Choline and Methionine for Transition Dairy Cows – How Interchangeable Are They?

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Introduction

Choline and methionine both have essential roles in mammalian metabolism. Choline is a quasi-vitamin that has a variety of functions, including that as the predominant phospholipid contained in the membranes of all cells in the body (as phosphatidylcholine), a component of the neurotransmitter acetylcholine, and as a direct precursor to betaine in methyl metabolism (Overton and Waldron, 2004). Furthermore, choline deficiency in monogastric species results classically in fatty liver development among other symptoms.

Methionine is an essential amino acid and building block for protein and typically considered one of the two most limiting amino acids for production of milk and milk protein in lactating dairy cows (National Research Council, 2001). In addition, the roles of methionine in regulating metabolic processes as well as innate immunity and oxidative metabolism continue to be elucidated (Martinez et al., 2017). Methionine can contribute to biosynthesis of phosphatidylcholine through its role as a methyl donor and, in a study conducted a number of years ago using lactating goats and radiolabeled choline and methionine to determine the kinetics and interconversions between the two compounds, 6% of the choline pool was derived from methionine (Emmanuel and Kennelly, 1984).

Choline and methionine each have been the focus of a number of studies involving transition cows during the past 20 years and, as detailed below, both have demonstrated positive effects on cow productivity during early lactation. Given the interrelationships described above, questions are often asked regarding the potential interchangeability of these nutrients. In this paper, I will review the research conducted for both of these nutrients in the transition dairy cow as well as discuss the potential for interchangeability of these nutrients in transition cow metabolism.

Choline Supplementation During the Transition Period

Piepenbrink and Overton (2003) determined that cows fed rumen-protected choline (RPC) during the precalving period and continuing through early lactation tended to have increased fat-corrected milk yields (average response + 5.3 lbs/d) during early lactation along with a trend for decreased storage of radiolabeled palmitate as liver triglycerides in vitro and increased concentrations of liver glycogen, implying improved liver metabolism. Diets in this study were formulated to meet grams per day requirements for methionine using corn gluten meal. Effects on blood nonesterified fatty acids (NEFA) and beta-hydroxybutyrate (BHBA) were not significant. Zahra et al. (2006) reported that cows fed RPC had increased milk yield (+ 2.6 lbs/d) during early lactation, but effects of RPC supplementation on blood NEFA and BHBA along with liver composition were not significant.

Cooke et al. (2007) evaluated whether RPC supplementation could prevent and alleviate triglyceride accumulation in liver using a feed-restriction model in dry cows. Supplementation of RPC during feed restriction decreased plasma NEFA and decreased liver triglyceride accumulation, the latter by nearly 50% compared to controls. Furthermore, RPC supplementation during the refeeding period following feed restriction resulted in more rapid clearance of triglycerides from liver. Zom et al. (2011) reported that supplementation with RPC did not affect blood metabolites, but decreased liver TG content during early lactation; further examination (Goselink et al., 2013) of the changes in gene expression in liver from this study suggested that RPC supplementation resulted in increased expression of genes related to processing of fatty acids and VLDL assembly. Elek et al. (2008; 2013) determined that cows fed RPC produced 5.5 lbs/d more fat-corrected milk (9.7 lbs/d more milk) during early lactation, and these effects were underpinned by decreased liver triglyceride and circulating BHBA concentrations for cows fed RPC.

Recently, Zenobi et al. (2018a) fed cows either 0 or 60 g/d of RPC (17.3 g/d of choline chloride) for the last 17 d before expected calving through 21 d postpartum to cows fed either high-energy or controlled energy dry period diets. Cows fed RPC tended to have increased yields of milk (+ 4.8 lbs/d) and energy-corrected milk (+ 4.8 lbs/d) during the first 15 wk postpartum and tended to produce 4.6 lbs/d more milk over the first 40 wk of lactation. Concentrations of plasma NEFA and BHBA were not affected by RPC and liver TG content was similar between cows fed control vs. supplemented diets. Interestingly, cows fed RPC produced colostrum with greater IgG content and calves from cows fed RPC had greater weight gain from calving through 50 wk of age. Effects of RPC on production and metabolism were largely independent of prepartum nutritional strategy in this experiment. In a companion experiment, they sought to evaluate dose-response effects to RPC supplementation to levels up to 2X that fed in their transition cows study in a restricted-fed dry cow model; RPC supplementation linearly decreased liver TG accumulation during feed restriction (Zenobi et al., 2018b)

