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Effect of maternal use of flaxseed oil during pregnancy and lactation on glucose metabolism and pancreas histomorphometry of male offspring from diabetic rats

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ABSTRACT

Aim: Investigate if the maternal use of flaxseed oil prevents pancreatic alterations in the offspring of diabetic mothers.

Methods: Diabetes was induced in female wistar rats ($n = 12$) by a high-fat diet and low-dose of streptozotocin. After the confirmation of the diabetes (glucose >300 mg/dL), rats were mated and once pregnancy was confirmed, they were allocated into three groups ($n = 6$): high-fat group (HFG); flaxseed oil group (FOG); and control group (CG) (nondiabetic rats). At weaning, male offspring ($n = 12$/group) received a standard chow diet. The animals were euthanized in two phases: at 100 and at 180 days, ($n = 6$/group). The pancreas was collected for histomorphometric and immunohistochemistry analysis.

Results: HFG showed hypertrophy of pancreatic islets at 100 and at 180 days ($p < 0.0001$), while the FOG offspring had islets with smaller diameters compared to HFG at both phases of sacrifice ($p < 0.0001$). HFG had a lower percentage of small islets when compared to CG and FOG, which had a higher percentage when compared to HFG ($p = 0.0053$) at 100 days. At 180 days HFG showed higher percentage of larger islets ($p = 0.00137$) and lower percentage of smaller islets ($p = 0.00112$), when compared to FOG. HFG showed lower islet insulin immunodensity at 100 days ($p < 0.0001$) and 180 days ($p < 0.0001$), whereas FOG was similar to CG ($p < 0.0001$) at 100 days and higher at 180 days ($p < 0.0001$).

Conclusions: Flaxseed oil reduced the damage caused by maternal hyperglycemia, promoting normal pancreas histomorphometry and β cell mass.

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1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disease characterized by high levels of blood glucose due to a complete or relative lack of insulin [1]. As the incidence of diabetes is increasing and affecting individuals of all ages, including children and youths, women of childbearing age are at increased risk of developing this disease during pregnancy [2]. DM affects almost 7% of pregnancies and is the most common metabolic complication during pregnancy [3].

There is convincing evidence suggesting that exposure to fetal and/or postnatal adverse environment can increase the susceptibility to a number of chronic diseases in the future life of the children [4–6]. Diabetes and obesity are two complications that during pregnancy can substantially influence the fetal and postnatal development of the offspring [7,8]. Diabetes during pregnancy leads to changes in the metabolism of the mother and her offspring, and is caused by maternal hyperglycemia and hyperinsulinemia. These conditions alter fetal metabolism during pregnancy and remain present throughout the life of the offspring [9]. Intrauterine exposure to mild hyperglycemia (due to defective insulin secretion) is associated with newborns of normal or macrosomic weight, which, during adulthood, develop glucose intolerance [4,9]. In contrast, newborns of mothers with severe hyperglycemia are microsomic [4,10–13] and present larger islets, which is related to hyperplasia and degranulation of β cells, suggesting overstimulation and reduced insulin action during adulthood [4].

Obesity and diabetes are more common in childhood and adolescence when there is a history of maternal or gestational diabetes. Under these conditions, metabolic disorders can affect the growth and the metabolism of the offspring and their subsequent generations [14].

There are many drugs to control glycemia, but they are usually expensive and are linked to concerns of congenital anomalies. Due to the high cost of drugs, pregnant women resort to alternative medication to treat diabetes and other diseases [9]. In recent decades, considerable interest has emerged from industry and consumers for physiologically active foods or food components [15]. Dietary intervention using herbal products is often considered a better strategy for either preventing or reducing the progression of chronic diseases. This tendency is increasing due to the affordability of these products along with the fewer side effects they produce compared to the drugs administered under a pharmacological approach [16]. Because of thie trend, there is a need for studies to determine the effects of medicinal plants and herbal products in order to establish their capacity to reduce adverse effects.

Flaxseed is an important oilseed crop grown worldwide due to its source of fiber and oil. Flaxseed and its oil are cited as potentially useful by the American Heart Association in the prevention of cardiovascular diseases, including reduction of serum cholesterol, platelet aggregation, and inflammatory markers, improving glucose tolerance and acting as an antioxidant [17]. Most of the observed benefits and the preventive properties related to illnesses have been attributed to its Omega-3 fatty acid and α-linoleic (ALA, 18:3) content [18]. Flaxseed oil is the richest source of ALA, which encapsulates about 55–60% of the total of the fatty acids. Another component of this seed also related to providing benefits in diabetic patients is Secoisolariciresinol diglucoside (SDG) which reduces serum glucose levels [19].

The purpose of this study was to evaluate the effects of flaxseed oil consumption on glucose metabolism and pancreatic morphology of adult male offspring of diabetic wistar rats that were fed with flaxseed oil during pregnancy and lactation.

2. Materials and methods

2.1. Parental generation

The animals included in this study were treated according to the conventional guidelines for experimentation with animals (NIH Publication No. 85-23, revised 1996). This study was approved by the Animal Experimentation Ethics Committee of the Center of Laboratory Animals of the Fluminense Federal University with the following registration number: 035/2010. Animals were maintained under controlled conditions of temperature and humidity, and a 12:12 h dark–light cycle, with free access to water and food.

2.2. Diabetes induction

Nondiabetic female wistar rats ($n = 12$) were fed with a high-fat diet (60% of energy from lipid, 14% from protein, and 26% from carbohydrates) for an initial period of three weeks. Another six rats were fed a control diet based on casein (10% of energy from lipid, 14% from protein, and 76% from carbohydrates), both ad libitum, thus forming two groups: high-fat group (HFG) ($n = 12$) and control group (CG) ($n = 6$). After three weeks of the high-fat diet, these rats were given an intraperitoneal injection of streptozotocin (STZ) (Sigma Chemical, St. Louis, MO, USA) at a dose of 35 mg kg^{-1} dissolved in vehicle (sodium citrate buffer 0.01 M, pH = 4.5) [20,21]. The rats that consumed the control diet received the vehicle solution intraperitoneally only. The groups continued to receive their respective experimental diets for another week, for a total of four weeks of exposure to the dietary standards adopted. At the end of the fourth week, blood was collected to confirm diabetes by a plasma glucose concentration above 300 mg/dL [21].

2.3. Mating period

All rats were mated overnight with nondiabetic male wistar rats in a ratio of 2 females per each male. The mornings in which spermatozoa were detected on vaginal swabs were established as day zero of pregnancy. The mating procedure continued for 15 consecutive days, which comprises approximately three estrous cycles.

2.4. Period of pregnancy and lactation

After confirming the pregnancy, the rats were placed in individual cages and allocated to three experimental groups: high-fat group (HFG) ($n = 6$), of diabetic pregnant rats, which received a high-fat diet (49% of energy (Table 1)); Flaxseed Oil