

DESCRIPTION FOR GENERAL PUBLIC

Several studies have shown that inadequate nutrition of a mother during pregnancy and lactation, as well as maternal metabolic status (like plasma lipid profile) may have a programming effect on the offspring with lifelong consequences. Exposures during early life (fetal, infancy, early childhood) modulate the risk for developing chronic diseases, namely obesity in adulthood. Epidemiological data shows, that prevalence of metabolic disorders is still increasing, especially in children and becomes an important health, social and economic problem. A proper diet of mother in crucial time of offspring development can prevent epidemiology of metabolic disorders in future generations.

One of the most important nutrient during early development is choline. Choline-derived phospholipids are required in large amounts for membrane biogenesis, cell division, tissue expansion, regulation of gene expression and lipid transport. Insufficient dietary choline supply, disturb lipid trafficking and thereby lead to nonalcoholic fatty liver disease (NAFLD).

Prenatal environment and lactation are important for metabolic programming, because poor nutritional status of a mother during these periods predisposes to the pathologic metabolic state of the offspring. It was noticed that neonatal plasma free choline is dependent on maternal plasma free choline and choline milk content, which are highly linked with maternal dietary choline intake. Moreover, it has been shown that a prenatal effect can be reversed by a specific dietary intervention during lactation.

One of the organ, which can be proper target of a study focused on interaction effects between prenatal and postnatal nutritional factors, is pancreas. Endocrine pancreas development in the rat occurs in prenatal, as well as postnatal period. Disruption of pancreas maturation can cause lifelong modification in energy balance. Moreover, a pancreatic hormone – insulin, is one of the most important regulator of glucose and lipid metabolism in insulin-dependent tissues like liver and skeletal muscle.

Biological effects of insufficient choline supply to the offspring during fetal and perinatal period, especially in the context of pancreas development, as well as changed pancreas physiological activity and modification of glucose and lipid metabolism are still little investigated, thus it seems necessary to perform such a study.

The main aim of proposed project is to investigate the role of choline supply from the mother to the offspring during pregnancy and lactation on endocrine pancreas ontogenesis in the progeny, as well as on glucose and lipid metabolism in insulin-dependent tissues like liver and skeletal muscle of the rat. The evaluation of modification prenatal effects by early postnatal dietary choline supply adjustment will be also performed. Because of 20% prevalence of NAFLD in population and changing lipid trafficking occurring during pregnancy and lactation, the influence of dietary choline supply on maternal plasma lipid profile will be also evaluated.

Specific aims of the project include analysis of liver and a skeletal muscle transcripts involved in glucose and lipid metabolism, as well as global miRNA expression by using commercial expression arrays dedicated to rat, follow by evaluation of selected genes by using real-time PCR, as well as analysis of expression of selected genes at the protein level. The selected genes will be also evaluated according to methylation pattern. The histological examination of the structure of pancreas, skeletal muscles and liver tissues will be performed. The main metabolic biomarkers in plasma will be checked. In the section of planned investigation includes animal experiment, the three Rs principles (replacement, reduction, refinement) according to good laboratory practice were used.

Obtained results will increase the knowledge in developmental biology and become an introduction for further investigation and future applications, i.e. establishing the guidelines of adequate dietary choline intake for patients suffer from NAFLD during the critical periods for offspring development. The proper maternal diet, namely adequate choline intake during pregnancy and lactation can be one of the key factor preventing chronic diseases in progeny.