Milk Production Performance in Periparturient Dairy Cattle

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For dairy cattle to perform well throughout and following lactations, precise dietary control during the periparturient phase is crucial. The primary issues experienced by periparturient dairy cows include issues like decreased dry matter intake (DMI), a negative energy balance, higher levels of non-esterified fatty acids (NEFA), and the ensuing inferior milk output. Dairy cattle have always been fed a diet high in crude protein (CP) to produce the most milk possible. Despite the vital function that dairy cows play in the conversion of dietary CP into milk, a sizeable percentage of nitrogen is inevitably expelled, which raises serious environmental concerns. To reduce nitrogen emissions and their production, lactating dairy cows must receive less CP supplementation. Supplementing dairy cattle with rumen-protected methionine (RPM) and choline (RPC) has proven to be a successful method for improving their ability to use nitrogen, regulate their metabolism, and produce milk. The detrimental effects of low dietary protein consumption on the milk yield, protein yield, and dry matter intake may be mitigated by these nutritional treatments. In metabolic activities like the synthesis of sulfur-containing amino acids and methylation reactions, RPM and RPC are crucial players. Methionine, a limiting amino acid, affects the production of milk protein and the success of lactation in general. According to the existing data in the literature, methionine supplementation has a favorable impact on the pathways that produce milk. Similarly, choline is essential for DNA methylation, cell membrane stability, and lipid metabolism. Furthermore, RPC supplementation during the transition phase improves dry matter intake, postpartum milk yield, and fat-corrected milk (FCM) production.

dairy cattle | periparturient period | RPM | RPC | milk production | metabolism | nitrogen utilization

1. Introduction

Effective nutritional management during the periparturient period plays a crucial role in optimizing lactational performance among lactating dairy cows [1][2][3]. Previous research has emphasized that variations in dry matter intake (DMI) and concentrations of non-esterified fatty acids (NEFA) have a significant impact on both fertility and subsequent milk production outcomes [3][4]. The common practice of implementing a traditional dry period before parturition inadvertently results in reduced DMI, thereby limiting energy intake. Consequently, this leads to a state of negative energy balance, causing a surge in NEFA and β-hydroxybutyric acid (BHBA) levels. Elevated levels of NEFA and BHB can incite compromised immune function, particularly by dampening neutrophil activity in the lead-up to calving [5]. In addition, that elevation of NEFA and BHB regulate oxidative stress, which is followed by increased inflammatory changes and suppressed immunity [2][6]. The suppressed immunity, elevated oxidative stress and inflammatory changes due to negative-energy-balance-causing abnormal levels of NEFA and BHB are the key factors that expose dairy cattle to various diseases including mastitis [7][8], ketosis, retained placenta, and ketosis [9][10]. Furthermore, escalated NEFA and BHB levels with poor health also exert an adverse influence on lactational performance [7].

In the realm of dairy cattle nutrition, the significance of RPM and RPC extends beyond their roles in metabolism and milk production enhancement. These compounds have garnered substantial attention for their contributions to periparturient health disorders in dairy cattle. Research has elucidated the pivotal roles of RPM and RPC in alleviating oxidative stress, mitigating inflammatory changes, and bolstering immunity [2][11]. This body of evidence underscores their potential in promoting overall bovine health. Furthermore, several field experimental trials have consistently reported the clinical implications of RPM and RPC supplementation [12][13]. Notably, RPM has emerged as a crucial factor in controlling and reducing the risk of mastitis in dairy cattle during the periparturient period [2][12][13]. Additionally, Dai et al. [14] demonstrated through in vitro experimental procedures that methionine and arginine treatment effectively alleviated inflammatory changes and oxidative stress induced by lipopolysaccharide (LPS) in bovine mammary epithelial cells (BMECs). Moreover, it is well known that ruminants possess a limited capacity to secrete very low-density lipoproteins (VLDL) from the liver, which can hinder the export of hepatic triacylglycerols, ultimately resulting in hepatic lipidosis. However, the supplementation of 25.8 g/d of RPC has been found to significantly increase hepatic triacylglycerol secretion, thereby reducing the incidence of hepatic lipidosis in dairy cows [15][16]. Other studies have indicated that RPM can reduce the occurrence of subclinical hypocalcemia [17]. However, it should be noted that RPM supplementation did not appear to reduce the incidence of other health disorders, including retained placenta and ketosis, in dairy cattle.

