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Lactose in milk replacer can partly be replaced by glucose, fructose, or glycerol without affecting insulin sensitivity in veal calves

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ABSTRACT

Calf milk replacer (MR) contains 40 to 50% lactose. Lactose strongly fluctuates in price and alternatives are desired. Also, problems with glucose homeostasis and insulin sensitivity (i.e., high incidence of hyperglycemia and hyperinsulinemia) have been described for heavy veal calves (body weight >100 kg). Replacement of lactose by other dietary substrates can be economically attractive, and may also positively (or negatively) affect the risk of developing problems with glucose metabolism. An experiment was designed to study the effects of replacing one third of the dietary lactose by glucose, fructose, or glycerol on glucose homeostasis and insulin sensitivity in veal calves. Forty male Holstein-Friesian (body weight = 114 ± 2.4 kg; age = 97 ± 1.4 d) calves were fed an MR containing 462 g of lactose/kg (CON), or an MR in which 150 g of lactose/kg of MR was replaced by glucose (GLU), fructose (FRU), or glycerol (GLY). During the first 10 d of the trial, all calves received CON. The CON group remained on this diet and the other groups received their experimental diets for a period of 8 wk. Measurements were conducted during the first (baseline) and last week of the trial. A frequently sampled intravenous glucose tolerance test was performed to assess insulin sensitivity and 24 h of urine was collected to measure glucose excretion. During the last week of the trial, a bolus of 1.5 g of [U-^{13}C] substrates was added to their respective meals and plasma glucose, insulin, and ^{13}C-glucose responses were measured. Insulin sensitivity was low at the start of the trial and remained low [1.2 ± 0.1 and 1.0 ± 0.1 $(mU/L)^{-1} \times min^{-1}$], and no treatment effect was noted. Glucose excretion was low at the start of the trial (3.4 ± 1.0 g/d), but increased ($P < 0.01$) in CON and GLU calves (26.9 ± 3.9 and 43.0 ± 10.6 g/d) but not in FRU and GLY calves. Postprandial glucose was higher in GLU, lower in FRU, and similar in GLY compared with CON calves. Postprandial insulin was lower in FRU and GLY and similar in GLU compared with CON calves. Postprandial ^{13}C-glucose increased substantially in FRU and GLY calves, indicating that calves are able to partially convert these substrates to glucose. We concluded that replacing one third of lactose in MR by glucose, fructose, or glycerol in MR differentially influences postprandial glucose homeostasis but does not affect insulin sensitivity in veal calves.
Key words: veal calves, fructose, glycerol, insulin sensitivity, glucose homeostasis

INTRODUCTION

Veal calves are fed milk replacer (**MR**), roughage, and concentrates. Despite the tendency to increase the amounts of roughage and concentrates in the diet, the vast majority (60–70%) of the digestible nutrient intake originates from MR. Upon closure of the esophageal groove, MR bypasses the rumen and flows directly into the abomasum. Lactose is the predominant, if not the only, carbohydrate source in MR. Calf MR commonly contains approximately 45% lactose, which is efficiently digested and absorbed from the calf intestinal lumen (Burt and Irvine, 1970; Coombe and Smith, 1974).

However, the commercial availability of lactose (or whey) for feed applications is limited and not constant, resulting in large fluctuations in raw material prices. This provides an economic incentive for MR manufacturers to replace lactose by alternative energy sources.

Importantly, a prolonged high intake of lactose, combined with substantial amounts of fat, has been associated with impaired glucose homeostasis. Hyperglycemia, hyperinsulinemia, and insulin resistance have been observed in veal calves in the second phase of the fattening period (Hostettler-Allen et al., 1994; Hugi et al., 1997). Such metabolic problems may eventually re-

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sult in diabetes and (pro)inflammatory stress, as demonstrated in humans (Hotamisligil, 2006; Shoelson et al., 2006), and in hepatic steatosis (Gerrits et al., 2008).

Starch or starch-based products, such as maltodextrins, are the most obvious alternatives for lactose. These products are widely available and are also attractive from an economic perspective. However, we recently demonstrated (Gilbert et al., 2015a) that calves have difficulties digesting starch-based products from MR diets, probably due to low activities of α-amylase and maltase in the small intestine. Nonetheless, the vast majority of starch does not reach the end of the small intestine, which can probably be explained by fermentation (Gilbert et al., 2015a,b).

