J. Dairy Sci. 100:1–11
https://doi.org/10.3168/jds.2017-12910

Plasma concentrations of glucagon-like peptide 1 and 2 in calves fed calf starters containing lactose

Y. Inabu,* A. Saegusa,† K. Inouchi,† S. Koike,‡ M. Oba,§ and T. Sugino*[1]
*The Research Center for Animal Science, Graduate School of Biosphere Science, Hiroshima University, Higashi-Hiroshima, Japan 739-8528
†Purchasing and Supplying Department, Dairy Technology Research Institute, The National Federation of Dairy Co-operative Associations (ZEN-RAKU-REN), Nishi-shirakawa, Fukushima, Japan 969-0223
‡Department of Animal Science, Graduate School of Agriculture, Hokkaido University, Sapporo, Japan 060-8589
§Department of Agricultural, Food and Nutritional Science, Faculty of Agricultural, Life and Environmental Sciences, University of Alberta, Edmonton, Canada T6G 2P5

ABSTRACT

The objective of this study was to evaluate the effects of lactose inclusion in calf starters on plasma glucagon-like peptide (GLP)-1 and GLP-2 concentrations and gastrointestinal tract development in calves. Holstein bull calves (n = 45) were raised on an intensified nursing program using milk replacer containing 28.0% CP and 15.0% fat, and were fed a texturized calf starter containing 0 (control), 5.0 (LAC5), or 10.0% (LAC10; n = 15 for each treatment) lactose on a DM basis. Lactose was included in the starter by partially replacing dry ground corn in pelleted portion of the starter. All calf starters were formulated with 23.1% CP. The ethanol-soluble carbohydrate concentrations of the control, LAC5, and LAC10 starters were 7.3, 12.3, and 16.8% on a DM basis, respectively. Starch concentrations of the control, LAC5, and LAC10 starters were 29.7, 27.0, and 21.4% on a DM basis, respectively. All calves were fed treatment calf starters ad libitum. Blood samples were obtained weekly from 1 to 11 wk of age, and used to measure plasma GLP-1, GLP-2, and insulin concentrations, serum β-hydroxybutyrate (BHB) concentration, and blood glucose concentration. At 80 d of age, calves were euthanized, and weights of the reticulorumen, omasum, abomasum, small intestine, and large intestine tissue were measured. Serum BHB concentration was higher for calves fed the LAC10 (171 μmol/L) starter than for those fed the control (151 μmol/L) and LAC5 (145 μmol/L) starters. Plasma GLP-1 and GLP-2 concentrations did not differ between treatments. However, relative to the baseline (1 wk of age), the plasma GLP-1 concentration was higher for the LAC10 (125.9%) than for the LAC5 (68.2%) and control (36.8%), and for the LAC5 than for the control (36.8%). Moreover, similar differences between treatments were observed for GLP-2 concentration relative to the baseline (88.2, 76.9, and 74.9% for LAC10, LAC5, and control treatments, respectively). The serum BHB concentration was positively correlated with the plasma GLP-1 concentration (r = 0.428). Furthermore, the plasma GLP-1 concentration was positively correlated with the insulin concentration (r = 0.793). The weights of the reticulorumen, omasum, abomasum, small intestine, and large intestine were not affected by the treatments. In conclusion, inclusion of lactose in calf starters resulted in higher plasma GLP-1 and GLP-2 concentrations, and BHB might be associated with higher plasma GLP-1 concentration.
Key words: lactose inclusion, gut-derived peptide, glucagon-like peptide 1, glucagon-like peptide 2

INTRODUCTION

Gut-derived peptides, secreted in response to ingested nutrients, are known to play important roles in nutrient utilization and in the physical, morphologic, and metabolic transformation of growing animals. Among such peptides are the glucagon-like peptide (**GLP**)-1 and GLP-2; both are produced by enteroendocrine L-cells of the gastrointestinal tract (**GIT**), primarily from the distal intestine (Burrin et al., 2003). The L-cells produce GLP-1 and GLP-2 as part of a proglucagon gene (*GCG*), which is larger precursor of GLP-1 and GLP-2 (Burrin et al., 2003). Glucagon-like peptide-1 plays a role in glucose homeostasis via the stimulation of insulin secretion in both nonruminants (O'Halloran et al., 1990; Holz et al., 1993) and ruminants (Faulkner, 1991; Edwards et al., 1997; Kurose et al., 1999) as well as through its own direct action (Luque et al., 2002; Acitores et al., 2005; Sancho et al., 2005, 2006). On the other hand, GLP-2 plays a role in stimulation of intestinal growth in nonruminants (Drucker et al., 1996; Kato et al., 1999; Hartmann et al., 2000). Moreover, Taylor-

Received March 22, 2017.
Accepted July 24, 2017.
[1]Corresponding author: sugino@hiroshima-u.ac.jp

Edwards et al. (2011) reported that ruminants respond to GLP-2 in a manner similar to that of nonruminants.

Previous studies reported that VFA, especially butyrate, are main secretagogues for GLP-1 and GLP-2 in ruminants (Fukumori et al., 2012; Elsabagh et al., 2017), and Górka et al. (2009) reported that sodium butyrate supplementation in milk replacers and calf starters increased GLP-2 secretion in calves.

