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REVIEWS: CURRENT TOPICS

Type of fatty acids in maternal diets during pregnancy and/or lactation and metabolic consequences of the offspring

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Abstract

During pregnancy and/or lactation, maternal nutrition is related to the adequate development of the fetus, newborn and future adult, likely by modifications in fetal programming and epigenetic regulation. Fetal programming is characterized by adaptive responses to specific environmental conditions during early life stages, which may alter gene expression and permanently affect the structure and function of several organs and tissues, thus influencing the susceptibility to metabolic disorders. Regarding lipid metabolism during the first two trimesters of pregnancy, the maternal body accumulates fat, whereas in late pregnancy, the lipolytic activity in the maternal adipose tissue is increased. However, an excess or deficiency of certain fatty acids may lead to adverse consequences to the fetuses and newborns. Fetal exposure to *trans* fatty acids appears to promote early deleterious effects in the offspring's health, thereby increasing the individual risk for developing metabolic diseases throughout life. Similarly, the maternal intake of saturated fatty acids seems to trigger alterations in the liver and adipose tissue function associated with insulin resistance and diabetes. The polyunsaturated fatty acids (PUFAs), particularly long-chain PUFAs (long-chain PUFA–arachidonic acid, eicosapentaenoic acid and docosahexaenoic acid), play an important and beneficial physiologic role in the offspring who receive this fatty acid during critical periods of development. Therefore, the maternal nutritional condition and fatty acid intake during pregnancy and/or lactation are critical factors that are strongly associated with normal fetal and postnatal development, which influence the modifications in fetal programming and in the individual risk for developing metabolic diseases throughout life.

Keywords: Fatty acids; Programming; Pregnancy; Lactation; Metabolism

1. Introduction

Lines of evidence indicate that maternal nutrition during pregnancy and/or lactation is directly related to the adequate development of the fetus, newborn and future adult, likely by modifications in fetal programming and epigenetic regulation, which induce phenotypic changes. Fetal programming is a phenomenon characterized by adaptive responses of the fetus to specific environmental conditions during early life stages, which may alter gene expression and permanently affect the structure and function of several organs and tissues, most likely influencing the individual's susceptibility to develop metabolic disorders over a lifetime, such as type 2 diabetes, cardiovascular disease, obesity and hypertension [1–4].

Initially, it is relevant to consider that although implantation process differs between rats and humans, the rat is an appropriated animal model for studying different mechanisms involved in the course of normal pregnancy, including fetoplacental development. The structure of the placenta varies considerably among mammalian species; however, basic morphology, main cell types, functions and molecular mechanisms underlying placental development are conserved across species. The trophoblast cells, which compose the placenta, ensure an appropriated bidirectional nutrient/waste flow necessary to normal growth and maturation of the embryo [5].

Human and animal studies showed the importance of environment factors (e.g., nutrition) and maternal lifestyle in the fetal programming and later development of chronic diseases [6–8]. In the pregnancy, diet is a major factor that influences the fetal development and metabolism. Consequently, nutritional factors, including energy, fatty acids, protein, micronutrients and folate, affect several aspects of fetal programming [8]. Study of individuals exposed *in utero* to the Dutch famine at winter of 1944–1945 revealed that the poor maternal nutrition, especially during mid or late pregnancy, decreased fetal growth and glucose tolerance in adults aged about 50 years. These findings suggested that maternal malnutrition during pregnancy can affect permanently the fetal metabolic control systems [6]. Likewise, in rats, Yuan et al. demonstrated that the caloric restriction during mid to late gestation from day 11 through day 21 of pregnancy

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[intrauterine growth retardation (IUGR)] decreased the offspring birth weight and pancreas weight at all stages of lifetime. In the same study was observed impairment in insulin sensitivity with age and alterations in the pancreas islet β-cell function, suggesting that changes in the intrauterine nutritional environment (IUGR) can predispose the animal to glucose intolerance and type 2 diabetes in the adulthood [9].

Additionally, authors revealed that the maternal metabolism and nutritional status also may affect offspring's metabolism lifelong through alterations in fetal programming [10]. Gademan et al. observed that a higher maternal prepregnancy body mass index (BMI) was significantly associated with a greater adiposity of the child at age 5–6 years. Further, maternal free fatty acid (FFA) level was positively linearly related to the child's fat percentage, BMI and risk for overweight. Thus, overweight/obese mothers and mothers with elevated FFA levels during early pregnancy seem to be more likely to have children with overweight or obesity at age 5–6 years. Later in life, this effect can influence the development of metabolic disorders such as cardiovascular disease [10]. Complementarily, a review study conducted by Hughes and Oxford reported that the maternal consumption of a lipid-rich diet can predispose the offspring to the later development of nonalcoholic fatty liver disease [11].

Maternal dietary pattern and nutritional condition, as well as metabolism of the mother, may affect the offspring health status, likely by the influence of these factors on the placental nutrient transfer and fetal nutrient supply. During pregnancy, maternal metabolism shows adaptations for supporting the continuous draining of substrates to the fetus, thus ensuring fetal growth [12]. Regarding lipid metabolism during the first two trimesters of pregnancy, the maternal body accumulates fat, whereas in late pregnancy, the lipolytic activity in the maternal adipose tissue is increased, thereby establishing a catabolic condition [12,13].