To enhance milk production, dairy cattle during the periparturient period are provided with a high-protein diet. The dairy industry faces a well-established phenomenon where dairy cows convert 20 to 35% of dietary crude protein (CP) into milk, with the remaining nitrogen being excreted in manure, leading to detrimental environmental consequences [18][19][20][21]. In response to this issue, reducing CP supplementation has become a significant focus in the field of lactating ruminants in the United States, as CP serves as the primary nitrogen source [22]. The U.S. dairy sector is under increasing pressure to reduce emissions of nitrogen, phosphorus, and greenhouse gases [23]. Nitrogen, in particular, represents a primary pollutant originating from dairy farm operations, contributing to instances of nitrate contamination in groundwater, the eutrophication of surface water, and emissions of ammonia and nitrous oxide into the atmosphere [24][25].

Implementing the recommended reduction in mobilized protein supplementation, as advocated by the National Research Council (NRC) in 2001 [26], could lead to improved nitrogen utilization for milk production within dairy cattle [27]. However, empirical evidence has shown that dietary protein intake below the recommended threshold may compromise milk production, milk protein yield, and DMI [28][29]. In such cases, the incorporation of RPM [30][31][32][33][34], along with RPC supplementation [35][36], has emerged as an effective strategy to mitigate the adverse consequences resulting from inadequate dietary protein intake.

RPM and RPC have received significant attention due to their notable contributions in promoting milk production performance and optimizing nitrogen utilization within dairy cattle [36][37][38][39][40][41]. A series of studies have consistently confirmed the crucial role of amino acids in orchestrating the regulation of milk and its components in dairy cattle [42][43][44][45][46]. Consequently, a study has emphasized the indispensable role of RPM in milk production and metabolism, as evidenced by in vitro experiments using mammary epithelial cells. These studies highlight the relevance of concentrations of lysine (Lys) and RPM in the medium, not only in optimizing milk protein synthesis but also in influencing amino acid transport and signal transduction pathways that impact the expression of genes associated with milk protein synthesis [47]. Optimal levels of Lys and RPM, along with a supplemental Lys-to-RPM ratio approximating 3:1, have been identified as catalysts for eliciting the expression of genes instrumental in milk protein transcription and translation, ultimately resulting in the peak of casein production and cell proliferation rates [26][48]. RPM, in synergy with other amino acids, has similarly shown positive effects on the production performance and the metabolic aspects of dairy cattle. Importantly, a study has documented that milk yield [12], as well as energy-corrected milk (ECM), milk fat, protein, and lactose percentage levels, exhibited enhancements in cows supplemented with RPM and lysine compared to the control group [49][50]. Furthermore, the study ascertained that supplementation with RPM and RP-lys preserved the post-calving body condition score (BCS), enhanced DMI, and reduced the blood concentrations of BHBA [49][50].

The importance of RPM in milk production is accentuated by its status as the rate-limiting amino acid for lactating dairy cows, especially when fed protein supplements high in lysine but low in methionine, such as blood meal and soybean meal. To mitigate this constraint and augment the post-ruminal methionine supply, the provision of RPM has emerged as an effective strategy. A multitude of studies have outlined the advantages conferred by RPM supplementation, including the economization of dietary protein and the enhancement of overall lactational performance in dairy cows, particularly in diets formulated around standard North American ingredients [51][52]. Recent academic efforts have also focused on RPM supplementation in the diets of transition cows, revealing that achieving a Lys-to-RPM ratio approximating 2.9:1 as a fraction of metabolizable protein results in increased milk yield, partly attributable to increased DMI and the potential for the more effective utilization of bodily lipid reserves [52].

In addition, methionine, as the only amino acid containing sulfur, plays the role of a precursor for other sulfur-containing amino acids, namely cysteine, homocysteine (Hcy), and taurine, all of which play critical roles in various methylation reactions. The metabolic journey of methionine begins with its conversion into S-adenosylmethionine (SAMe), a key cofactor in methionine intermediate metabolism used in methylation reactions. SAMe serves as a methyl donor for amino acid residues within proteins, DNA, RNA, and small molecules, thereby influencing a wide range of biological processes [53]. Furthermore, methionine acts as a precursor for hydrogen sulfide, taurine, and glutathione, all of which have demonstrated their effectiveness in counteracting oxidative stress caused by various oxidants, thus protecting tissues from damage [54]. As a result, the dietary inclusion of rumen-protected methyl donors, such as RPM, has advantages in meeting the needs of cows during the peak of lactation, when the outflow of methylated compounds in milk is increased.

