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Effects of prebiotic inulin addition to low- or high-fat diet on maternal metabolic status and neonatal traits of offspring in a pregnant sow model

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ABSTRACT

The effects of adding inulin to low- or high-fat diet on the metabolic status and nutrient digestibility in gestating sows and the neonatal traits of their offspring were examined. Sixty sows were allocated to a 2 × 2 factorial treatment design with levels of inulin (0% or 1.5%) and fat (0% or 5%) addition as the fixed factors during gestation. Inulin supplementation resulted in the following: improved serum lipid profiles, insulin resistance, and glucose tolerance, which were adversely impacted by fat addition; increased serum butyrate concentration throughout gestation and propionate concentration on day 60 of gestation when given with a high-fat diet; enhanced fecal bile acid excretion in a high-fat diet; lowered ether extract (EE) digestibility and increased calcium digestibility in the sow; and decreased BMI and carcass EE content in neonatal piglets. The beneficial effects of inulin were particularly marked when it was combined with a high-fat diet.

1. Introduction

Due to increased consumption of high-calorie, fatty food that is low in dietary fiber (DF), overweight or obesity and accompanying chronic diseases, including type 2 diabetes, hyperlipidemia, and cardiovascular disorders, have become a major social concern in modern societies (Kendall, Esfahani, & Jenkins, 2010). Dietary habits during pregnancy may not only have significant effects on maternal metabolic status, but also persistent effects on fetal programming and metabolism of the offspring (Wu, Bazer, Cudd, Meininger, & Spencer, 2004). Reports have indicated that DF intake in pregnant women is far below current recommended levels worldwide (Diemert et al., 2016; Gunnarsdottir et al., 2016). The role of DF in nutrition and health has received a great deal of public attention and encouraged rapid expansion of related studies. A growing body of evidence has highlighted the notable effects of prebiotic dietary fibers, soluble DF in particular, on weight control, hyperglycemia, insulin resistance, and hyperlipidemia (Aliasgharzadeh, Dehghan, Gargari, & Asghari-Jafarabadi, 2015; Chassaing et al., 2015; Gunness & Gidley, 2010; Karimi et al., 2016). Nevertheless, the mechanisms underlying these effects remain the subject of debate. A typical soluble dietary fiber (SDF), inulin, found in several fruits and vegetables, is a mixture of linear D-fructose polymers linked by β (2-1) glycoside bonds, with a terminal glucose or fructose unit, and could be resistant to digestion by gastrointestinal enzymes in monogastric animals (Roberfroid & Delzenne, 1998). Previous studies have demonstrated the beneficial effects of fructan-type inulin on body weight control, serum glucose and lipid metabolism, inflammatory responses, and antioxidant status in humans and rodents (Aliasgharzadeh et al., 2015; Dehghan, Farhangi, Tavakoli, Aliasgarzadeh, & Akbari, 2016; Gargari, Dehghan, Aliasgharzadeh, & Jafar-abadi, 2013; Lightowler, Thondre, Holz, & Theis, 2017; Rozan et al., 2008; Russo et al., 2010; Yang et al., 2017). However, surprisingly few studies have been conducted on pregnant individuals.

Given the scarcity of research aimed at evaluating the beneficial effects of a specific SDF on maternal metabolism during gestation, and the similarity between pigs and humans in terms of gastrointestinal anatomy, pharmaceutical bioavailability and nutrient digestibility (Swindle, Makin, Herron, Clubb, & Frazier, 2012), the current study

Abbreviations: ATTD, apparent total tract digestibility; CF, crude fiber; CP, crude protein; CRL, crown-rump length; DF, dietary fiber; DM, dry matter; DT, digestive tract; EE, ether extract; FFA, free fatty acid; GTT, glucose tolerance test; HDL-C, high-density lipoprotein cholesterol; HMG-CoA, 3-hydroxy-3-methylglutaryl-coenzyme A; $HOMA_{IR}$, homeostatic model assessment of insulin resistance; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides; VFA, volatile fatty acid

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was performed to investigate the effects of adding prebiotic inulin to low- or high-fat gestational diets on maternal metabolic status and neonatal traits of offspring using a pregnant sow model. An additional aim was to reveal the possible mechanisms underlying these beneficial effects.

2. Materials and methods

2.1. Animals and experimental design

A total of sixty 2–3 parity Landrace × Yorkshire sows were inseminated with semen from Duroc boars, and allocated to a 2 × 2 experimental design with levels of inulin (0% or 1.5%) and fat (0% or 5%) addition as the fixed factors, based on parity, body weight, and backfat thickness. The four treatments were low-fat diet (LFD), low-fat diet with 1.5% inulin (LFD.Inu), high-fat diet (HFD), and high-fat diet with 1.5% inulin (HFD.Inu). From days 0–90 of gestation, sows were supplied with 2.3 kg/d of the corresponding diet, with the amount increasing to 2.8 kg/d from day 91 to parturition. Sows were fed twice a day at 0800 and 1600 h, and had free access to water. The average ambient temperature in the gestation house was maintained at 22–26 °C. On day 107 of gestation, the sows were moved to individual farrowing pens. The Care and Use Committee of Sichuan Agricultural University approved all the research protocols (No. DKY-B20121601).