Fatty acids (FAs), mainly essential FAs and long-chain polyunsaturated fatty acids (LC-PUFAs) which are central nutrients required for the synthesis of structural lipids, are fundamental to fetal and postnatal development and normal cell function [12,14]. However, an excess of certain FAs may harm the availability of others, producing adverse consequences to the fetus and newborn [12]. Several studies have demonstrated a selectivity in placental transfer of FAs and a strong preference by the placental plasma membrane binding sites for LC-PUFAs, especially docosahexaenoic acid (DHA) [12,15–18]. In contrast, Campbell et al. showed that the *trans* fatty acids (TFAs) competed strongly for the same LC-PUFA binding sites in human placental membranes, inhibiting the transport of LC-PUFAs to the placenta [16]. In fact, the human study performed by Enke et al. revealed a negative association between industrial TFAs and n-3 (LC-PUFAs in fetal plasma collected at birth [19]. Similarly, Albuquerque et al. demonstrated that the total amounts of PUFA, arachidonic acid (AA) and DHA decreased significantly in brains of 21-day-old rat offspring from dams fed a TFA-enriched diet during pregnancy and lactation [20].

Furthermore, authors suggested that the placental tissue has lipoprotein receptors and expresses enzymes with lipase and phospholipase activities involved in the mechanism of maternal FA transfer across the placenta to sustain the fetal lipid requirements [12,13,18]. The maternal diet, hepatic metabolism and adipose tissue stores define the FA composition of the maternal triacylglycerols (TAGs) pool in plasma [21]. In a review, Herrera reported that the maternal plasma TAGs derived from lipoproteins [e.g., very low density lipoproteins (VLDL)] are hydrolyzed and captured by placenta, which promotes the reesterification and intracellular hydrolysis facilitating diffusion of the released FAs to the fetus. In fetal liver, the FAs are esterified and released back into the fetus circulation as TAGs [12]. Additionally, other authors demonstrated that, in a smaller proportion, the nonesterified fatty acids (NEFAs) that originate from maternal metabolism can cross the placenta without prior modification through passive diffusion and protein-mediated transport [12,13,18].

During lactation, the fetus is exposed to FAs through their secretion in breast milk. The lactating mammary tissue synthesizes FAs intracellularly from a supply of substrates extracted by the maternal plasma; FAs may be extracted from lipids in the maternal blood. In this sense, the maternal TAGs carried in chylomicrons and VLDLs are the primary plasma source of FAs. Moreover, the maternal NEFAs produced from TAGs in the mammary tissue by lipoprotein lipase enzyme are important in the fasting state [22]. The lipid drops formed in the mammary epithelial cells are secreted into the milk by exocytosis or association with the plasma membrane bilayer [23].

The review study conducted by Lauritzen and Carlson showed that the contribution of the maternal diet and stores of FAs synthesized by the mammary gland to the milk FA composition is dependent on the timing of food intake/fasting duration [21]. Thus, both diet of lactating mothers and maternal body stocks of FAs may affect the fat composition of breast milk [24,25]. In this sense, Nishimura et al. demonstrated that the maternal dietary DHA and eicosapentaenoic acid (EPA) content during the third trimester of pregnancy is directly associated to the content of these fatty acids in mature breast milk. Additionally, the same human study showed a direct relation between the dietary n-3 to n-6 ratio in the postpartum period and milk composition [25]. Similarly, Priego et al. observed that oleic acid (the primary component of olive oil) levels increase in the milk of rats supplemented with olive oil from day 14 of pregnancy to day 20 of lactation. In the same study, butter-supplemented rats presented a higher percentage of palmitic acid in their milk, which is the most abundant fatty acid in butter [26].

In summary, the maternal nutritional condition and FA composition of the diet during pregnancy and/or lactation are critical factors that are strongly associated with normal fetal and postnatal development and also seem to influence the modifications in fetal programming, altering the individual risk for developing metabolic diseases throughout life.

This review discusses the implications of consumption of different types of fatty acids in maternal diets during pregnancy and/or lactation on the metabolic consequences associated with the health and disease of the offspring.

2. Saturated fatty acids (SFAs)

SFAs are FAs totally hydrogenated, which have a linear chain without double bounds between carbon atoms. They are in solid state at room temperature and are represented by the lauric acid (12:0), myristic acid (14:0), palmitic acid (16:0) and stearic acid (18:0). The SFAs comprise the fast foods, processed foods, high-fat (HF) dairy products, red meats and pork [27].

Public health recommendations emphasize the importance of reducing SFA intake to prevent cardiovascular diseases, obesity, metabolic syndrome and cancer [28–30]. The effects of diet seems to be mediated through multiple biological mechanisms that include oxidative stress, endothelial dysfunction, insulin sensitivity, blood pressure, thrombotic tendency and subclinical inflammation [31].

The effects of maternal malnutrition on fetal growth have been extensively studied, and the role of poor prenatal diet in elevating lifelong risk of cardiovascular and metabolic diseases has been well characterized. In a recent systematic review, Ainge et al. identified that the risk of developing diabetes and obesity in offspring born to HF-fed dams appears to be independent of maternal obesity, birth weight and postweaning macronutrient intake [32].

The chronic consumption of diets high in saturated fats is associated with poorly controlled hyperglycemia, hyperinsulinemia