In addition to these results, there are other studies that have demonstrated either statistically significant (+ 5.3 lbs/d of milk, Scheer et al., 2002; + 6.4 lbs/d of milk, Pinotti et al., 2003; + 4.0 lbs/d of fat-corrected milk in one experiment and + 1.8 lbs/d of milk in a second experiment, Lima et al., 2007) or statistically nonsignificant (+ 5.1 lbs of fat-corrected milk, Janovick-Guretzky et al., 2006; + 1.8 lb/d of 3.5% fat-corrected milk, Leiva et al., 2015) production responses to RPC supplementation.

Methionine Supplementation During the Transition Period

Similar to the research conducted focused on choline supplementation to diets fed to transition cows, there is also a substantial body of work accumulated over the past 20 years or so with regard to methionine supplementation during the transition period and early lactation. Overton et al. (1996) fed cows either 0 or 20 g/d of rumen-protected methionine (RPM) beginning 7 to 10 d before calving and continuing into lactation. Cows fed RPM produced 6.0 lbs more fat-corrected milk during early lactation. Socha et al. (2005) fed cows either 10.5 g/d of RPM or 10.2 g/d of RPM plus 16.0 g/d of rumen-protected lysine (RPL) beginning 14 d before expected calving and continuing through early lactation. Cows fed RPM plus RPL produced more milk during early lactation than those fed RPM alone; milk yield of cows fed the basal diets was intermediate. Supplementation of RPM and RPM plus RPL increased milk protein content when cows were fed 18.5% CP diets during the postpartum period; amino acid supplementation did not affect milk protein content when cows were fed 16% CP diets postpartum. Effects of amino acid supplementation on liver and energy metabolism were not evaluated in either the Overton et al. (1996) or Socha et al. (2005) studies.

Piepenbrink et al. 2003 determined the effects of feeding an analog of methionine (2-hydroxy-4-(methylthio)-butanoic acid; HMB) to periparturient cows on production and metabolism. They reported that feeding an intermediate level of HMB increased milk yield by 6.6 lbs per day; however, comprehensive evaluation of the effects of HMB on metabolism (circulating concentrations of NEFA and BHBA, liver concentrations of triglyceride and glycogen, in vitro assessment of liver propionate and palmitate metabolism) suggested that the production responses were not underpinned by changes in liver metabolism.

These responses were supported by those of Bertics and Grummer (1999), who used a research model similar to that described above for choline to evaluate responses of liver triglyceride accumulation during feed restriction and depletion during refeeding to HMB supplementation. In this study, HMB supplementation did not affect either triglyceride accumulation or depletion during the two phases of the experiment.

Ordway et al. (2009) evaluated feeding either the isopropyl ester of HMB (HMBi) or RPM to cows beginning during the prepartum period and continuing into early lactation. They determined that supplementation of HMBi and RPM did not affect yields of milk or fat-corrected milk (average milk yields were 95.7, 95.9, and 92.6 lbs/d for cows fed the basal diet, HMBi, and RPM, respectively); however, milk protein percentage was increased by feeding both HMBi and RPM. Effects of methionine supplementation on liver and energy metabolism were not determined in their experiment.

Preynat et al. (2009, 2010) fed cows RPM with or without intramuscular injections of folic acid and vitamin B12 during the transition period and early lactation. Feeding RPM did not affect milk yield (83.3 vs. 83.0 lbs/d for control vs. RPM, respectively), but increased milk crude protein percentage (2.94 vs. 3.04%). Interestingly, liver concentrations of triglycerides were actually increased in cows fed RPM in this study.

