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Short communication: Supplementation of fructo-oligosaccharides does not improve insulin sensitivity in heavy veal calves fed different sources of carbohydrates

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ABSTRACT

Heavy veal calves (4–6 mo old) often develop problems with insulin sensitivity. This could lead to metabolic disorders and impaired animal growth performance. Studies in various animal species have shown that the supplementation of short-chain fructo-oligosaccharides (scFOS) can improve insulin sensitivity. We therefore studied the effects of scFOS supplementation on insulin sensitivity in heavy veal calves. Forty male Holstein-Friesian calves (BW = 190 ± 2.9 kg; age = 162 ± 1.4 d at the start of the trial) were fed either a control milk replacer (MR) diet or a diet in which one-third of the lactose was replaced by glucose, fructose, or glycerol for 10 wk prior to the start of the trial. At the start of the trial, calves were subjected to a frequently sampled intravenous glucose tolerance test to assess whole-body insulin sensitivity (muscle and hepatic insulin sensitivity). Calves within each dietary treatment group were ranked based on their insulin sensitivity value. Half of the calves received scFOS (12 mg/kg of BW) with the MR for 6 wk (supplementation was equally distributed over the insulin sensitivity range). Subsequently, a second frequently sampled intravenous glucose tolerance test was conducted to assess the effect of scFOS. In addition, fasting plasma levels of glucose, insulin, triglycerides, and cholesterol were determined to calculate the quantitative insulin sensitivity check index and triglyceride:high-density lipoprotein cholesterol ratio (fasting indicators of insulin sensitivity). Whole-body insulin sensitivity was low at the start of the trial and remained low in all groups [1.0 ± 0.1 and 0.8 ± 0.1 $(mU/L)^{-1} \cdot min^{-1}$ on average, respectively]. Supplementation of scFOS did not improve insulin sensitivity in any of the treatment groups. The quantitative insulin sensitivity check index and the triglyceride:high-density lipoprotein cholesterol ratio also did not differ between scFOS and non-scFOS calves and averaged 0.326 ± 0.003 and 0.088 ± 0.004, respectively, at the end of the trial. We conclude that scFOS supplementation does not improve insulin sensitivity in heavy veal calves regardless of the carbohydrate composition of the MR. This is in contrast to other animals (e.g., dogs and horses), where scFOS supplementation did improve insulin sensitivity. The absence of an effect of scFOS might be related to the dosage or to metabolic differences between ruminants and nonruminants. Increasing evidence indicates that dietary interventions in veal calves have little or no effect on insulin sensitivity, possibly because of low levels of insulin sensitivity.
Key words: veal calf, milk replacer, fructo-oligosaccharides, insulin sensitivity

Short Communication

Veal calves are fed milk replacer (**MR**) and solid feed (roughage and concentrates) and are exposed to large quantities of lactose and fat via the MR. Prolonged high intakes of MR can induce problems with glucose homeostasis and insulin sensitivity in veal calves. These problems have been identified in heavy veal calves (4–6 mo), characterized by a high incidence of hyperglycemia, hyperinsulinemia, and glucosuria (Hostettler-Allen et al., 1994; Hugi et al., 1997) and insulin resistance (Pantophlet et al., 2016a). In a recent study, we found that calves raised on a lactose MR diet, or diets in which one-third of the lactose was replaced by glucose, fructose, or glycerol, did not differ in insulin sensitivity and that insulin sensitivity was low (Pantophlet et al., 2016c). This could lead to metabolic disorders and impaired animal growth performance. Therefore, prevention strategies must be developed. Various animal studies have shown that dietary short-chain fructo-oligosaccharide (**scFOS**) supplementation can

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help prevent problems and improve whole-body insulin sensitivity (i.e., muscle and hepatic insulin sensitivity). In obese dogs and horses, for example, supplementation of dietary scFOS for a period of 6 wk increased insulin sensitivity (Respondek et al., 2008; Respondek et al., 2011). In young veal calves (<3 mo old), supplementation of scFOS for 10 wk did not improve insulin sensitivity or glucose homeostasis (Pantophlet et al., 2016b). In older veal calves (10–13 wk old), however, scFOS supplementation did improve postprandial glucose homeostasis (Kaufhold et al., 2000). A decrease in postprandial response for glucose was observed, but not for insulin. Mechanisms were not reported. It is not clear whether the improved glucose homeostasis during scFOS supplementation in older calves is related to changes in insulin sensitivity. Therefore, the objective of this study was to assess the effects of scFOS supplementation on insulin sensitivity in heavy veal calves.