Apart from starch-based products, glucose, fructose, and glycerol may also replace lactose in MR. Partly replacing lactose by fructose and glycerol may beneficially affect postprandial glucose homeostasis. These substrates have lower glycemic (and insulinemic) responses than lactose (Foster-Powell et al., 2002). It is believed that a lower glycemic (and insulinemic) response is beneficial for health, especially in subjects with impaired glucose metabolism (Howlett and Ashwell, 2008). In humans, fructose and glycerol are almost completely absorbed and metabolized by the liver (Grunnet and Lundquist, 1967; Schaefer et al., 2009; Sun and Empie, 2012). Therefore, the effects of these substrates on postprandial glucose homeostasis will likely depend on the rate and extent of conversion of these substrates to glucose by the liver. In humans, fructose is only partly (29–51%) converted to glucose by the liver (Sun and Empie, 2012); whether this is also the case for veal calves is not clear. Compared with fructose and glycerol, glucose may lead to higher glycemic (and insulinemic) responses than lactose (Foster-Powell et al., 2002), and thus may negatively affect postprandial glucose homeostasis. Whether prolonged exposure to these substrates (as partial replacer of lactose in veal calves) also affects insulin sensitivity is not known.

The objective of the current study was, therefore, to study the effects of partial replacement of dietary lactose by glucose, fructose, and glycerol on glucose homeostasis and insulin sensitivity (**IS**) in veal calves. The effects on energy and protein utilization for growth were also assessed and described elsewhere (Gilbert et al., 2016)

MATERIALS AND METHODS

Animals and Housing

Forty male Holstein-Friesian calves were housed at the research facility of the Department of Animal Sciences at Wageningen University. At start of the trial calves were 97 ± 1.4 d of age and weighted 114 ± 2.4 kg (means ± SEM).

Calves were housed in groups, except for the last 6 d of the pre-experimental period (i.e., first 10 d of the trial) and the last 14 d of the trial. During these periods calves were housed individually in metabolic cages (dimensions = 0.80 × 1.8 m). During group housing, calves were housed in pens (5 calves/pen), which were fitted with wooden slatted floors and galvanized fencing. Per calf, 2 m^2 was available. Ventilation occurred by ceiling fans, and illumination by natural light and artificial (fluorescent lamps) light between 0630 and 1730 h. The average temperature and humidity were 18.5 ± 0.4°C and 69.5 ± 1.2%, respectively (means ± SEM). The experimental procedures were approved by the Animal Care and Use Committee of Wageningen University.

Experimental Design, Diets, and Feeding

Calves were fed 2.0 times the ME requirements for maintenance, which was set at 460 kJ/kg of metabolic BW per day (Van Es et al., 1967). Individual BW were measured weekly and the feeding rate was adjusted accordingly.

The trial consisted of a pre-experimental period (first 10 d) and an experimental period of 55 d. During the pre-experimental period, all calves received the control MR diet, which contained 462 g of lactose/kg of MR. The composition of the MR is given in Table 1. Thereafter, calves were assigned to 1 of 4 dietary treatments. The control group (**CON**) remained on the control MR diet; in the other groups 150 g of lactose (per kg of MR) was replaced by isoenergetic amounts of either glucose (**GLU**; Tereos Syral, Marckolsheim, France), fructose (**FRU**; Tate & Lyle Europe, Boleraz, Slovakia) or glycerol (**GLY**; Triconor Distribution BV, Soest, the Netherlands). All calves remained on their respective diets for a period of 55 d. The introduction of the lactose replacers occurred gradually, by increasing the lactose replacement by 50 g/kg of MR every 3 d.

In addition to MR, each calf received 10 g of DM of solid feed per kilogram of metabolic BW per day. The solid feed consisted of 80% concentrates and 20% wheat straw (based on DM). The concentrates were composed of 279 g/kg of barley, 458 g/kg of corn, 205 g/kg of lupines, 24 g/kg of palm oil, and 34 g/kg of premix.

Milk replacer was fed on individual basis, at a concentration of 140 g of MR/L and supplied at a temperature of ~42°C. The concentration increased to 160 g/L of water when the MR volume ≥9.0 L. Solid feed was provided per pen (5 calves/ pen) during group housing, and per individual calf when the calves were housed in metabolic cages. Calves were allowed ad libitum access