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Short communication: Plasma concentration of glucose-dependent insulinotropic polypeptide may regulate milk energy production in lactating dairy cows

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ABSTRACT

In dairy cows, an increase in plasma concentration of glucose-dependent insulinotropic polypeptide (GIP) is associated with an increase in metabolizable energy intake, but the role of GIP in energy partitioning of dairy cattle is not certain. The objective of this study was to examine the relationship between plasma GIP concentrations and energy partitioning toward milk production. Four mid-lactation, primiparous, rumen-fistulated Holstein-Friesian cows were fed a control diet of 55% forage and 45% concentrate [dry matter (DM) basis] in a 4 × 4 Latin square design with 4-wk periods. The 4 treatments were (1) control diet fed at 1000 and 1600 h, and (2) once-daily (1000 h) feeding, (3) twice-daily (1000 and 1600 h) feeding, and (4) 4 times/d (1000, 1600, 2200 and 0400 h) feeding of the control diet plus 1 dose (1.75 kg on a DM basis at 0955 h) into the rumen of supplemental vegetable proteins (Amino Green; SCA NuTec Ltd., Thirsk, UK). Measurements of respiratory exchange and energy balance were obtained over 4 d during the last week of each period while cows were housed in open-circuit respiration chambers. Blood was collected from the jugular vein every 30 min for 12 h, using indwelling catheters, starting at 0800 h on d 20 of each period. Plasma GIP concentration was measured in samples pooled over each 5 consecutive blood samplings. The relationships between plasma GIP, DM intake, heat production, respiratory quotient, milk yield, and milk energy output were analyzed using linear correlation procedures, with metabolizable intake as a partial variant. Plasma GIP concentration was not correlated with heat production, or milk yield, but was positively correlated with milk energy yield (correlation coefficient = 0.67) and negatively correlated with RQ (correlation coefficient = −0.72). The correlations between GIP and RQ and milk energy output do not imply causality, but suggest that a role for GIP may exist in the regulation of energy metabolism in dairy cows.

Key words: dairy cow, glucose-dependent insulinotropic polypeptide, energy partitioning, milk energy output

Short Communication

In nonruminants, the main function of the gut hormone glucose-dependent insulinotropic polypeptide (**GIP**) is to increase insulin secretion in a glucose concentration-dependent manner (Holst and Gromada, 2004). Another key function of GIP is its role in the regulation of energy and lipid metabolism. Glucose-dependent insulinotropic polypeptide not only increases the activity of lipoprotein lipase in adipose tissue and reduces concentration of plasma FFA (Kieffer, 2003) but also increases lipogenesis (Hauner et al., 1988). Studies using GIP receptor knockout mice have demonstrated a role of GIP in regulating fat deposition in mice, making the mice less energy efficient due to an increased oxidation of fat (Miyawaki et al., 2002). These knockout mice exhibited decreased BW despite having the same DMI as wild-type control mice.

In lactating dairy cows (Relling and Reynolds, 2008) and growing lambs (Relling et al., 2010), plasma GIP concentration increased with increased ME intake. In early lactation, plasma GIP concentration increased with increasing DIM but not in response to an increase in DMI (Relling and Reynolds, 2007**[AU1: Should this be 2007b?]**). In ruminants the role of GIP is not certain. Sheep infused with GIP had decreased plasma concentration of glycerol, which was measured as an indicator of lipolysis (Martin et al., 1993). Also, GIP stimulated lipogenesis in sheep adipose tissue (Baba et al., 2000). Although plasma GIP concentration seems

