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CHOLINE: A REQUIRED NUTRIENT FOR TRANSITION DAIRY COWS

"Substantial progress has been made on our understanding of choline as a nutrient for dairy cows. The introduction of rumen-protected products containing choline chloride has facilitated research into various aspects of choline's mode of action within intermediary lipid metabolism in dairy cows. This advancement has also enabled the exploration of crucial questions regarding choline's role in maintaining hepatic health and enhancing productive performance during the critical transition period for cows."

Dairy cows are truly remarkable creatures. Consider the rapid transformation of a modern Holstein cow, going from zero to producing as many as 50 kilograms of energy-corrected milk per day in just 3 to 4 weeks of lactation. Such incredible production demands dynamic and integrated adaptations in multiple tissues to cope with the nutrient shifts during lactation onset.

Research conducted by Chris Reynolds at the University of Reading in the United Kingdom revealed that during the initial 3 weeks of lactation, there is a notable augmentation in hepatic blood flow. This flow rate rises from around 1.100 liters per hour to 2.220 liters per hour. Remarkably, this shift occurs in conjunction with a twofold elevation in oxygen consumption by the splanchnic tissues over the same period[1]. These alterations mirror the escalation in both dry matter intake and nutrient absorption within the gastrointestinal tract. This transformation parallels the heightened demand for essential components like glucose, amino acids, and fatty acids. These elements are crucial for the synthesis of milk by the mammary gland.

During the first 4 to 8 weeks of lactation, dairy cows experience negative nutrient balance, concurrent with increased susceptibility to diseases. Approximately 30 to 35% of the dairy cows are anticipated to experience a clinical disease event in the first month or two postpartum, and success during

the transition period greatly influences the success of the remainder of the lactation of a cow.

An obstacle frequently encountered by dairy cows during the initial stages of lactation is the excessive mobilization of fat tissue, which can lead to an amplified deposition of triacylglycerol within the liver. This condition is commonly referred to as hepatic lipidosis or fatty liver. While minor increments in hepatic triacylglycerol may not necessarily yield detrimental effects on subsequent performance, cows displaying a more pronounced lipidosis, ranging from moderate to excessive levels, experience compromised productivity and well-being. This situation also heightens the likelihood of premature culling. Approximately 40 to 45% of dairy cows develop moderate to severe hepatic lipidosis in the first 3 weeks of lactation.

Recent research from the University of Florida published in the Journal of Dairy Science sheds new light on hepatic lipidosis and its impact on dairy cow performance[2]. In that specific cohort study, the authors examined a group of 329 cows to establish a connection between the concentration of hepatic triacylglycerol within the first week postpartum and its subsequent impact on health, production, and survival outcomes. The study's results demonstrated that once concentrations of hepatic triacylglycerol surpassed the range of 4 to 7%, the risk of disease occurrence escalated while productive performance declined. Though not establishing causality, these associations suggest that identification of strategies to reduce the accumulation of triacylglycerol in hepatic tissue may benefit dairy cows.

One potential solution to alleviate fatty liver is to increase the export of triacylglycerols from the liver, requiring increased synthesis and assembly of very-low-density lipoproteins (VLDL). Choline, a nutrient identified in the 1850s, has subsequently been recognized as a required dietary component for mammals due to its pivotal role in facilitating the synthesis of various compounds. These include phospholipids, sphingolipids, and neurotransmitters. As it turns out, the synthesis and secretion of VLDL by the liver necessitates the presence of phospholipids, many of which fall under the category of phosphatidylcholines. Coincidentally, during the early 1920s when Canadian scientist Frederick Banting was in the process of discovering insulin, his experimental model involved dogs that had their pancreases removed. Remarkably, these dogs developed hepatic lipidosis, a phenomenon observed by one of Banting's students named Charles Best. Best, who later gained international recognition as a scientist, conducted further research and demonstrated that adding phosphatidylcholine to the diets of these depancreatized dogs mitigated the severity of lipidosis in their livers. These groundbreaking findings prompted an exploration of choline as an essential nutrient within the human diet.

Dairy cows affected by fatty liver exhibit lower plasma phosphatidylcholine concentrations. Although phosphatidylcholine can be endogenously synthesized by tissues, it is likely that the demands of choline during the transition period are greater than the supply from dietary sources and from endogenous synthesis, particularly because endogenous synthesis requires methyl groups originated by compounds such as methionine, which can be in short supply at the onset of lactation.

Ruminants, unlike nonruminants, face limitations in choline availability from dietary sources because of rumen microbial degradation. Therefore, supplementing rumen-protected choline (RPC) becomes essential. Despite widespread recognition of choline as a required nutrient for most mammals, established feeding guidelines for lactating or dry dairy cows remain absent.

