The effect of maternal treatment with metformin in pregnancy and lactation on programming metabolic adverse conditions in the offspring- long-term functional and epigenetic studies

Gestational diabetes mellitus (GDM), defined as glucose tolerance disturbances during pregnancy, is the most common metabolic complication of this period. Maternal hyperglycemiaffects the fetal hormonal response and insulin synthesis, which is crucial for its development and may program its metabolism. GDM increases the risk of obesity, metabolic syndrome, type 2 diabetes (DM2), and cardiovascular disease in the offspring later in life. Prompt diagnosis of hyperglycemia in pregnancy and effective and safe (for mother and fetus) therapies regulating maternal glucose levels are essential for the proper development and maturation of fetal tissues and organs.

Metformin is an oral biguanide that works primarily by inhibiting hepatic gluconeogenesis, and it also increases glucose uptake in peripheral tissues and reduces glucose absorption in the gastrointestinal tract. Metformin does not directly affect insulin secretion and therefore does not cause hypoglycaemia, which makes it safer than other drugs for diabetes.

Metformin is now called the gold standard in the treatment of type 2 diabetes and insulin resistance in many countries and is one of the most prescribed drugs in the world. It is also used for women suffering from polycystic ovary syndrome. The potential anti-cancer and anti-aging activity is also gaining more and more attention.

However, the treatment of GDM with metformin is debatable. For many years, the Polish Diabetes Society has maintained the lack of recommendation for using metformin in pregnant women. Unlike insulin, metformin crosses the placenta and is present at clinically relevant concentrations in fetal and placental tissues, which means that it has potential effects on a developing fetus. There are also no studies on the long-term effects of metformin exposure in utero. The available data come from studies of children, which does not allow determining the entire risk of diseases, including metabolic disorders that appear in the fourth or fifth decade of life.

The project aims to investigate the effects of maternal treatment with metformin in pregnancy and lactation on the trajectory of offspring development and possible changes in their epigenome.

The author of the project hopes that the obtained results will contribute to understanding the hitherto unknown impact of metformin treatment in pregnant women on the health of the offspring in adulthood and will be used to develop an effective and safe treatment for gestational diabetes.