Several studies have shown that the feeding of lactose increases ruminal butyrate concentration in dairy cows (DeFrain et al., 2004; Oba et al., 2015; Gao and Oba, 2016). Fermentation products in the rumen, particularly butyrate, are considered the main stimulators of GIT development (Sander et al., 1959; Steele et al., 2016). In previous studies, sodium butyrate supplementation in calf starters increased reticulorumen weight relative to whole stomach weight and small intestine weight relative to BW in calves (Górka et al., 2011, 2014).

Based on this information, it was expected that lactose inclusion in the diet of calves would stimulate GIT development via stimulation of GLP-1 and GLP-2 secretion. Therefore, the objective of our study was to evaluate the effects of inclusion of lactose in calf starters on plasma GLP-1, GLP-2, and insulin concentrations, serum BHB and blood glucose concentrations, and GIT development in calves.

MATERIALS AND METHODS

Animals and Diets

The procedures used in the present study were performed in accordance with principles and guidelines for animal use set by Hiroshima University, and all experimental procedures were approved by the Animal Care and Use Committee of Hiroshima University. The detailed procedure was described in a companion paper (Saegusa et al., 2017). Forty-five Holstein bull calves, BW of 46.7 ± 0.7 kg and 5.0 ± 0.1 d of age (mean ± SE), were born on March 20 to April 13, 2015 (n = 21) and May 7 to June 2, 2015 (n = 24). Calves were further blocked by birthdate, BW, and farm origin, and randomly assigned to 1 of 3 calf starter treatments: fed texturized calf starter (control), and calf starter where starch was replaced with lactose at 5% (**LAC5**) or 10% (**LAC10**; n = 15 for each treatment) on a DM basis. Calves were fed calf starters from 1 wk of age, after the first blood sampling. Ingredient composition of calf starter formulations (% of DM) is shown in Table 1, which is adapted from a companion paper of Saegusa et al. (2017). As shown in Table 1, lactose was included in the pelleted portion in the calf starter by partially replacing dry ground corn. All calf starters were isonitrogenous with actual CP concentrations in the control, LAC5, and LAC10 starters of 24.0 ± 0.4, 23.3 ± 1.0, and 24.4 ± 0.8% (mean ± SD) on a DM basis, respectively. Ethanol-soluble carbohydrate concentrations in the control, LAC5, and LAC10 starters were 10.3 ± 0.6, 11.7 ± 0.7, and 15.8 ± 0.7% on a DM basis, respectively. Starch concentrations of the control, LAC5, and LAC10 starters were 29.7 ± 1.1, 27.0 ± 2.3, and 21.4 ± 1.1% on a DM basis, respectively. The NDF concentrations in control, LAC5, and LAC10 were 16.5 ± 0.9, 16.6 ± 0.6, and 17.6 ± 0.5 on a DM basis, respectively. Calves had free access to water throughout the study.

Table 1. Ingredient composition of calf starters (adapted from Saegusa et al., 2017)

Composition	Treatment		
	Control	LAC5	LAC10
Ingredient, % of DM			
Steam-flaked corn grain	9.9	9.9	9.9
Steam-flaked barley grain	20.2	20.2	20.2
Alfalfa dehydrated pellet	3.7	3.7	3.7
Molasses cane	0.4	0.4	0.4
Pellet	65.8	65.8	65.8
In pellet, % of DM			
Dry ground corn	14.9	8.2	1.6
Wheat feed flour	1.6	1.6	1.6
Soybean flour	2.2	3.4	4.4
Wheat bran	9.0	9.0	9.0
Soybean meal	17.3	16.8	14.6
Rapeseed meal	1.3	1.3	1.3
Heated soybean[1]	7.1	7.1	7.1
Corn gluten meal	2.3	2.6	4.1
Ground beet pulp	4.1	4.1	4.1
Dehydrated alfalfa	0.0	0.6	1.9
Cane molasses	3.3	3.3	3.3
Calcium carbonate	1.2	1.2	1.2
Salt	0.7	0.7	0.7
Calcium phosphate	0.6	0.6	0.6
GC mix 21[2]	0.5	0.5	0.5
Lactose[3]	0.0	5.0	10.0

[1]Heated soybean (SoyPlus, West Central Cooperative, Ames, IA).

[2]GC mix 21 (trace minerals and vitamins premix, Zenrakuren, Tokyo, Japan), containing 16.0% vitamin mix, 6.3% trace mineral mix, and 77.7% rice bran.

[3]Lactose (Hilmar 5030 Extra Fine Grind Lactose, Hilmar Ingredients, Hilmar, CA).

Calves were raised on an intensified nursing program using a commercial milk replacer containing 28% CP and 15% fat at 200 g/L. The milk replacer was fed in 2 equal portions at 0630 and 1630 h. After arrival, the amount of milk replacer fed to calves was gradually increased from 600 to 1,200 g/d over a 7-d period to adapt calves to intensive liquid feeding. Calves were fed milk replacer at 1,200 g/d from 3 to 5 wk of age, and were weaned at 6 wk of age by reducing the provided milk replacer to 800 g/d. The amount of milk replacer offered was further reduced to 600 g/d at wk 7, and no milk was provided at wk 9. Calves were offered one of the treatment calf starters ad libitum at 1000 h ini-