CHOLINE PLAYS IMPORTANT ROLES ON HEPATIC LIPID METABOLISM

Numerous experiments at the University of Florida studied the role of choline in hepatic lipid metabolism. The experiments used a feed-restriction model to simulate the negative nutrient balance that dairy cows typically experience in the first weeks of lactation[3-6]. The initial utilization of this model can be credited to Ric Grummer from Wisconsin. Grummer demonstrated that the application of RPC led to a reduction in the extent of triacylglycerol accumulation within the livers of dry cows. In subsequent experiments carried out in Florida, a total of 187 pregnant dry cows in the late stages of gestation were intentionally provided with less than 40% of the energy required for both cow maintenance and sustaining the pregnancy. This restricted feeding regimen lasted for a span of 9 days and was designed to induce fatty liver in the cows. The diets administered to the cows contained varying amounts of choline ions, ranging from 0 to 25,8 g/day, in the form of the ReaShure brand of RPC. To ensure consistency, the cows were also given rumen-protected methionine supplementation during the period of restricted feeding, thus replicating the exact metabolizable methionine intake that would occur when the cows consumed 11 kg of dry matter on a daily basis.

Administering choline as part of the diet resulted in a substantial 31,7% reduction in hepatic triacylglycerol concentration, while concurrently increasing glycogen concentration by 54,2%. Importantly, these effects were directly proportional to the quantity of choline ion introduced through the diet. Notably, a noteworthy outcome emerged from one of the experiments: cows that received a supplementation of 25,8 g/day of choline ion

via RPC exhibited an elevated hepatic secretion of triacylglycerol-rich lipoproteins[5]. This finding aligns with observations from research involving non-ruminant species and underscores the significance of choline in supporting the synthesis and subsequent export of lipids from the liver through the production of VLDL.

The introduction of RPC into the diet during the period of feed restriction induced modifications in the expression of multiple genes within the hepatic tissue, specifically those associated with lipid metabolism. These alterations in gene expression patterns indicate a decrease in hepatic lipogenesis and a simultaneous improvement in the export of lipids[4-6]. This phenomenon sheds light on the mechanism behind the reduction in hepatic lipidosis observed in cows that were supplemented with RPC.

SUPPLEMENTING RPC ENHANCES FAT DIGESTIBILITY

Choline serves as a constituent of phosphatidylcholines, a subset of phospholipids that constitute crucial components of both cell membranes and lipoproteins. These phospholipids play a pivotal role in facilitating the absorption and transportation of lipids. As cows approach the period of parturition, their dry matter intake typically decreases, followed by a gradual increase after giving birth. Research conducted by Lance Baumgard at Iowa State University has demonstrated that sudden shifts in dry matter intake can disrupt the structure of the gastrointestinal tract lining, leading to alterations in the integrity of the intestinal epithelium. This, in turn, affects the absorption of nutrients[7].

Indeed, models involving feed restriction have been utilized to replicate disturbances within the intestinal tract that mirror the naturally occurring decline in dry matter intake during the transitional phase. In a recent study conducted at the University of Florida, the impact of RPC supplementation on the digestibility of fat in dairy cows was investigated[6]. For this experiment, 33 prepartum Holstein cows were subjected to a feed restriction regimen aimed at disrupting intestinal integrity. These cows were divided into two groups, with one group receiving 0 g/day of choline ion and the other group receiving 25,8 g/day of choline ion supplementation for a duration of 9 days during the feed restriction period.

On the ninth day, the cows were deprived of feed and were instead given a mixture of saturated fatty acids to assess the apparent digestibility of fat. Supra-mammary lymph samples were collected 6 hours after the cows consumed the fatty acids. The results indicated that providing RPC led to an increase in fat digestibility and the concentrations of triacylglycerol in both blood and lymph. This suggests that supplementing choline to cows experiencing a negative nutrient balance could potentially enhance the transport and absorption of fatty acids within the intestines.

SUPPLEMENTING RPC BENEFITS PRODUCTIVE PERFORMANCE AND HEALTH

While a wealth of literature exists detailing the various cellular mechanisms influenced by choline, a recurring question arises: Can its impact on phospholipid synthesis, liver function, or nutrient transport translate into improved health and productivity outcomes? However, experiments where interventions are applied to individual cows via diet and require careful feeding often face the challenge of limited sample sizes, which can restrict the ability to thoroughly investigate the effects of dietary changes on health and reproduction.