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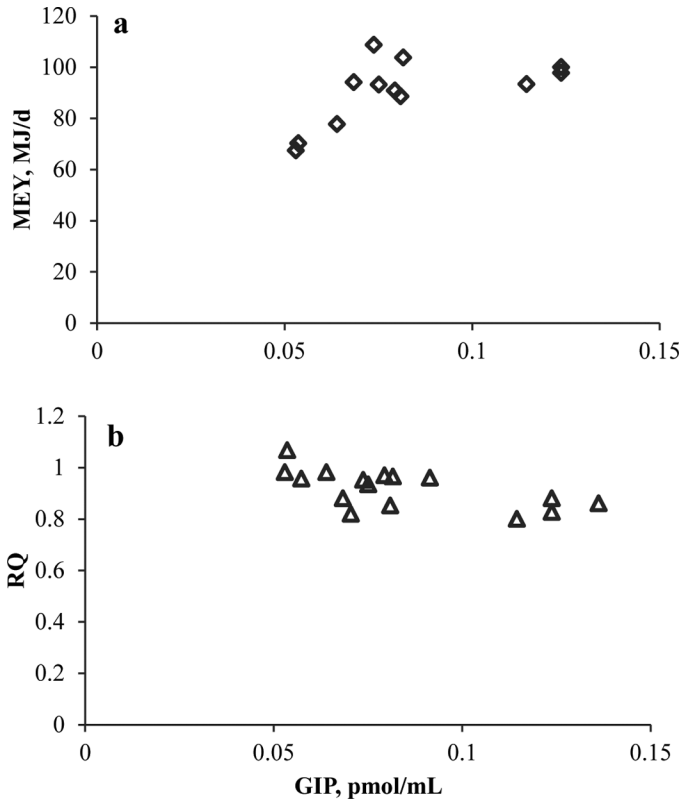

Figure 1. Association between plasma glucose-dependent insulinotropic polypeptide (GIP; pmol/d**[AU7: Should this be pmol/mL, as in the figure?]**) concentration and (a) milk energy yield (MEY; MJ/d) and (b) respiratory quotient (RQ) in mid-lactation dairy cows.

to increase in response to some of the same stimuli in ruminants as in nonruminants, and some GIP functions are similar among species regarding lipolysis and lipogenesis, the role of GIP in regulating energy partitioning in lactating dairy cows is not certain. Therefore, the objective of the present study was to examine the relationship between plasma GIP concentrations and energy metabolism in lactating dairy cows.

All animal procedures were licensed, regulated, and inspected by the United Kingdom Home Office under the Animals (Scientific Procedures) Act of 1986. Four mid-lactation, primiparous, rumen-fistulated Holstein-Friesian cows were fed a control diet of 55% forage and 45% concentrate (DM basis; Table 1) in a 4 × 4 Latin square design with 4-wk periods. The 4 treatments were (1) control diet fed at 1000 and 1600 h, and (2) once-daily (1000 h) feeding, (3) twice-daily (1000 and 1600 h) feeding, and (4) 4 times/d (1000, 1600, 2200 and 0400 h) feeding of the control diet plus 1 dose (1.75 kg on a DM basis at 0955 h) into the rumen of supplemental vegetable proteins (Amino Green; SCA NuTec Ltd., Thirsk, UK). Measurements of respiratory exchange and energy balance were obtained over 4 d during the last week of each period while cows were housed in open-circuit respiration chambers, as described previously (Moe et al., 1972; Tyrrell et al., 1979; Lapierre et al., 1992). Heat production was estimated as described by Brouwer (1965). Feed refusals were collected daily, at 0930 h. Dry matter intake was measured daily by the difference between feed offered and feed refusal.

Cows were milked twice per day (0600 and 1600 h) and the milk energy yield (**MEY**) was estimated using the milk yield (**MY**) and milk composition as described previously (Tyrrell and Reid, 1965). Blood was collected from the jugular vein every 30 min for 12 h using indwelling catheters and starting at 0800 h on d 20 of each period (Huntington et al., 1989; Relling and Reynolds, 2007a). Plasma GIP concentration was measured in samples pooled for each 5 consecutive blood samplings over the 12-h collection period. Plasma GIP concentration was measured as described by Relling and Reynolds (2007a), using the primary antibody described by Larsen et al. (2010). The intraassay coefficient of variation was 9.8% and the minimum sensitivity (90% of zero standard binding) was 0.003 pmol/tube**[AU2: Tube of what? Please specify how much of what was in a tube.]**.