Osorio et al. (2013) fed cows either a basal ration or the basal ration supplemented with either HMBi or RPM beginning 21 d before expected calving and continuing through the postpartum period. Cows fed methionine had large increases in milk yield compared to controls (+5.3 lbs/d for HMBi and +9.5 lbs/d for RPM); however, effects of the two sources of methionine on blood NEFA and BHBA and liver triglyceride content were not significant. Interestingly, cows fed supplemental methionine had greater phagocytosis in blood neutrophils harvested at 21 d postpartum, suggesting improved immune function. Further analysis of samples collected from this study suggested that cows supplemented with Met had better oxidative status as evidenced by lower plasma ceruloplasmin and serum amyloid A concentrations, greater plasma oxygen radical absorbance capacity, and greater liver concentrations of glutathione and carnitine (Osorio et al., 2014). Furthermore, these researchers detected alterations of gene networks in liver consistent with changes in oxidative status and inflammatory responses described above (Osorio et al., 2016).

Recently, Batistel et al. (2017b) fed cows RPM from 28 d before expected calving through 60 d postpartum Cows fed RPM had greater prepartum DMI (+ 2.6 lbs/d) along with greater postpartum (1 to 30 d) DMI (+ 3.7 lbs/d), milk yield (+ 9.1 lbs/d) and energy-corrrected milk yield (+9.7 lbs/d). Concentrations of plasma nonesterified fatty acids during the postpartum period were decreased in cows fed RPM. They also determined that calf birth weight was increased for cows fed RPM and that RPM upregulated AA transport and modulated the mTOR signaling pathway in the placentome (Batistel et al., 2017a)

Differential Responses to Choline and Methionine in Transition Cows

Results above suggest that both choline and methionine supplementation can improve performance of dairy cattle during the transition period, but that each may have distinct roles relative to metabolism. To determine the effects of choline and methionine more specifically on bovine hepatocytes, Chandler and White (2017) prepared primary monolayer hepatocyte cultures from neonatal calves and incubated the cells with increasing concentrations of either choline chloride or DL-methionine. They determined that increasing choline concentrations in the media increased secretion of VLDL into media and decreased the accumulation of reactive oxygen species in media. Furthermore, choline and methionine had differential effects on several of the enzymes related to one-carbon metabolism. Interestingly, there were no interactions detected between choline and methionine additions within this in vitro system.

Sun et al. (2016) fed cows either a control diet or diets supplemented with RPM, RPC, or both in a 2 x 2 factorial arrangement of treatments from 21 d before expected calving through 21 d postpartum. Both RPM and RPC increased prepartum and postpartum DMI and yield of fat-corrected milk during the postpartum period. Both RPM and RPC decreased postpartum concentrations of NEFA and BHBA and increased plasma concentrations of glucose. Furthermore, both RPM and RPC had similar effects on various indices of oxidative status. Interaction terms were not significant for virtually all outcomes, suggesting additivity of responses to RPC and RPM.

Summary

Choline and methionine have essential roles in various aspects of mammalian metabolism and are connected biochemically as part of one-carbon metabolism. Research conducted during the past 20 years supports roles for both choline and methionine in transition cow nutrition. Both choline and methionine generally increase productive performance during early lactation; however, they appear to affect transition cow metabolism differently. Choline appears to function primarily to increase triglyceride export from liver as very low density lipoproteins (VLDL) thereby decreasing liver triglyceride accumulation and improving liver energy metabolism. Methionine appears to alter oxidative status and immune function, thereby also affecting liver metabolism through inflammatory and immune mechanisms. The literature does not support an effect of methionine supplementation on liver triglyceride export. Recent results also suggest that both methionine and choline may have effects of relevance to the calf; methionine via modulation of placental function and choline via increased colostral immunoglobulin G, although more research is needed to fully understand potential epigenetic effects of these nutrients in the transition cow.

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