Gestational Diabetes Mellitus and Meconium Microbiota

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Gestational diabetes mellitus (GDM) is a pregnancy complication in which women without previously diagnosed diabetes develop chronic hyperglycemia during gestation. Microbial organisms within the gut—the “gut microbiome”—might contribute to metabolic diseases, including GDM.

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1. Gestaional Diabetes Mellitus and Pregnancy

Gestational diabetes mellitus (GDM) is a pregnancy complication in which women without previously diagnosed diabetes develop chronic hyperglycemia during gestation. It is the most common medical complication and metabolic disorder of pregnancy. Prevalence may vary from 1 to 14% among all pregnancies [1][2]. There is evidence that microbial organisms within the gut—the “gut microbiome”—might contribute to metabolic diseases, including GDM. The gut microbiome can be influenced by early life events, such as preterm delivery and breastfeeding, and by events in later life, such as diet composition and antibiotic use. The gut microbiome has been consistently reported to differ between metabolically healthy and obese individuals, including during pregnancy [3]. GDM is a topic of great interest because it represents a major risk factor for adverse fetal maternal outcomes such as preeclampsia, preterm birth, fetal macrosomia, polyhydramnios, shoulder dystocia, Caesarean section, neonatal respiratory distress, neonatal hypoglycemia and perinatal mortality. An appropriate management of this disorder (adequate counselling, self-glucose monitoring, diet, physical activity, and eventually medication) is crucial for a favorable pregnancy outcome [4].

In women with GDM during pregnancy, there is a higher chance not only to develop type II diabetes mellitus during life, but also the risk for pancreatic cancer [5].

2. Glucose Metabolism with Gestational Diabetes Mellitus Pregnancy

Glucose metabolism in early pregnancy is characterized by hypoglycemia, hypoinsulinemia, ketogenesis, and fatty acid turnover. Between 24–28 weeks of gestation, the concentrations of placental and insulin-antagonistic factors increase, altering carbohydrate metabolism. This is interpreted as antagonism of the action of circulating insulin. Due to the reaction of the pancreas, insulin secretion increases. However, in some cases, the reserves of the pancreas can be reduced or depleted [6]. Due to the abnormal metabolism of carbohydrates, altered maternal

glucose homeostasis develops, which is a condition referred to as DMG. The basis of the disorder is increased secretion of hPL (although growth hormone is reduced), as well as the effect of placental insulinases [7].

Insulin degradation on the maternal side of the placenta is unilateral, since insulin does not cross the placental barrier. The insulin resistance is of the post-receptor type and is hormonally conditioned. A decrease in the number of insulin receptors bound to peripheral target cells, along with a relative lack of circulating insulin, including post-receptor defects, leads to glucose intolerance and the development of gestational diabetes [8][9].

Changes in the mother's glucose and insulin concentrations are followed by similar changes in the fetus. Maternal hyperglycemia leads to fetal hyperglycemia and hyperinsulinemia. The consequences of this excessive stimulation are reflected in the fetal pancreas in the form of islet hyperplasia with an increase in the number of beta cells and increased insulin values [10]. The importance of detecting gestational diabetes in the early stages of pregnancy is best illustrated by the data reporting a significant percentage of morbidity and mortality in newborns, in mothers in whom this disorder is undiagnosed and untreated, and in those when it is discovered late in pregnancy [11]. Fetal adiposity, which is also found in well-regulated diabetes, is explained by an increase in free fatty acids in the placenta, with increases the transfer to the fetus. The passage of amino acids through the placenta regulates insulin (hyperinsulinemia increases the transfer), and the fetal pancreas responds to an increase in the concentration of amino acids and glucose by producing insulin [12]. This is one of the important reasons for the occurrence of fetal macrosomia. It was found that the concentration of amino acids is higher in the fetal circulation than in the maternal circulation, while fetal glycemia is approximately 1.1–1.6 mmol/L lower than the maternal glycemia, i.e., 70–80% of maternal glycemia [13]. Medical nutritional therapy is the first-line approach in managing gestational diabetes mellitus (GDM). Diet is also a powerful modulator of the gut microbiota, whose impact on insulin resistance and the inflammatory response in the host are well known. Changes in the gut microbiota composition have been described in pregnancies either before the onset of GDM or after its diagnosis. The possible modulation of the gut microbiota by dietary interventions in pregnancy is a topic of emerging interest, in consideration of the potential effects on maternal and consequently neonatal health. To date, very few data from observational studies are available about the associations between diet and the gut microbiota in pregnancy complicated by GDM. In this review, we analyzed the available data and discussed the current knowledge about diet manipulation in order to shape the gut microbiota in pregnancy [14].

The priority of current studies is to discover mechanisms by which epigenetic modification prolongs the effects of environmental influences in early childhood and provides a long-lasting response to transient stimulus-modified gene expression and phenotype in adults [15].

Thus, nutrition in the pre- and postnatal period positively influences health in adulthood [16]. An adverse intrauterine environment in pregnancy complicated with diabetes has long-term consequences for the offspring because of the effects of epigenetics [17]. Optimal control of pregnant women's glycemia can reduce the adverse consequences of pregnancy complicated with diabetes because the glucose level and perinatal outcome are a continuum [18]. Children of mothers with GDM are at greater risk of obesity, diabetes type 1 and 2, hypertension, lipid changes, and albuminuria in preadolescent age and in adulthood [19]. Mental and motor deficits as well as attention and

behavioral disorders are much more common in the offspring of mothers with diabetes [20][21]. Many consequences of GDM during pregnancy can be prevented. Early breastfeeding can prevent metabolic complications in neonates because colostrum is rich in glucose, and hypoglycemia may be asymptomatic. GDM can lead to not only development of fetal macrosomia, neonatal hypoglycemia, jaundice, polycythemia, and hypocalcemia during the perinatal period, but also childhood obesity and metabolic syndrome in adulthood [22].

3. Gestational Diabetes Mellitus and Meconium Microbiota

The human body harbors trillions of microbial cells and they are indispensable for human health. The gut microbiota resides on the intestinal mucosal surfaces and participates in epithelial homeostasis, energy harvest, and immune development [23]. Colonization of the infant's gut has drawn great interest, because it links to individual's health and late-onset diseases [24]. However, factors that affect neonatal gut microbiota and metabolome in neonates of mothers with GDM has not been fully elucidated [25]. Microorganisms in meconium were the first colonizers of the newborn, which come from the mother's skin, vagina, and gut. A wide variety of reports had demonstrated that microbiotain meconium could be affected by the delivery mode, perinatal antibiotics, and breastfeeding [26]. In the Ting Chen study, the relationship between the meconium microbiota, metabolome in neonates born to mothers with GDM was identified. A limited number of Taxa and Proteobacteria as the dominant phylum in the meconium of newborns of mothers with GDM was also found [27]. Decreased enteric microbiota richness is associated with increased insulin resistance markers and proinflammatory markers [28].

The abundances of the Rothia families and Clostridium sensustricto, which may contain opportunistic pathogens that might cause enteric infections and childhood metabolic disorders, were significantly increased in the GDM neonates. Decreased richness of the enteric microbiota has been associated with elevated insulin resistance and proinflammatory markers [29]. In addition, bacterial family changing was in the similar trend by delivery modes. It was indicated that variation of GDM-related bacteria was consistent. However, the consistency of changed bacteria in neonates might dramatically be altered within days based on feeding (breast/formula) enteric microbiota varies among different races, depending on the mother's diet and climate [30].

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