Role of Methionine and Methionine Precursors in Transition Cow Nutrition with Emphasis on Liver Function

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Introduction

Methionine is an essential and multifunctional nutrient in vertebrate diets. In addition to its role in protein synthesis, methionine functions as a methyl donor and precursor to a number of other antioxidant and lipotropic compounds including cysteine, taurine, glutathione, metallothionine, choline, carnitine, creatine and S-adenosyl methionine (**SAM**), a universal methyl donor (Lehninger, 1977). Methionine precursors 2-hydroxy-4-(methylthio)-butanoic acid (**HMTBa**) and its isopropyl ester can also serve this function (Zanton et al., 2014). In addition these compounds exert beneficial effects on the rumen fermentation and microbial protein synthesis (Lee et al., 2015; Baldin et al., 2015).

Methionine is of particular interest in dairy cattle nutrition. Historically research has focused on the role of methionine as a co-limiting amino acid for milk protein synthesis, and in supporting milk fat synthesis and metabolic balance (Polan et al., 1991; McCarthy et al., 1968). More recently this view has expanded to include other metabolic functions of methionine such as its role in supporting liver function, oxidative balance and immunity (Osorio et al., 2013). In non-ruminants methionine deficiency produces fatty liver disease including depletion of cellular antioxidants (glutathinone), methyl donors, SAM, and general hepatic inflammation and fibrosis (Schugar and Crawford, 2012). This paper will focus on the nutritional role of methionine in the transition dairy cow.

Challenges to the Transition Cow

The dairy cow faces a major metabolic and immunologic challenge at calving in which essential nutrients can play a significant role. Methionine status can potentially be related to three important metabolic indices in transition cows: energy balance (lipid metabolism), protein balance, and antioxidant balance (Pedernera et al., 2010). Dysfunction in any of these spheres of metabolism may result in sub-clinical or clinical disorders or diseases (fatty liver, ketosis, impaired passive transfer of immunity to calf, reduced immune function and disease resistance in cows) (Bell, 1995; Overton and Waldron, 2004; Drackley, 2011; Lean et al., 2013). This up close view of metabolic function has to be put into the context of dairy farm management where dry matter

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intake of cows near and just after calving is a most critical factor. Dry matter intake is in turn influenced by management and environmental factors such as stocking density, heat stress, rumen adaptation, calcium metabolism and overall level of disease challenge. These factors must be addressed in order to gain the most value from supplementing essential nutrients like methionine in the transition period (Overton and Waldron, 2004; Lean et al. 2013).

Liver function is central to metabolism and especially critical in transition dairy cows. During the first 3 to 6 weeks after calving, a typical Holstein cow will mobilize 40-60 kg of body fat and 20 to 25 kg of body protein (Bell, 1995; Komaragiri and Erdman, 1997). The liver both participates in and regulates the majority of this intense metabolic activity aimed at mobilizing and directing nutrient flow to the mammary gland and supporting organs like the G.I. tract. Therefore any diminution in liver function can impair lactation performance and reproduction. Methionine has been shown to be essential for normal liver function and health in several species (Katoh, 2002; Schugar and Crawford, 2012).

Prepartum Protein Status and Supplementation

The increasing demand for amino acids for fetal growth, colostrum synthesis, mammary gland, liver and G.I. tract coupled with the natural reduction in dry matter intake prior to calving can result in negative protein balance (Jaurana et al., 2002). Ideally this would be kept to a minimum to avoid depletion of body protein stores. As a result a number of studies have been conducted to test the effects of prepartum protein supplementation on subsequent performance of dairy cows (Lean et al., 2013).

Kokkonen (2014) conducted a meta-analysis of 15 published studies with 47 treatment comparisons. Prepartum diet crude protein levels varied from 9.7 to 20.6% of dry matter and diet RUP from 2.9 to 10.6% of DM. Confounding factors (length of supplementation, length of postpartum measurements, forage base, energy intake and parity) were included in the analysis with random study effects. A sensitivity analysis for study bias was performed in which each study was excluded, in turn, from the data analysis and the results compared to analysis of the full data set. Milk protein synthesis and postpartum dry matter intake increased in response to increasing prepartum protein supplementation in cows fed higher fiber, mixed forage diets including straw, but tended to decrease in cows fed corn silage-based diets supplemented primarily with soybean meal. The author speculated that corn silage-based diets supported greater rumen microbial protein yields and that use of soybean meal as the source of supplemental protein may have introduced a methionine limitation, based on the amino acid composition of corn and soy proteins (Kokkonen, 2014).

A recent study conducted by Osorio et al. (2013, 2014) tested the effect of supplementing each of two methionine sources (HMTB isopropyl ester and rumen-protected methionine) to dairy cows in late gestation and early lactation. The control diet was methionine limiting in relation to lysine. Supplementing an additional ~7 grams per day of metabolizable methionine from either source improved measures of antioxidant capacity (*P* < 0.04) and tended (*P* < 0.07) to reduce acute phase inflammatory protein response (an indicator of liver function), increase plasma carnitine and improve white blood cell function. Postpartum dry matter intake and milk component yields were significantly improved in supplemented cows (Osorio et al., 2013). These results demonstrated a beneficial response to methionine supplementation during transition and early lactation and linked the response to indicators of methionine metabolism (Osorio et al., 2014).

Literature Summary of the Effects of Methionine Supplementation Pre- and Postpartum on Dairy Cow Performance

A simple summary of 10 published studies with 14 treatment vs. control comparisons was conducted for this review. Data were expressed based on the quantity of additional metabolizable methionine (**mMet**) supplied per cow per day prepartum (8-28 days) from various sources (both protected D-L methionine and methionine analogues). While methionine was also supplemented postpartum in the studies, the level of prepartum supplementation fit the performance data more closely. Prepartum supplementation rates varied from 3 to 12 grams per day of additional mMet; average milk yield ranged from 63 to 95 lbs per cow per day; and length of postpartum supplementation from 28 to 140 days. Milk protein yield and dry matter intake displayed the best fits of the data based on regression analysis. Both followed a polynomial response with a maximum response at ~ 7.5 g/cow/day of mMet prepartum ($R^2 = 0.44$ and 0.32, respectively). Milk fat yield and milk production were poorer fits. While this data set and the analysis are inadequate to draw conclusions the results suggest that optimum supplementation levels lie between 5 and 10 grams of additional mMet per cow per day during the prepartum period as previously suggested by Luchini and Loor (2015).

Summary

Performance of dairy cows is affected by methionine status during the transition period. Recent studies confirm effects of methionine on metabolic processes beyond basic requirements for milk protein synthesis. Various forms of methionine have proven effective in supporting improved cow performance. It appears that 5 to 10 grams of supplemental metabolizable methionine given prepartum will support optimal performance postpartum, although further research is undoubtedly required.

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SESSION NOTES