To circumvent this limitation and ensure the broader applicability of interventions, researchers employ meta-analytical techniques that integrate findings from multiple published studies. In 2020, a systematic review of the available literature was conducted, followed by a comprehensive meta-analysis examining the effects of supplemental RPC during the transition period[8]. This analysis encompassed 20 publications, incorporating 21 experiments involving a total of 1.313 transition cows. These cows were randomly assigned to receive either 0 g/day of choline ion or varying amounts of choline ion via RPC starting before calving.

Results from the meta-analysis indicated that supplementing RPC during the transition phase led to a notable increase in energy-corrected milk yield by an average of 2,2 kg/day. Furthermore, there was a tendency for a reduction in the incidence of retained placenta and mastitis among the supplemented cows compared to their non-supplemented counterparts. Interestingly, the changes in energy-corrected milk yield and milk component yields exhibited a linear relationship with the amount of choline ion supplementation, up to a threshold of 25,2 g/day. The exact optimal dosage of choline ion supplementation remained uncertain due to this linear response.

The meta-analysis also unveiled that the response to choline was influenced by the supply of metabolizable methionine in the postpartum diet. This connection was expected due to the biochemical interactions between choline and methionine within the body, influencing 1-carbon metabolism and phosphatidylcholine synthesis. Even when the lactating diet provided metabolizable methionine at a level of 2,60% of metabolizable protein, supplementing RPC still increased energy-corrected milk yield.

A noteworthy observation stemming from the meta-analysis was the dearth of literature investigating the role of supplemental choline in nulliparous cows – those that haven't given birth yet. These nulliparous cows typically comprise around 30 to 35% of the prepartum cow population on dairy farms. While it's anticipated that these cows could also benefit from choline supplementation during the transition period, this remains a relatively unexplored area in research.

THE EFFECTS OF RPC ARE OBSERVED REGARDLESS OF THE BODY CONDITION OF COWS

Given choline's role in hepatic lipid metabolism and its potential to reduce the risk of fatty liver, it's not uncommon for nutritionists and veterinarians to propose supplementing RPC primarily to over conditioned prepartum cows, which are at an increased risk of developing hepatic steatosis. To investigate this notion, we revisited data from two randomized experiments. In these studies, prepartum cows were divided into groups, with one group receiving 0 g/day of choline ion and the other group receiving 12,9 g/day of choline ion from ReaShure RPC. This supplementation began around 255 days of gestation and continued until 21 days postpartum[9]. The objective was to ascertain whether the response to RPC was influenced by the body condition of cows upon entering the prepartum group.

A total of 215 pregnant parous Holstein cows were enrolled in both experiments, with each cow's body condition score assessed twice before the treatments commenced. The cows' mean body condition was 3,51, ranging from 2,69 to 4,25. The results of this analysis revealed that irrespective of the cows' body condition scores prepartum, supplementing transition diets with 12,9 g/day of choline as RPC yielded consistent positive effects. This supplementation led to increased milk yields by 1,8 kg/day, fat yields by 0,08 kg/day, true protein yields by 0,04 kg/day, energy-corrected milk by 1,9 kg/day, and 3,5% fat-corrected milk by 2,1 kg/day. Additionally, cows that received RPC exhibited enhanced feed efficiency in converting feed into energy-corrected milk, regardless of whether they were under or over conditioned before calving. This study demonstrates that the response to RPC is observed in cows regardless of their degree of fatness at the initiation of prepartum supplementation.

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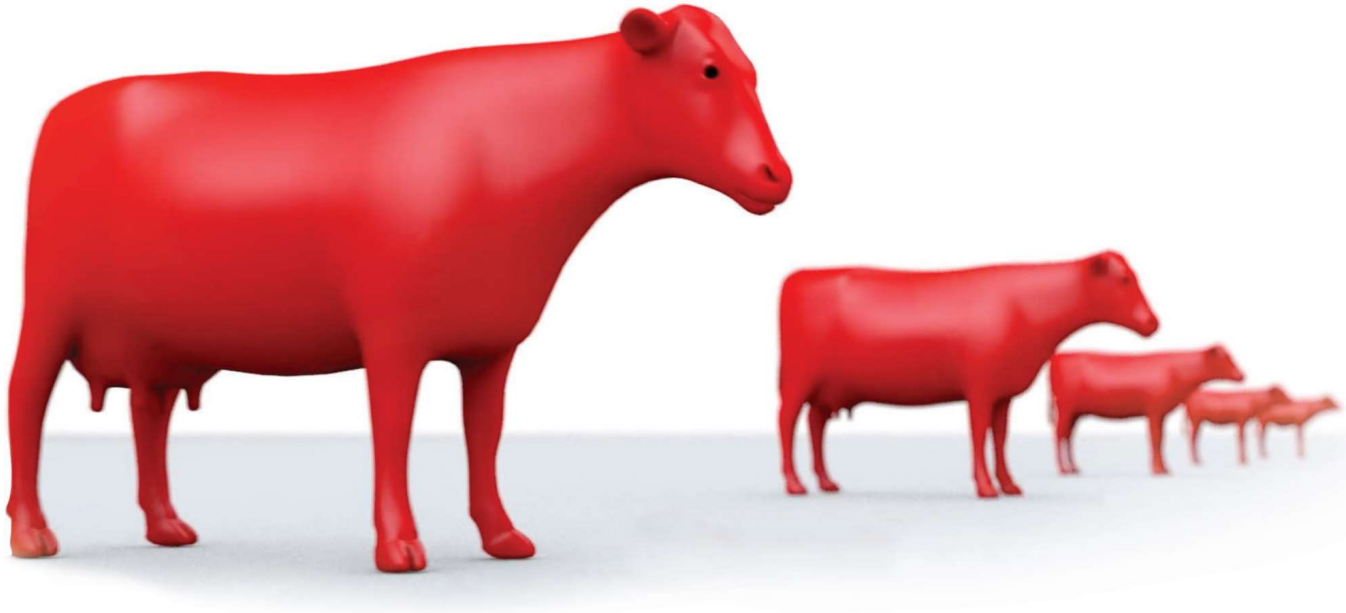