Table 1. Control diet formulation and composition (g/kg of DM)

Item	Amount
Ingredient	
Corn silage	402
Grass silage	125.6
Barley straw	22
Limestone	0.4
Cracked wheat	111
Molassed sugar beet feed	58
Corn distillers grains	49
Hi-pro soya[1]	62
Rapeseed meal	62
Fat 100%[2]	10
Palm kernel expeller	53
Wheat feed	31
Urea	5
Minerals/vitamins[3]	10
Composition	
CP	156
NDF	428
ADF	190
Starch	202
WSC[4]	24
Ether extract	38
Ash	63
Starch + WSC	226

[1] **[AU5: Please provide the name and location of the manufacturer of Hi-pro soya.]**

[2]Calcium salts of soybean oil.

[3]Mineral and vitamin mix, which met and or exceeded requirements according to NRC (2001).**[AU6: Please provide the composition of the mineral and vitamin mix.]**

[4]WSC = water-soluble carbohydrates.

Table 2. Pearson correlation analysis, using DMI as a partial correlation, among plasma glucose-dependent insulinotropic polypeptide (GIP) concentration, heat production (HP), DMI, milk yield (MY), respiratory quotient (RQ), and milk energy output (MEY)

Variable	GIP	HP	DMI	MY	RQ
HP	−0.34				
DMI	−0.20	0.11			
MY	0.50	−0.26	0.26		
RQ	−0.78**	0.44	−0.28	−0.75**	
MEY	0.67*	−0.24	0.23	0.94**	−0.83**

*$P < 0.05$; **$P < 0.01$.

The relationships between plasma GIP and DMI, heat production, respiratory quotient (**RQ**), MY, and MEY were analyzed using the linear correlation procedures of SAS (version 9.1; SAS Institute Inc., Cary, NC). For all the correlations except DMI, ME intake was used as the partial variant. In a preliminary statistical analysis of the data, the addition of supplemental vegetable proteins with the different feeding times and their interaction with time had no effect ($P > 0.10$) on any of the variables measured; therefore, the main effects of supplemental vegetable proteins and the different feeding times were excluded from the statistical model for the data analysis reported in the present paper.

In the present study, the average DMI and MY were18.6 and 27.6 kg/d respectively. The average plasma GIP concentration was 84.2 p*M*. A positive correlation of GIP with MEY ($P = 0.02$; Figure 1a) and a negative correlation with RQ ($P < 0.01$; Figure 1b) was detected; MY, DMI, and heat production were not correlated ($P \geq 0.11$) with plasma GIP concentration (Table 2). To our knowledge, this is the first study to show an association between the gut peptide GIP and energy measurements such as RQ or MEY. Although the positive correlation between plasma GIP concentration and MEY does not prove that ME distribution to milk energy is regulated by GIP, it does suggest that GIP may play a role in, or be related to, energy partitioning in dairy cows. Effects of GIP on energy metabolism have been shown in other animal models. Using in vitro and in vivo studies, GIP has been shown to stimulate lipogenesis in rat and ovine adipose tissue (Beck, 1989; Martin et al., 1993; Baba et al., 2000; Miyawaki et a., 2002). Also, GIP increases whole-body glucose utilization if infused with insulin in sheep (Rose et al., 1998). Using models with GIP receptor knockout mice, Miyawaki et al. (2002), reported that with the same energy intake, the knockout mice were less efficient in terms of dietary energy utilization compared with control wild-type mice. The lack of action of GIP in the GIP receptor knockout mice resulted in the increased use of fat as an energy substrate, which was measured as a smaller RQ compared with controls. However, in the present study, a negative correlation existed between plasma GIP concentration and RQ. This indicates the cows with less plasma GIP concentration were using more fat as an energy substrate, which would agree with a positive effect of GIP on lipogenesis. The use of lipids as an energy fuel would allow more glucose to be utilized for milk synthesis. Despite the importance that GIP may have in energy partitioning and milk energy output, we are not aware of studies that measured GIP receptor concentration in the mammary gland or the effect of GIP on enzymatic activity in the mammary gland. In conclusion, the correlations between GIP and RQ and MEY do not prove causality, but they do suggest that a role for GIP may exist in the regulation of nutrient and energy metabolism in dairy cows.

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