MILK FEVER AND RELATED POSTPARTUM DISEASES IN DAIRY CATTLE – A REVIEW

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Abstract

Milk fever is a metabolic condition that occurs in dairy cattle before or immediately after parturition as a result of low calcium (Ca^{++}) levels in the blood (hypocalcaemia). Based on its pathological changes, milk fever (hypocalcaemia) can be clinical or subclinical, being particularly prevalent in high-producing cows during the calving period.
The most common factors leading to milk fever include milk production, breed, parity, age, body condition score (BCS), and the composition of the cow's diet. The economic effects of milk fever are represented by decreases in milk production and fertility, finally resulting in culling of high-producing dairy cattle within herds. In order to establish the diagnosis of milk fever in dairy cattle, clinical and paraclinical examinations are used.
Milk fever prevention is economically essential for dairy farmers since it helps them avoid production and culling losses, and also increased veterinary expenses related with this condition. Numerous approaches have been introduced in order to mitigate hypocalcaemia, which include anionic salt feeding, low-calcium diets, vitamin D supplements, magnesium supplements, and peripartum body condition management. As a final conclusion, preventing milk fever is crucial for overcoming disease's economic impact on the dairy industry.

Key words: milk fever, dairy cattle, reproduction, prevention.

INTRODUCTION

As known, milk fever is among the most prevalent mineral-related metabolic disorders of dairy cows, occurring just before or shortly after parturition as a result of excessive calcium loss from the blood (50 g per day), in order to ensure rapid milk synthesis (DeGaris and Lean, 2008; Thirunavukkarasu et al., 2010; Khan A. et. al., 2012).
Known also as periparturient hypocalcaemia or periparturient paresis, milk fever is defined by Horst et al. (2005) cited by Pacheco H.A. et al. (2018), as a metabolic condition, affecting dairy cows around parturition.

MILK FEVER KEY HIGHLIGHTS

This is one of the metabolic disorders that most commonly occurs in adult cows within 48 hours of parturition, but can also occur weeks before or after it. Generally, dairy cows produce 10 liters or more of colostrum, containing 23g or more of calcium on the day of parturition, which is approximately 6 times as much calcium as the extracellular calcium pool includes (Aberaw A., 2017).

According to Reinhardt T. et al. (2011), after calving, blood calcium concentrations in about half of dairy cattle in their second lactation and above, drop below the threshold for subclinical hypocalcaemia. Therefore, metabolic diseases are caused by the animals' inability to cope with the metabolic requirements of high milk production, and their etiology can be linked directly to insults encountered during the transition period.

Negative energy balance (NEB), increased lipid mobilization, and a drop in calcium blood concentrations can emerge from increased energy and calcium requirements for colostrum and milk production, in combination with a decrease in dry matter intake (DMI) following parturition (Bell A.W., 1995; Butler W.R. et al., 1989, Goff J.P. et al., 1997, Reinhardt T.A. et al., 2011).

Thus, all these changes are increasing the risk of metabolic and inflammatory conditions, with negative effects on animal welfare, being also a significant source of production and financial losses for the dairy industry.

Generally, the occurrence of metabolic disorders is linked to feeding, dairy farm management, and also animal genetics. Imbalanced and insufficient feeding of high

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producing dairy cows during pregnancy and prepartum, is typically associated with significant metabolic changes during the transition period, making them more susceptible to develop metabolic or even infectious disorders (Bruckmaier R.M. et al., 2017). In other words, when the homeostatic processes fail to maintain normal blood calcium concentrations during early lactation, milk fever develops.

So, this metabolic condition is regarded as a gateway disease that significantly reduces the probability of full productivity in the subsequent lactation. Mild milk fever develops in the majority of cows during the peripartum period and it has been linked to certain calving difficulties, such as retained placenta, uterine prolapse, metritis, mastitis, ruminal stasis, immune system depression, and generally a reduced reproductive performance, resulting in a 3–4 year reduction in productive life (Bhanugopan M.S., et al., 2014).

If for the subclinical hypocalcaemia there are less severe changes in blood calcium levels (between 5.5 and 8.0 mg/dL), and thus, no visible symptoms (Wubishet F. et al., 2016), in clinical hypocalcaemia the initial signs include ataxia, nervousness, and hyperactivity in the animal.