2. Interplay of Methionine and Choline in One-Carbon Metabolism and Amino Acid Regulation

Methionine plays a crucial role in one-carbon metabolism [55], coordinating a complex series of biochemical processes that transfer one-carbon (methyl) groups in various forms [56][57][58][59][60]. This metabolic pathway is essential for critical cellular functions, including the synthesis of DNA and RNA, amino acid metabolism, and the production of S-adenosylmethionine (SAMe), a universal methyl donor crucial for methylation reactions throughout the body [61][62]. Methionine itself acts as the precursor to SAMe, a key molecule in this pathway, formed by combining methionine with adenosine triphosphate (ATP). SAMe, in turn, donates its methyl group to various substrates, participating in a wide range of biochemical reactions, including DNA and RNA methylation, protein methylation, and the synthesis of neurotransmitters, which are essential for mood regulation and brain function.

As SAMe exhausts its methyl group in methylation reactions [55], it transforms into S-adenosylhomosysteine (AdoHcy) [63]. This conversion involves further steps, including transferring a methyl group to Hcy to regenerate methionine. Methionine also initiates protein synthesis, a fundamental process responsible for constructing all body proteins, from enzymes to structural proteins, as well as those involved in various cellular functions. It actively participates in transmethylation reactions, influencing the synthesis of amino acids, neurotransmitters, DNA, RNA, and lipids. Furthermore, methionine contributes to its own regeneration from Hcy and the production of vital molecules such as creatine, choline, and epinephrine. It also aids in cysteine synthesis through transsulfuration, which is essential for the formation of protein disulfide bonds and the production of the antioxidant glutathione [64][65].

Choline plays a vital role in regenerating methionine from Hcy by generously donating methyl groups in one-carbon metabolism [66]. Additionally, choline is involved in creatine synthesis, which is crucial for muscle energy metabolism, and serves as a precursor for choline-containing amino acids such as betaine [67], and sarcosine, contributing to Hcy conversion into methionine and methyl group detoxification. In conclusion, methionine and choline intricately interconnect in amino acid metabolism [68]. Methionine supports protein synthesis, transmethylation reactions, and cysteine synthesis, while choline contributes to methionine regeneration [69], creatine synthesis, and the production of choline-containing amino acids. Together, these processes ensure the availability of amino acids, crucial for protein production, cellular functions, and overall health in dairy cattle and other organisms.

From the above discussion, it can be concluded that methionine and choline have distinct but interconnected roles in amino acid metabolism. Methionine serves as an essential amino acid required for protein synthesis and participates in transmethylation reactions and cysteine synthesis. Choline, on the other hand, is crucial for regenerating methionine from Hcy, contributing to the one-carbon metabolism pathway, and plays a role in the synthesis of creatine and choline-containing amino acids. These processes collectively ensure the availability of amino acids for protein production, cellular functions, and overall health in dairy cattle and other animals.

3. The Role of RPM and RPC in Metabolism and Milk Production Performance of Dairy Cattle

3.1. RPM Role in Metabolism and Nitrogen Utilization of Dairy Cattle

Methionine, an indispensable amino acid, plays a crucial role in shaping the physiological development, metabolism, and growth of mammals [70][71][72]. Seymour particularly emphasizes the importance of this amino acid in metabolic processes, especially as a precursor to essential compounds required for vital physiological functions [73]. Methionine serves as a fundamental building block for compounds such as succinyl-CoA, Hcy, cysteine, creatine, and carnitine. Furthermore, its active involvement in the biosynthesis of SAMe is essential for polyamine, creatine, and phosphatidylcholine metabolism [74].

The role of methionine extends far beyond its basic building-block function. It actively participates in cellular methylation reactions and sulfur recycling processes, with the ability to undergo enzymatic conversion to L-methionine sulfoxide [74][75]. The resulting product of this conversion, cysteine, plays a critical role in fundamental cellular functions, including protein translation, glutathione synthesis, and taurine production [76][77]. The consequences of insufficient methionine levels are significant, leading to detrimental effects such as small intestine atrophy, suppressed epithelial growth in neonatal animals, reduced goblet cells, and diminished glutathione content within the small intestine [78].

