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Effect of Glutamine Supplementation on Splanchnic Metabolism in Lactating Dairy Cows

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ABSTRACT

The suggestion that glutamine (Gln) might become conditionally essential postpartum in dairy cows has been examined through increased postruminal supply of Gln. Net nutrient flux through the splanchnic tissues and mammary gland was measured in 7 multiparous Holstein cows receiving abomasal infusions of water or 300 g/d of Gln for 21 d in a crossover design. Milk yield increased significantly (by 3%) in response to Gln supplementation, but the 2.4% increase in milk protein yield was not statistically significant. Glutamine treatment had no effect on portal or hepatic venous blood flows. Net portal appearance of Gln and Glu was increased by Gln supplementation, accounting for 83% of the infused dose with, therefore, only limited amounts available to provide additional energy to fuel metabolism of the portal-drained viscera. The extra net portal appearance of Gln was offset, however, by a corresponding increase in hepatic removal such that net Gln splanchnic release was not different between treatments. Nonetheless, the Gln treatment resulted in a 43% increase in plasma Gln concentration. Infusions of Gln did not affect splanchnic flux of other nonessential amino acids or of essential amino acids. Glutamine supplementation increased plasma urea-N concentration and tended to increase net hepatic urea flux, with a numerical increase in liver hepatic O_2 consumption. There were no effects on glucose in terms of plasma concentration, net portal appearance, net liver release, or postliver supply, suggesting that Gln supplementation had no sparing effect on glucose metabolism. Furthermore, mammary uptake of glucose and amino acids, including Gln, was not affected by Gln supplementation. In conclusion, this study did not support the hypothesis that supplemental Gln would reduce glucose utilization across the gut or increase liver gluconeogenesis or mammary glutamine uptake to increase milk protein synthesis.
Key words: glutamine, amino acid, splanchnic, nutrient flux

INTRODUCTION

Glutamine (Gln) is a nonessential amino acid (**NEAA**) as it can be synthesized by mammalian tissues. Nonetheless, under situations of high metabolic demand, such as postsurgery or during infection, exogenous Gln has been shown to exert beneficial effects (Newsholme, 2001; Wilmore, 2001; Ziegler, 2001). Therefore, Gln may be considered conditionally essential during periods of physiological stress. Such a scenario may exist for the dairy cow during early lactation, when there may be a considerably larger demand for Gln than can be met from absorption, endogenous stores, and synthesis de novo. First, milk production is a large drain for Gln, with Gln and Glu together comprising 20% of milk protein AA (Jensen, 1995). Second, Gln is an important energy source for the gut in monogastrics: in piglets, Gln and Glu catabolism may account for 50% of the CO_2 produced by the gut (Reeds et al., 2000), comparable to the contribution from glucose (van der Schoor et al., 2001). In the immediate postpartum period, when the cow has a glucose deficiency of approximately 500 g/d (Bell, 1995), the gut may rely heavily on Gln as an energy source. Additional Gln supply may spare glucose catabolism by the gut, thereby increasing supply to peripheral tissues. As a glucogenic AA, Gln may also increase postsplanchnic glucose supply by enhancing hepatic gluconeogenesis. Third, Gln provides N to support nucleic acid synthesis (Gate et al., 1999) during the proliferation of the gut and liver, which increase their mass by 19 and 12%, respectively, during the first 8 wk postpartum (Gibb et al., 1992).

That Gln supply may be limited in early lactation is suggested by the observation that plasma Gln concen-

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trations are depressed and not restored to precalving levels even by 56 d into lactation, unlike other AA (Meijer et al., 1995b; Doepel et al., 2002). Although plasma concentration is not a direct reflection of whole-body flux, concentration depression over an extended period would suggest that dietary supply plus de novo synthesis of Gln are insufficient to meet the increased multiple demands during the postpartum period. Indeed, the output of Gln and Glu in milk protein is often less than their uptake by the mammary gland (**MG**; Guinard and Rulquin, 1994). Meijer et al. (1993) suggested that, at low plasma Gln concentrations, supply to the MG becomes a restriction that might be overcome by supplementation because MG uptake would increase in response to an increment in arterial Gln concentration.