Moreover, poor appetite, decreased rumen motility, low body temperature, sluggish breathing, impalpable pulse, weak but rapid heartbeats (80-100 per minute) with difficulties to be heard due to diminished capacity of muscles to contract, dilated pupils, and dry muzzle are all common symptoms of this condition (Goff J., 2008). Other signs and symptoms include a tilted head to the side, splayed out hind legs, and paresis (difficulty to rise from lying down). Finally, coma and sudden death are possible outcomes (Oetzel G., 2011, Khan A., et al., 2012).

As for its incidence in dairy cattle herds according to age and breed, milk fever tends to vary between 0 - 10%, and it may reach even 25% in some herds (DeGaris and Lean, 2008). Also, according to a meta-analysis of 135 controlled studies, performed by Lean et al. (2006), the incidence of this disease ranges from 0% to 83%, a wide range that indicates there is a big potential to affect the disease's occurrence if one understands the factors that contribute to its development.

Economic losses are significant, and include those incurred as a result of on-farm death, early culling, lower milk production, and increased veterinarian and treatment expenses (Liang et al., 2017) (figure 1).

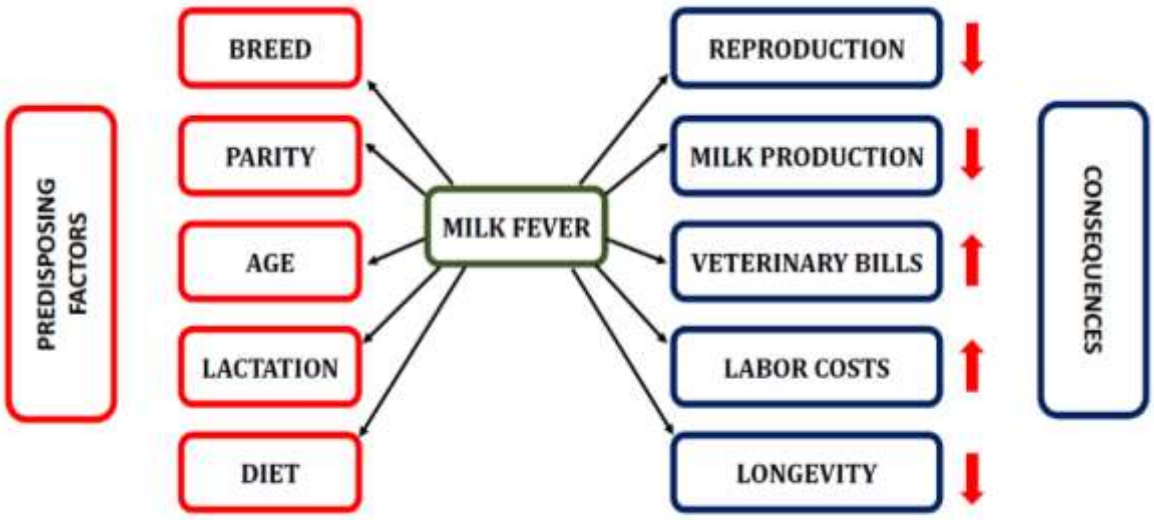

Figure 1 Predisposing factors for milk fever and its economic consequences (Dervishi E. et al., 2017)

REPRODUCTIVE CONSEQUENCES OF MILK FEVER IN DAIRY CATTLE

Dystocia is an important cause of periparturient recumbency, Chamberlain (1987) cited by DeGaris, P.J. et al. (2008), reporting that dystocia is responsible for 46% of primary recumbencies in cows, 38% for hypocalcaemia, and 16% for other causes. According to Mulligan F. et al. (2006), one may easily see the difficulties that a decreased ability of smooth and skeletal muscle contractions could cause for cows in labor.

Several scientific papers illustrate that milk fever cows are more likely to develop dystocia than normal cows. In some cases, the increased likelihood of dystocia was found to be six times compared to normal cows, while others indicated an increased probability of around 2.5 to 3 times compared to normal cows (Correa et al., 1993).

In 1984, Risco et al., stated that hypocalcaemia was found to be related to **uterine prolapse** in multiparous dairy cows and, in conjunction with other factors, is indicated as an etiologic factor for this puerperal disease in dairy cattle.