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RESPONSES TO RPC EXTEND BEYOND THE PERIOD OF SUPPLEMENTATION

Research conducted at the University of Florida, along with a recent study conducted by Barry Bradford at Michigan State University, has demonstrated that cows supplemented with RPC during the transition period exhibit heightened milk production during the supplementation phase, and this effect persists for several weeks after the supplementation period concludes[10-12].

In one experiment, cows were provided RPC from the close-up period until 21 days postpartum, resulting in a milk yield increase of 2,1 kg/day that continued for up to 40 weeks into lactation. In another separate experiment, an increase in milk yield of 2,0 kg/day was observed due to RPC supplementation, and this enhancement extended for 25 weeks into lactation.

This phenomenon is consistent with observations from various dietary interventions introduced during the transition period, which tend to positively impact animal health and metabolism and subsequently extend their effects on production beyond the intervention period. However, the precise mechanism underlying this carry-over effect remains to be fully understood.

Substantial progress has been made on our understanding of choline as a nutrient for dairy cows. The introduction of rumen-protected products containing choline chloride has facilitated research into various aspects of choline's mode of action within intermediary lipid metabolism in dairy cows. This advancement has also enabled the exploration of crucial questions regarding choline's role in maintaining hepatic health and enhancing productive performance during the critical transition period for cows.

While the precise optimal dosage of choline to optimize both production and health in dairy cows is not yet definitively established, the existing data unequivocally demonstrate the positive impact of feeding choline ion through RPC, up to 25 g/day, during the transition period. This supplementation not only triggers lipotropic effects within the hepatic tissue but also exhibits tangible improvements in productive performance and health outcomes. These findings collectively provide compelling evidence that choline should be considered a required nutrient in the diet of transition dairy cows.

References are available upon request.

About José Eduardo P. Santos

Dr. José E.P. Santos is a Professor in the Department of Animal Sciences at the University of Florida where he conducts research and extension in dairy cattle nutrition and reproduction. He earned his DVM degree from São Paulo State University in Brazil in 1992, completed the M.Sc. and Ph.D. degrees in 1995 and 1997 at the University of Arizona, and a clinical residency in Dairy Production Medicine in 2000 in the School of Veterinary Medicine at the University of California Davis. Before joining the University of Florida, José spent 8 years as a faculty member in the Department of Population Health and Reproduction in the School of Veterinary Medicine at the University of California Davis.

About Usman Arshad

Usman Arshad is from Pakistan and received his Doctor of Veterinary Medicine degree (2010-2015) from University of Veterinary and Animal Sciences (UVAS), Lahore. Usman completed his masters (M. Phil Theriogenology; 2015-2017) from UVAS and Ph.D. (Animal Molecular and Cell Biology; 2018-2023) from University of Florida with a major concentration in Dairy Cattle Nutrition and Reproduction. He has recently joined Dr. Heather White's Lab at University of Wisconsin-Madison as a Post-Doctoral Research Associate.

Usman is passionate about transition cow management and exploring molecular and cellular pathways related to hepatic tissue metabolism and feed efficiency in dairy cows. Usman has a longstanding interest in data analysis, especially conducting meta-analysis that benefits the dairy industry and facilitates dairy farmers in decision-making. During his post-doctoral training, Usman intends to gain additional experience in analysis of fatty acid composition, Western blots, flow cytometry, and use of cell culture models to elucidate intermediary metabolism in dairy cows.