and 24 weeks of gestation in asymptomatic patients with twin pregnancies. The expression of elafin and secretory leukocyte peptidase inhibitor did not correlate with the duration of gestation, the occurrence of premature delivery before 37 or 34 weeks of gestation, the occurrence of spontaneous premature delivery, or sonographically assessed length of the cervical canal. Both biomarkers were characterized by low sensitivity (54.6 vs. 60.6%), specificity (50%), low positive likelihood ratio (1.09 vs. 1.21) and high negative likelihood ratio (0.91 vs. 0.79).

The paper entitled „**Both low and high PAPP-A concentrations in the first trimester of pregnancy are associated with increased risk of delivery before 32 weeks in twin gestation**" presented the retrospective analysis of data obtained from 304 women with twin gestations

in whom the concentration of pregnancy-associated plasma protein A was measured between 11+0 and 13+6 gestational weeks. It was observed that both the concentration of pregnancy-associated plasma protein A below the 10th percentile and above the 90th percentile for gestational age were associated with an increased risk of delivery below 34 weeks (RR 2.25; 95% CI 1.1-4.6; RR 3.46; 95% CI 1.6–7.5) and below 32 gestational weeks (RR 2.72; 95% CI 1.3–5.5; RR 2.48; 95% CI 1.1–5.3). Spontaneous uterine contractions resulting in a delivery (RR 2.05; 95% CI 1–4.2) and gestational diabetes (RR 3.5; 95% CI 1.7–6.9) occurred significantly more commonly in patients with low concentrations of pregnancy-associated plasma protein A, while its high concentrations were associated with almost 10-fold higher risk of intrauterine fetal demise (RR 8.9; 95% CI 3.1–11.5). The analysis was performed with generalized additive models visualized with the use of splines. In case of delivery before 34 and 32 weeks of gestation a double significant U-shaped correlation, both linear and non-linear, was observed between the risk of delivery and the concentration of pregnancy-associated plasma protein A.

Conclusions:

1. The expression of elafin and secretory leukocyte peptidase inhibitor does not correlate with the risk of premature delivery in twin gestations.
2. Elafin and secretory leukocyte peptidase inhibitor are not effective predictive factors of premature delivery in twin gestations.
3. The risk of twin pregnancy complications depends on the plasma concentrations of PAPP-A in women with twin gestations between 11 and 13+6 gestational weeks.
4. The correlation between the concentrations of PAPP-A protein and pregnancy complications is non-linear.
5. It is important to search for an effective predictive factor of twin gestation complications considering possible linear and non-linear correlations between the biomarker and the analyzed complications.
6. The measurement of PAPP-A concentrations is used in routine diagnostics of aneuploidy in the first trimester of pregnancy. Therefore, it seems to be a potentially effective biomarker to predict premature delivery and intrauterine fetal demise used in clinical practice.