2.2. Diets

All diets were formulated to meet or exceed the nutrient requirements of gestating sows as recommended by the NRC (2012) (Supplementary Table S1). To better mimic a human model and to ensure effectiveness, the 1.5% dose level for supplemental inulin was selected based on previous human studies that showed the most effective intake level of fructan-type inulin in improving blood lipid profile, calcium absorption, and immune status to be 8–10 g per day for subjects with a weight range of 60–75 kg (Abrams, Griffin, & Hawthorne, 2007a; Aliasgharzadeh et al., 2015; Dehghan et al., 2016; Gargari et al., 2013; Tovar, Caamano, Garcia-Padilla, & Garcia, 2012). In comparison, the average sow weight at mating was approximately 200 kg. Fat and inulin were added by substituting the same amount of maize starch in the LFD diet. Inulin used in the study was obtained from BENEO-Orafti (Orafti GR, Belgium), and had a purity greater than 90% and average degree of polymerization between 10 and 12.

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jff.2018.07.004.

2.3. Fasting serum glucose, lipid profile, urea, insulin, and volatile fatty acids

Fasting blood samples (10 ml) were collected from six sows allocated to each treatment before the morning meal at mating and on days 30, 60, and 90 of gestation. Blood was collected into two 5 ml tubes without anticoagulant and left at room temperature for 2 h, followed by centrifugation for 10 min at 2550 g at 4 °C. Serum samples were harvested and stored at −20 °C until analysis.

Serum glucose, total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and urea concentrations were measured enzymatically using assay kits (Nanjing Jiancheng Institute of Bioengineering, China). Serum free fatty acid (FFA) and insulin were measured with commercial porcine enzyme-linked immunosorbent assay kits according to the manufacturer's instructions (Nanjing Jiancheng Institute of Bioengineering, China). The homeostatic model assessment of insulin resistance ($HOMA_{IR}$) was used to estimate insulin sensitivity as $HOMA_{IR}$ = (FPI × FPG)/22.5, where FPI is fasting plasma insulin (mU/L) and FPG is fasting plasma glucose (mmol/L) (Islam, Civitarese, Hesslink, & Gallaher, 2011). The serum was analyzed for volatile fatty acids (VFA: acetate, propionate, and butyrate) as described by Brighenti et al. (1998) with gas chromatography (Varian CP-3800 GC); however crotonic acid, rather than isovaleric acid, was used as the internal standard.

2.4. Fecal bile acid excretion and apparent total tract digestibility of nutrients

Five sows from each treatment group were randomly chosen for analysis of fecal total bile acid excretion and apparent total tract digestibility (ATTD) of nutrients. Fecal bile acids were extracted from freeze-dried feces collected at mating and on days 30, 60, 90, and 110 of gestation using organic solvents, as described by Locket & Gallaher (1989), and measured enzymatically (TBA Assay Kit, Maccura, Chengdu, China).

On day 99 of gestation, the chosen sows were transferred to individual metabolic cages. Feces were collected for four consecutive days from day 100 of gestation. Ferric oxide was used as an indigestible marker to indicate the initiation and termination of fecal collection for the entire four days (Otto, Yokoyama, Ku, Ames, & Trottier, 2003). Each sow received 5 g of ferric oxide mixed with 100 g of the corresponding diet before the morning meal on days 100 and 104 of gestation. The remaining feed was offered after the ferric oxide/feed mixture was completely consumed. The exact time when the sows began to eat the ferric oxide/feed mixture and the first appearance of red feces, which contained ferric oxide, were recorded and the interval between the two was defined as the digestive tract (DT) transit time. Fecal samples were collected daily and weighed, and 10% (w/w) of the samples were stored at −20 °C. Total fecal samples for 4 days were thawed, pooled, and mixed thoroughly, and subsamples (400 g) were then collected and stored at −20 °C.

Freeze-dried fecal samples and feed samples were finely ground through a 1 mm mesh screen, and their chemical compositions were analyzed according to AOAC (2007). Feed and fecal samples were analyzed for dry matter (DM) (method 930.15, AOAC, 2007), ether extract (EE) (method 920.39, AOAC, 2007), ash (method 942.05, AOAC, 2007), crude fiber (CF) (method 978.10, AOAC, 2007), Ca (method 927.02, AOAC, 2007), and P (method 984.27, AOAC, 2007). Gross energy was measured by bomb calorimetry (Parr Instrument 1563, Moline, IL, USA). Crude protein (CP) (N × 6.25) was determined using the Kjeldahl method with a KjelFlex K-360 (Buchi, Flavil, Switzerland).

2.5. Intravenous glucose tolerance test during the perinatal period

On day 107 of gestation, an intravenous glucose tolerance test (GTT) was performed on five randomly chosen sows per treatment as described by Wang, Cao et al. (2016) with a minor modification. Briefly, sows were infused with 500 g/L dextrose solution via the central ear vein at a dose of 0.5 g/kg body weight using an infusion pump (JSB-1200, JYM®, Changsha, China) after a 16 h fasting. By adjusting the infusion rate (11.05–14.35 g/min), the glucose was infused within 10 min. Blood samples were taken from the lateral ear vein at −10, −9, −6, −3, and 0 min relative to completion of infusion and at 5, 10, 15, 20, 30, 45, 60, 90, and 120 min after infusion. The −10 min time point was defined as the initiation of glucose infusion, which started immediately after the first blood sample was taken. A drop of blood was placed on a test sensor immediately for blood glucose evaluation using a glucometer (One Touch UltraEasy® glucometer, Lifescan, Milpitas, CA, USA). For each sow, basal (−10 min sample) glucose concentration, peak glucose concentration, maximum increase in glucose concentration, and area under the curve for the entire 120 min (AUC_{120}) were calculated. The maximum increase in glucose concentration was calculated by subtracting the basal level from the peak glucose concentration. Glucose clearance rate [k, μmol/(L min)] was calculated by using the slope of $\log_e$ glucose against time from 0 to 20 min after