Potentially, Gln supplementation may benefit a number of important processes in the early postpartum cow. Therefore, we hypothesized that Gln supplementation might improve milk and milk protein yields through 3 means: 1) sparing glucose utilization by gut tissue and increasing liver synthesis of glucose, 2) increasing hepatic release of Gln and thus peripheral tissue supply, and 3) increasing mammary uptake of Gln through increased arterial supply, thereby removing a limitation on milk protein secretion. Our objectives, therefore, were to determine the effect of postruminal Gln supplementation in early lactation cows on the net flux of Gln and other nitrogenous and energetic compounds across the gut, liver, and mammary gland, and on milk production and composition.

MATERIALS AND METHODS

Animals and Treatments

Eight multiparous Holstein cows with an average BW of 733 ± 51 kg were surgically implanted with abomasal catheters (Doepel et al., 2006) and with chronic indwelling catheters in the mesenteric, portal, and hepatic veins and the caudal aorta, via a mesenteric artery (Huntington et al., 1989; Blouin et al., 2002). The right carotid artery was surgically raised to a subcutaneous position to allow access to arterial blood in the event that the aortic catheter failed. Surgeries were performed a minimum of 6 wk before calving.

Continuous abomasal infusions were administered to the cows according to a crossover design with 21-d periods. The 2 treatments were 10 L/d water (control) or 300 g/d (85.6 mmol/h) of L-Gln delivered in 10 L of water (Gln). Infusions were initiated within 48 h following parturition and administered continuously using a peristaltic pump. Fresh L-Gln infusion solutions were prepared daily. The infusion rate of 300 g/d of Gln was based on observations of Gln metabolism in previous studies. In sheep, Gln irreversible loss rate is approximately 1 mmol/h per $kg^{0.75}$ (Hoskin et al., 2001). If scaled to a 700-kg dairy cow, this would amount to 3.2 mol/d (470 g/d). The decrease in Gln plasma concentration prepartum to 21 d postpartum is approximately 40% (Doepel et al., 2002). If this decrease represents a change in apparent net needs it would amount to approximately 190 g/d. The cow may actually synthesize more Gln to reduce the decrease in plasma concentration making the actual net flows of Gln to support metabolism during the transition period even greater; therefore, an additional 50% was added to the supplement.

Cows were fed a diet as described previously (Doepel et al., 2006). Briefly, a TMR that supplied 30.6 Mcal of NE_L and 2,067 g/d of MP at 18 kg of DMI/d was fed ad libitum twice daily at 0800 and 1600 h from d 1 to 17, and in 12 equal meals per day delivered at 2-h intervals by automatic feeders from d 18 to 21 of each experimental period. The TMR consisted of 38% corn silage, 20% grass hay, 19% high moisture corn, and 23% protein supplement consisting of 49% soybean meal, 29% Soyplus (West Central Soy, Ralston, IA), 5% Megalac (Church & Dwight Co. Inc., Princeton, NJ), and 17% mineral and vitamin supplements. The cows also received 20 g of rumen-protected methionine (Mepron 85, Degussa, Burlington, Ontario, Canada) and 2 kg of long alfalfa hay (11.9% CP, 32.9% ADF, and 56.1% NDF) once daily in the morning before the TMR was offered. Orts were recorded daily. Moisture content of the silages was determined weekly and used to make ration adjustments. Cows were given free access to fresh water. Cows were milked twice a day, at 0830 and 1930 h, and milk yield was recorded at each milking. Milk was sampled at each milking from d 15 to 21 of each period. The experimental protocol was approved by the Institutional Committee for Animal Care of the Lennoxville Research Centre, and animals were cared for in accordance with the guidelines of the Canadian Council on Animal Care (1993).

Blood Sampling

On d 21 of each period, blood samples were collected into heparinized tubes simultaneously from the arterial, hepatic venous, and hepatic portal catheters every 45 min for 4 h (6 samples), covering 2 cycles of feeding. Blood samples were also obtained from the subcutaneous abdominal vein by venipuncture following the same 45-min sampling schedule. To determine plasma flow across the splanchnic tissues, para aminohippuric acid (**pAH**; 10% wt/vol) was infused into a mesenteric vein catheter (Huntington et al., 1989). A priming dose of 2 g was given a minimum of 40 min before the first blood