Within the gastrointestinal tract (GIT), approximately 20% of dietary methionine is absorbed and utilized [79]. Research by Shoveller et al. [80] indicates that neonatal piglets' parenteral methionine requirement approximates 69% of the enteral requirement. Additionally, methionine catabolism has been found to be more pronounced in extracellular cells outside pig enterocytes, particularly in the portal-drained viscera and intestinal mucosa, as highlighted by Blachier et al. [81]. The dynamic interaction of methionine with choline, as emphasized by Swain and Johri [82], underscores its significance in antibody (IgG) production. Conversely, methionine deficiency leads to a decrease in relative lymphoid organ weight, ultimately impacting overall growth performance [83]. The balance is delicate, as excessive methionine intake has been associated with growth depression [84].

3.2. Rumen-Protected Methionine's Role in Ruminants' Milk Production

Dairy animals during parturition are prone to experiencing a negative energy and protein imbalance because their nutrient intake is insufficient to meet the demands of milk production [6][8][85]. The importance of RPM in milk production has garnered significant attention in dairy cattle research [86][87][88][89][90]. Therefore, increasing milk production requires the strategic implementation of high-protein diet supplementation for dairy cattle. This approach is supported by substantial evidence, as there is a well-documented association between RP Lys, RPM, and threonine concentrations with the growth, physiology, and reproductive performance of calves [91][92]. Accordingly, Lee et al. emphasized that providing RP-Lys, RPM, and histidine in combination significantly increased milk protein yield in dairy cows fed a diet deficient in metabolizable protein [93]. Further evidence suggests that supplementing cows with 10 g/day of RPM, along with a concentrated diet containing corn grain and soybean meal, significantly increased milk production in dairy cattle [94]. This finding is consistent with the study of Carder and Weiss [95], who demonstrated that supplementation with RPM and Lys resulted in sustained increases in milk energy and milk yield. Consistently, the continuous supplementation of RPM has been linked to increased milk yield and milk protein content in periparturient dairy cows [96][97]. Studies conducted during the pre- and postpartum periods consistently showed that RPM supplementation can increase both milk yield and milk protein content in dairy cattle [13][17][98].

From the above discussion, it is clear that RPM supplementation plays a crucial role in addressing the challenges of negative energy and protein balance during parturition. An increasing body of research consistently demonstrates that careful RPM supplementation, along with strategic dietary adjustments, holds promise in significantly increasing milk yield and enhancing overall milk quality in dairy cattle.

3.3. Molecular Mechanisms Unveiling the Influence of Methionine Supplementation on Dairy Cattle Milk Production Performance

A comprehensive investigation into the genetic basis of the impact on milk production in dairy cattle due to RPM supplementation has revealed intricate molecular pathways and regulatory elements. Numerous in vitro experimental studies have diligently elucidated the regulatory functions and molecular mechanisms of cAMP response element-binding protein-regulated transcription coactivator 2 (CRTC2) in methionine-induced milk fat synthesis [45]. These studies emphasize the critical role of CRTC2 as a transcription coactivator within the methionine-induced milk fat synthesis pathway mediated by the mammalian target of rapamycin (mTOR) in BMECs.

An independent study has demonstrated that methionine supplementation has a significant influence on the expression of purine-rich element-binding protein B (PURB), a key regulator of gene transcription and cellular physiology [46]. The upregulation of PURB, in conjunction with methionine treatment, has led to increased milk protein and fat synthesis, accompanied by elevated expressions of mTOR and sterol response element-binding protein (SREBP)-1c within BMECs. Interestingly, counteractive effects were observed when PURB expression was reduced. Furthermore, an important discovery has emerged regarding the positive modulation of U2 snRNP auxiliary factor 65 kDa (U2AF65) by methionine, further enhancing milk synthesis and cell proliferation within BMECs through the mTOR-SREBP-1c signaling pathway [99].

Annexin A2 (AnxA2), renowned for its diverse roles encompassing growth, development, and metabolism, assumes a significant role in milk synthesis and cell proliferation. Methionine treatment has exhibited a positive influence on phosphatidylinositol 3-phosphate (PIP3) levels, mTOR phosphorylation, and protein levels of SREBP-1c and Cyclin D1. In this complex process, AnxA2 emerges as a critical regulator through the phosphatidylinositol-3-kinase (PI3K)-mTOR-SREBP-1c/Cyclin D1 signaling pathway [100]. Furthermore, the synergistic overexpression of glucose-regulated protein 78 (GRP78) alongside methionine treatment has yielded notable stimulatory effects on milk protein and milk fat synthesis, augmented cell proliferation, and an affirmative modulation of mTOR phosphorylation. This coalescence has also heightened protein levels of Cyclin D1 and SREBP-1c. Notably, the ablation of GRP78 through siRNA transfection has manifested contrasting outcomes. Intriguingly, the predominant cytoplasmic localization of GRP78 in bovine mammary epithelial cells has been observed. Moreover, its protein expression has been significantly enhanced following stimulation with methionine, leucine, estrogen, and prolactin [101].