Also, within the study performed by Mulligan F. et al. (2006), 19% of cows with uterine prolapse were classified as having severe hypocalcaemia (serum calcium 4mg/dl), while another 28% were classified as having moderate hypocalcaemia (serum calcium 4.1 to 6.0mg/dl).

Later, several studies have shown that cows with subclinical hypocalcaemia are more likely to experience dystocia and uterine prolapse (Martinez N.C.A. et al., 2012). Regarding the link between milk fever and retained fetal membranes, the same author claimed that cows diagnosed with subclinical hypocalcaemia were more likely to develop **retained placenta** defined as the lack of expulsion of fetal membranes within 12 hours of parturition.

Various studies indicate an increased risk of retained fetal membranes following milk fever, milk fever cows being up to three times more likely to develop this pathological condition compared to normal cows (Houe et al., 2001). Milk fever has been reported to have a direct effect on the occurrence of retained placenta, doubling the likelihood of a retained placenta (Erb et al., 1985).

Furthermore, according to Correa M.T. et al. (1993), because milk fever is a risk factor for dystocia, which in turn is a risk factor for retained placenta, there is a significant indirect influence of milk fever on retained placenta as well.

Melendez P, et al. (2002) reported that the plasma calcium levels in cows with retained fetal membranes was considerably lower than the concentration in cows with normal placental expulsion in their study. Gild C. et al. (2015), also found that cows with subclinical hypocalcaemia experienced retained placenta in some cases. As a result, there is a clear correlation between the development of milk fever and the prevalence of retained placenta (figure 2).

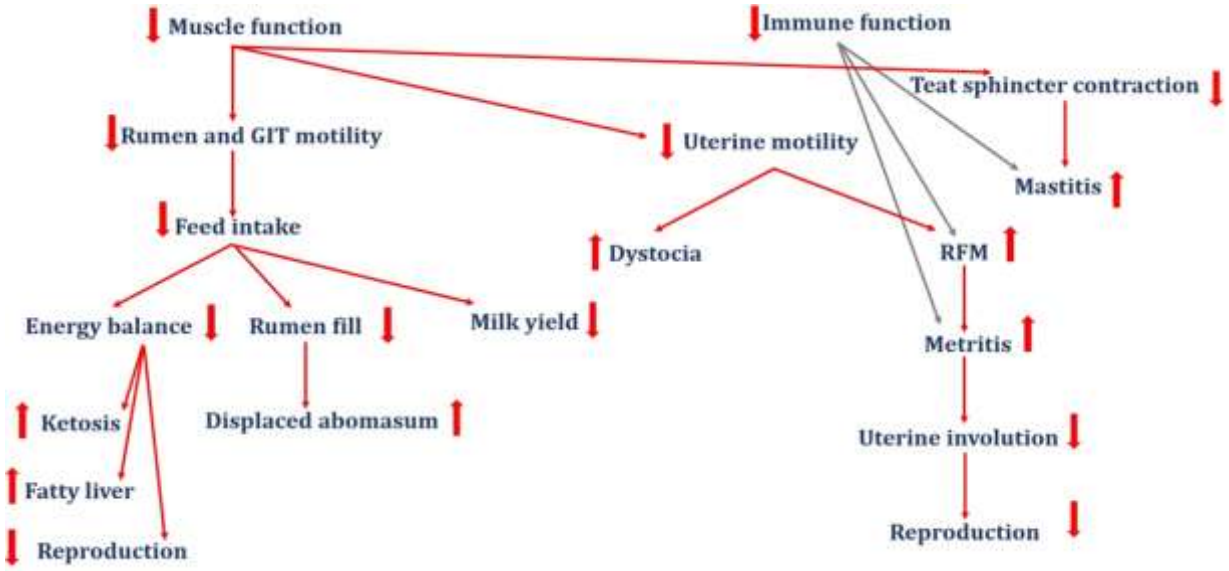

Figure 2 Consequences of milk fever and subclinical hypocalcaemia (adapted from Mulligan F et al., 2006)

METRITIS AND ENDOMETRITS

Martinez et al. (2012) conducted a prospective cohort study in which serum calcium concentrations were assessed on days 0, 1, 2, 3, 4, 7, and 12 after parturition in cows classified as metritic or healthy. Hypocalcaemia was more severe and persisted for a longer period of time in cows with metritis than in cows without this postpartum disease.