Forty male Holstein-Friesian calves (BW = 190 ± 2.9 kg; age = 162 ± 1.4 d; mean ± SEM) were housed at the research facility of the Department of Animal Sciences at Wageningen University (Wageningen, the Netherlands). Calves were housed in groups (5 calves/pen) except for the first and last week of the trial. During these periods calves were housed individually in metabolic cages (0.80 × 1.8 m). Experimental procedures complied with the Dutch Law on Experimental Animals and the ETS123 (Council of Europe 1985 and the 86/609/EEC Directive) and were approved by the Animal Care and Use Committee of Wageningen University. Prior to the start of the trial, the calves were fed either a control MR diet (n = 10) or diets in which one-third of the lactose in the MR was replaced by isoenergetic amounts of glucose (Tereos Syral, Marckolsheim, France; n = 10), fructose (Tate and Lyle Europe, Boleraz, Slovakia; n = 10), or glycerol (Triconor Distribution BV, Soest, the Netherlands; n = 10) for 10 wk. All calves remained on their diets throughout the trial. A detailed description of the diets and feeding strategy is provided elsewhere (Pantophlet et al., 2016c). In short, calves were fed MR and solid feed (20% wheat straw and 80% concentrates) twice a day, at 0630 and 1530 h. The MR was fed on an individual basis (BW was measured weekly), and solid feed was provided per pen during group housing and per individual calf when the calves were housed in metabolic cages. Calves had ad libitum access to water. Whole-body insulin sensitivity was assessed at the start and the end of the trial. The start values were used to assign calves to scFOS or no scFOS within each dietary treatment group (i.e., n = 5 for scFOS; n = 5 for no scFOS). The calves were ranked to evenly distribute the supplementation scFOS over the insulin sensitivity range in each group. The scFOS were added to the MR at a dose of 12 mg/kg of BW for 6 wk. At the end of the 6-wk period, whole-body insulin sensitivity was assessed again to study the effect of scFOS supplementation. One calf in the glucose group was excluded from all measurements due to ruminal drinking.

Whole-body insulin sensitivity was assessed using the frequently sampled intravenous glucose tolerance test. A detailed description of this experimental procedure is provided elsewhere (Pantophlet et al., 2016c). In short, a central venous catheter (Careflow, Becton Dickinson, Franklin Lakes, NJ) was inserted in the jugular vein for glucose and insulin infusion and blood sampling. Calves were fasted to achieve a steady glucose turnover rate before the test. At $t = 0$ min, an intravenous glucose bolus of 0.3 g/kg of BW (20% glucose solution; B. Braun, Oss, the Netherlands) was administered within 2 min followed by an intravenous insulin bolus of 0.03 IU/kg of BW (100 IU/mL solution; Insuman Rapid, Sanofi-Aventis, Gouda, the Netherlands) at t = 20 min (administered within 1 min). Blood samples were collected at $t = -8, -4$, 2, 4, 6, 8, 10, 12, 14, 16, 19, 22, 25, 30, 35, 40, 50, 60, 75, 90, 120, 150, and 180 min relative to the glucose bolus. The samples were centrifuged (1,516 × g for 10 min), and plasma was harvested for the analysis of plasma glucose and insulin concentrations. In addition, plasma triglycerides and high-density lipoprotein (**HDL**) cholesterol concentrations were analyzed in the fasting plasma sample collected at $t = -8$ min (at the start and the end of the trial). Whole-body insulin sensitivity was calculated according to Bergman's minimal model approach using MinMod Millennium (version 6.0.2; MinMod Inc., Los Angeles, CA). In addition, another index of insulin sensitivity, the quantitative insulin sensitivity index (**QUICKI**; Muniyappa et al., 2008), was calculated from the fasting plasma glucose and insulin concentrations. Also, clean urine was quantitatively collected for a period of 5 and 3 d at the start and the end of the trial, respectively. A detailed description of the urine collection procedure is provided elsewhere (Pantophlet et al., 2016c). Urinary glucose and plasma glucose, triglycerides, and HDL cholesterol were measured on a Roche-Hitachi modular automatic analyzer (Roche Diagnostics, Basel, Switzerland) using enzymatic colorimetric assays. The within- and between-run coefficients of variation were ≤2% for all analyses. Insulin was measured using a bovine ELISA kit (Mercodia, Uppsala, Sweden). The within- and between-run coefficients of variation were ≤5.6 and 8.2%, respectively.

Data were analyzed using SPSS (version 22; IBM, Armonk, NY). The effect of scFOS on whole-body insulin sensitivity, QUICKI, triglyceride:HDL cholesterol