Implicating the nuclear factor of κB (NFκB) family, renowned for its roles in gene expression regulation, unveils its involvement in milk synthesis regulation. NFκB1 has been identified as a governing factor for various genes, including SREBP-1c, and β4-galactosyltransferase-T2 (β4Gal-T2), consequently impacting the milk biosynthesis process [102]. Methionine treatment has been shown to enhance NFκB1's binding to gene promoters of mTOR, SREBP-1c, and β4Gal-T2 in BMECs, illuminating milk biosynthesis to be facilitated through the PI3K pathway rather than the mTOR signaling pathway. Further insights have emerged from studies delving into the intricate regulatory network, indicating that methionine treatment leads to the suppression of DEAD-box helicase 6 (DDX6) expression. As a pivotal member of the RNA helicase family governing mRNA storage and translation regulation, decreased DDX6 expression adversely affects milk synthesis by hampering the effects of p-mTOR, SREBP-1c, and Cyclin D1 within BMECs [103]. Furthermore, gene functional analyses have corroborated the positive regulatory impact of methionine on SREBP-1c gene expression, thereby promoting milk fat synthesis through epidermal-type fatty acid binding protein-5 (*FABP-5*) [104]. Intriguingly, the heterodimeric amion acid taste receptor (TAS1R1/TAS1R3) constellation emerges as a sensor for extracellular methionine in BMECs. Activation of this receptor tandem triggers mTOR signaling, possibly via intracellular calcium-concentration elevation, and is implicated in the mediation of methionine and valine-induced changes in β-casein (CSN2) mRNA abundance [105].

3.4. Rumen-Protected Choline Role in Metabolism of Dairy Cattle

Choline, an indispensable nutrient, plays a central role in the field of metabolism. It is embedded in the composition of lipid-soluble metabolites, especially phosphatidylcholine, lysophosphatidylcholine, free choline and sphingomyelin, all of which are essential components of cell membranes. These compounds play critical roles in cell signaling and lipid metabolism, and their profound importance has been clearly elucidated by the scientific community [106]. The indispensable nature of choline and its metabolites underscores their important roles in maintaining structural integrity and promoting signaling functions within cell membranes. Furthermore, choline actively participates in the synthesis of acetylcholine, a highly important neurotransmitter, and also contributes to methylation processes through the efficient transfer of methyl groups, facilitated by the intermediary betaine metabolite, leading to the synthesis of the crucial SAMe pathway [107].

The prominence of choline metabolites in the biological development of mammals is particularly highlighted during the transition period. Supporting this, observations have confirmed the potential for choline supplementation during this critical phase to enhance hepatic lipid metabolism in cells, a finding supported by various studies [108][109][110]. Of note, among these choline metabolites, betaine emerges as a key facilitator in the synthesis of creatine, carnitine, and methionine. Its role as a methyl group donor, which traverses the transmethylation pathway, has been identified as instrumental in this process [111]. A spectrum of dietary sources boasts substantial phosphatidylcholine content, typically around 13% by weight [112]. Interestingly, the inclusion of choline in the diet significantly influences the remethylation activity of betaine. While the reversal of betaine into choline through a reverse reaction is not feasible, betaine assumes a supporting role under circumstances where choline availability is constrained, aiding the remethylation reaction for the synthesis of Hcy [113]. This dynamic modulation involving betaine orchestrates methylation through the Hcy methyltransferase reaction, thereby exerting regulatory control over adoHcy and S-adenosyl methionine levels within cells. This, in turn, leads to improvements in the epigenetic mechanism and DNA methylation within the cellular environment. Moreover, the presence of choline and betaine within the diet, alongside other methyl donor groups, exerts a profound influence on methylation reactions [114]. Of particular significance, the collaborative contributions of methyl-tetrahydrofolate and betaine underscore their involvement in the biosynthesis of methylation from Hcy to methionine [115].

During the pivotal transition period, dairy cows undergo significant physiological changes. These changes include a reduction in dry matter intake, an imbalance between negative energy and metabolizable protein, and an increased demand for high-quality nutrients to support both fetal growth and lactation performance. This juncture is accompanied by the emergence of potential challenges such as ketosis, hypocalcemia, clinical mastitis, and indications of fatty liver [116][117][118]. The liver functionality index (LFI), serving as a reflection of transition cow metabolic health, captures shifts in biomarkers linked to liver plasma protein synthesis (albumin), lipoprotein synthesis (cholesterol), and heme catabolism (bilirubin). Importantly, research has illuminated the connection between choline-fed cows and elevated LFI values, translating to improved dry matter intake, milk yield, milk fat yield, milk protein yield, and a reduced vulnerability to metabolic ailments [64].