Also, according to the findings, hypocalcaemia was found to affect immunological function in this study as well. This finding was corroborated with a subsequent study conducted later (Martinez et al., 2014), which found that healthy cows with induced subclinical

hypocalcaemia had decreased appetite, impaired metabolism, and immune cell function.

Waldron et al. (2003) and Kvidera et al. (2017), on the other hand, proven that infusion of lipopolysaccharides, which induces an extensive immunological response, causes a drop in serum calcium levels. Thus, it is necessary to clarify if hypocalcaemia is a cause or a co-occurring condition of infectious diseases. According to Curtis C.R. et al (1983), and Goff J.P. et al. (1997) cited by Seifi H.A. (2017), metritis is linked to subclinical hypocalcemia.

This is possible, because metritis is more likely to occur under hypocalcemic situations, when immunological function may be compromised and muscular contraction reduced (Murray R. et al., 2008; Martinez N. et al., 2012).

Within a study on 110 dairy cattle, Martinez et al. (2012) discovered that cows who had calcium levels below 2.14 mmol/L at least once between 0 and 3 days in milk, had a 4.5-fold higher risk of developing metritis. Also, a study published by Rodríguez E.M. et al. (2017), states that multiparous cows with subclinical hypocalcemia had a 4.85 higher risk of developing metritis compared to normal-calcium animals.

The associations between milk fever, dystocia, and retained fetal membranes, along with the reported link between milk fever and periparturient immunosuppression, provide a good foundation for the postulated association between milk fever and endometritis (Kimura et al., 2006).

Compared to healthy cows, Whiteford and Sheldon (2005) discovered a higher prevalence of endometritis in cows with clinical hypocalcemia. Thus, although several publications link milk fever to complications during or around parturition, it is very likely that many farm veterinarians treat retained placenta and poor fertility issues without considering milk fever and subclinical hypocalcemia as possible contributing factors to a lower reproductive efficiency and higher culling rates.

In cows after parturition, uterine contamination is inherent, although it is progressively removed by uterine involution, discharge of lochia, and mobilization of immunological defenses (Bretzlaff 1987).

However, uterine bacterial contamination persists more than three weeks in 40% of cows, and nearly half of these animals develop clinical endometritis (Sheldon I.M. et al., 2004).

Hypocalcemia affects smooth muscle contraction (Goff J.P., 2008) and has been linked to a decreased contractility of the myometrium. Between 15 and 32 days postpartum, cows having a history of milk fever in the same lactation have larger uterine horn diameters (Goff J.P., 2014).

FERTILITY

Cows who have recovered from clinical hypocalcaemia require more services per conception and have prolonged intervals between calving and conception after they have recovered (Borsberry and Dobson 1989). However, it is unclear if clinical hypocalcaemia, which occurs during the first few days after parturition, has an impact on reproductive function several weeks after the parturition.

When it comes to optimal fertility, hypocalcaemia can interfere with one or more of the three main events of the postpartum period that must occur in order to achieve it: the restoration of normal ovarian cycle activity, uterine involution, and the reduction of uterine bacterial contamination (Sheldon I.M. et al., 2004).

Clinically or subclinically hypocalcemic animals have a prolonged interval between calving and their first postpartum ovulation (Risco et al., 1994).

Additionally, subclinical hypocalcaemia results in smaller follicles at first ovulation in cows (Kamgarpour and others 1999) this observation being significant, as cows with follicles larger than 8 mm in diameter between 14 and 28 days postpartum have shorter calving to conception intervals (Sheldon I.M. et al., 2004).

Given the fact that uterine involution and lochia discharge are dependent on rhythmical uterine contractions, which are suppressed by hypocalcaemia, it is not surprising that clinical hypocalcaemia is related to delayed uterine and cervical involution (Risco et al., 1994).

PREVENTION

Preventing milk fever is economically beneficial for dairy farmers due to the reduced production loss, death loss, and veterinary expenses associated with milk fever. Numerous nutritional management measures have been used to control hypocalcaemia and mobilize calcium in dairy cattle, including the use of anionic salts, low calcium ion diets, and vitamin D supplementation (Amaral-Phillips D., 2017).

Before parturition, low calcium diets improve the release of Parathyroid Hormone. This stimulates osteoclasts in the bone, promotes calcium resorption in the bone, stimulates renal tubules to resorb urine calcium and start making 1,25-dihydroxyvitamin D. As

a result, when lactation begins, the calcium homeostatic pathways become active and capable of preventing hypocalcaemia (Oetzel G.R., 2011).

According TO Jesse P.G. et al., (2018) feeding cows with **calcium poor diets** during the dry period is one of the methods to prevent milk fever.

This can be achieved by providing less than 50 g/ each day. As a result, calcium-rich forages such as alfalfa should be removed from the animal's diet. Corn silage and grass hay should be fed often throughout the dry period to help lower calcium levels (Angassa T., 2019).

Bhanugopan M.S. and Lievaart J., (2014) found that all farmers used hay, straw, and grain as a general nutrition plan throughout the dry period. Practically, grain feeding helps the rumen adapt quickly to the high-energy diets given post-partum, and grains also have a low calcium content.

Dietary cation-anion balancing (DCAB) represents a nutritional strategy to prevent milk fever in early lactation, but also to enhance the cow's health and performance (Patel V.R. et al., 2011).

It is a typical prophylactic method that involves providing anionic salts to decrease the cation anion difference in the diet and has been successfully adopted in the dairy farms (Martín-Tereso J. et al., 2014). The objective of this form of supplementation is to decrease the amount of absorbable cations like sodium and potassium in the diet and increasing the amount of accessible anions such as chlorine and sulfur monoxide (Goff J., 2008).

Given the increased potassium content of dry fodder, is recommended to avoid feeding cows with excessive amounts of dry fodder, in order to prevent milk fever, being essential to include silage and succulent / green fodder in a significant percentage of the dry cow's diet, since they contain less potassium (Thirunavukkarasu M. et al., 2010).

Bhanugopan M.S. et al. (2014), stated that one method of preventing milk fever in cows, is to administer orally supplements with **calcium around parturition.** Later, Amanlou H. et al. (2016), indicated that 2 subcutaneous calcium infusions in the first 18 hours postpartum are correlated with a lower risk of developing postpartum disorders (metritis, clinical and subclinical endometritis and hypocalcemia) in cows from experimental group, compared to control group animals.

Magnesium is an important component of calcium metabolism, serving as a critical element of calcium metabolism in the resorption of calcium from bone by Parathyroid hormone. As Jesse P.G. et al. mentioned in a study published in 2018, magnesium supplementation is critical for preventing milk fever.

Increased magnesium supplementation was determined to be the most effective strategy for preventing milk fever (Lean I.J. et al., 2006).

In addition to the methods mentioned above, Bhanugopan M.S. and Lievaart J., (2014) recommended **vitamin D supplementation** in prepartum dry cows. This method needs injecting or feeding up to 10 million IU of vitamin D daily for 10-14 days before parturition, improving thus intestinal calcium absorption.

Regarding **body condition score (BCS)**, Ostergaard et al. (2003) and Finbar M. et al. (2006), stated that over-conditioned dairy cows during calving are up to four times more likely to develop milk fever, because they have a higher calcium output in milk. Compared to thinner dairy cattle, over-conditioned cows have a lower feed intake in the last week or ten days before parturition. This may result in a reduction in their calcium and magnesium intake to levels that predispose them to the development of hypocalcaemia.

It is essential to keep the dry cows from becoming too fat. Cows who have seen significant body condition loss during the dry period are also at susceptible to develop milk fever (Etagegnehu B. et al., 2020).

CONCLUSIONS

Taking into consideration the above mentioned, preventing milk fever is critical for mitigating the economic effect of the diseases. Nutritional techniques and body condition control are crucial for disease prevention.

According to Etagegnehu B., et al. (2020), training dairy farmers is essential for educating them about milk fever and the right composition of rations for their dairy cows.

Also, is recommended that dairy farm operators should lower the energy source of feed, particularly concentrate during calving. Farmers should be educated about the importance of observing their dairy cows 48-72 hours before and after calving for signs of milk fever.

As a final mention, additional research on the epidemiology and economic impact of milk fever in the dairy industry should be done.

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