During this complex transition phase, the interplay of stress and hormonal dynamics leads to an increase in NEFA in circulation, serving as a compensatory mechanism to counter the negative energy balance in transitioning cows. The liver coordinates the oxidation of NEFA to generate energy, with some of it redirected towards the production of TG, subsequently mobilized as VLDL [119]. However, it is important to note that a portion of NEFA undergoes partial oxidation in the liver, resulting in the accumulation of ketone bodies in the bloodstream, hindering the transport of triglycerides through VLDL. Additionally, in the pre- or early lactation phase for cows, there may be an elevation in the ratio of lipid peroxidation [120], a reduction in serum α-tocopherol, and increased levels of oxidative stress. This collective situation has the potential to negatively impact the health and productive performance of dairy cows [121]. Notably, RPC supplementation has been confirmed to help lower blood BHBA levels in periparturient dairy cattle [122]. Existing evidence highlights the role of RPC in improving hepatic TG levels, thereby supporting optimal production performance during the lactational period [37][123]. Introducing dietary RPC supplementation yields significant results, with a noticeable increase in colostrum production among Holstein cows [124][125]. This increase is particularly pronounced among cows in their second parity. However, it is worth considering that the demand for choline could potentially be even more pronounced among cows in their third or higher parities. Furthermore, strategic choline supplementation has been found to translate into higher concentrations of phosphocholine within colostrum. Notably, RPC supplementation has been associated with an elevation in trimethylamine N-oxide concentrations within colostrum [124][125].

3.5. RPC Role in Milk Production of Dairy Cattle

The use of RPC in peripartum dairy cattle has garnered significant attention due to its consistent ability to increase either milk yield or fat-corrected milk production [126]. This phenomenon has received ample confirmation in the scientific literature, with a consensus gradually emerging that the inclusion of 12-20 g per day of RPC in the diet of cows results in optimal improvements in dairy cow production performance [127][128].

An in-depth meta-analysis conducted by Arshad et al. [127] has drawn widespread attention, focusing specifically on RPC supplementation. This meticulous effort compiled data from 23 distinct experiments, encompassing 74 treatment means and a robust sample of 1,938 cows. The results derived from this meta-analysis are striking, revealing a statistically significant increase in both pre- and postpartum daily dry matter intake by 0.28 kg per day and 0.47 kg per day, respectively, with significant differences. Furthermore, this analysis unveiled a noticeable rise in ECM production, resulting in a weighted mean average increase of 1.61 kg per day. Additionally, distinct improvements were observed in fat and protein yield, with increases of 0.08 kg per day and 0.06 kg per day, respectively [127]. Consistently, Humer et al. [129] conducted an exhaustive review of data from 27 separate studies, shedding light on a significant increase in postpartum dry matter intake, from an average of 19.1 to 19.9 kg per day ($p < 0.01$), along with an increase in milk yield from an average of 31.8 to 32.9 kg per day ($p = 0.03$) following RPC supplementation. Moreover, a statistically significant increase in milk fat and protein yield was observed ($p \leq 0.05$), while the compositional attributes of milk remained unaffected [129].

During the early stages of lactation, there is often a negative nutrient balance, leading to a decrease in choline metabolite concentrations in bovine plasma [110][130]. However, it has been discovered that RPC supplementation can reverse this trend, resulting in increased plasma concentrations of choline metabolites in prepartum cows, thereby improving their choline status [123]. Increasing choline status in the prepartum phase offers a promising approach to reduce the risk of fatty liver in cows [123][131] and positively impact postpartum health and lactation performance [132]. The research landscape in this domain involves an extensive exploration of the effects of RPC supplementation in various formulations, dosages, and dietary contexts on postpartum performance. Generally, including RPC in the diets of transition cows has yielded favorable results, demonstrating enhancements in milk, fat, and ECM yields [133][134]. However, it is essential to acknowledge the variability in responses across studies. Notably, the response to RPC supplementation has not been consistent in all investigations [135][136]. Additionally, the timing and duration of RPC feeding have been identified as pivotal factors affecting the performance of lactating Holstein cows, as elucidated by another study [38].

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