



## CALCIUM REQUIREMENT IN RELATION TO MILK FEVER FOR HIGH YIELDING DAIRY COWS: A REVIEW

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**Abstract:** *The purpose of this paper is to review the predisposing factors and advances in controlling principles of milk fever in high yielding dairy cows. Dietary imbalances in dairy cows can be one of fundamental cause of numerous and complicated types of health problems that are usually categorized as metabolic disorders. High producing dairy cows are among highly susceptible animal to such metabolic disorders during their transitional periods; three weeks before and after calving. In these periods, the animal struggles to maintain their calcium homeostasis; which is the most common metabolic disorder of high yielding dairy cows, due to their underlying physiological and pathological factors. Thus, those factors predisposing dairy cows to milk fever are age, stage of lactation and parity, body condition and diet. Usually, the basic principle of controlling milk fever is feeding the cows from diet constituting lower calcium and potassium contents in dry period. So that calcium mobilization from bone would be promoted, which ensures the increased metabolic processes of calcium mobilization during the transition period? Furthermore, supplementations of various anionic salts which includes magnesium sulfate, calcium sulfate, ammonium sulfate, calcium chloride, ammonium chloride and magnesium chloride are commonly used to raise blood calcium level, thus, minimizes risks of milk fever. Also, body condition management of cows during dry period is used to prevent milk fever. Finally, a recent research indicates that serotonin intravenous injections have significantly reduced the incidence of hypocalcemia in high yielding dairy cows.*

**Keywords:** *Calcium, Dairy cows, Hypocalcemia*

### 1. Introduction

Mineral nutrients are inorganic elements required for normal physiological and anatomical functioning and health of the animals. Based on their abundance in the body, the minerals can be macro-mineral or micro-mineral; were the later one is referred as trace elements, due to its relatively smaller amounts. But macro-minerals are those minerals that are relatively, required with higher quantities than micro-minerals. Therefore, these macro-minerals are calcium, phosphorus, magnesium, sodium, potassium, chloride and sulphur. Calcium is the most abundant

mineral in the body of the animals, where its significant proportion (99 % of calcium) is dominantly found in the bone. In the bones, together with phosphorus, it forms hydroxyapatite, which is an important component of the skeletal structure of vertebrates. While, the remaining amount of calcium is extracellular, it plays a crucial role of muscle contractions and normal functioning of nervous system. However, the calcium in the bones is not a static mass, but it is in continuous exchange with the extracellular fluids. The intracellular calcium fraction is involved in signaling within the cell. In plasma, calcium is found as protein-bound calcium,

ionized calcium and calcium bound in complexes with the anions. The fraction of ionized calcium must be maintained at a constant level to ensure the normal functioning of muscles and nerves [1].

Milk fever (MF) is one of the most common mineral-related metabolic conditions affecting dairy cows during transition, a disorder that occurs immediately after or shortly before calving as a result of a low level of calcium in the blood (hypocalcaemia) [2]. Milk fever and subclinical hypocalcemia (total blood calcium  $\leq 2.0$  mmol/l) are the most important macro-mineral disorders affecting transitioned high yielding dairy cows [3]. However, a mild degree of hypocalcemia in the majority of cows during the peripartum period and usually associated calving problems, retained placenta, uterine prolapse, mastitis, ruminal stasis, depression of the immune system and generally reduced reproductive performance of the animals [4]. In a small proportion of animals, hypocalcemia becomes severe and results in paresis, lying down and occasionally death [5].

About 50% of dairy cows in their second lactation and greater have blood Ca concentrations that fall below the threshold for subclinical hypocalcemia after calving [6]. This insufficient blood calcium concentration can make a cow to lose its ability to rise up to her feet, as calcium is responsible for normal nerve and muscle functioning. This can cause a metabolic disorder termed as milk fever, also known as post-parturient hypocalcemia or parturient paresis. It is most common metabolic disorder of older and high yielding dairy cows [7].

Most of the cows experience subclinical hypocalcemia after calving, but some experience severe blood calcium drops that leads to milk fever. The normal blood calcium level ranges between 8 and 12 mg/dl. However, when blood calcium is reduced to 7.5 – 5mg/dl, the stomach

motility is reduced by 30 and 70 % respectively [8]. The reduced abomasum motility due to lowered blood calcium leads to displaced abomasum. The low calcium requirements of cows during the dry period become suddenly elevated after parturition. This sudden calcium drain from blood must be counter balanced by increased calcium absorption from gut or calcium mobilization from bone. Thus, during this time the parathyroid hormone is released to enhance calcium resorption from bone. But, hypocalcemia occurs when the mechanism of calcium absorption and resorption are insufficient to meet calcium demands. Therefore, if not treated soon, most of the cows will die within a few days [9].

Therefore, this paper is a review on predisposing factors and the preventive strategies of milk fever and subclinical hypocalcemia in high yielding dairy cows.

## **2. What is milk fever?**

Milk fever and subclinical hypocalcemia are the most important macro-mineral disorders that affect transition. Milk fever and subclinical hypocalcemia (total blood calcium  $\leq 2.0$  mmol/L) are the most important macro-mineral disorders that affect transition dairy cows [10]. Adequate circulating Ca concentrations throughout the transition period are necessary for productive lactation, but large quantities of Ca are lost from maternal Ca pools into milk and colostrum. A rapid, large drop in maternal blood Ca causes 5 – 10 % of cows to be afflicted with clinical hypocalcemia and additional 50 % to suffer from subclinical hypocalcemia. Subclinical hypocalcemia and clinical hypocalcemia were the major reason for early lactation removal of cows from the herd [11] [6] [12].

The transition period is an extremely critical period of milk fever in high yielding dairy cows, where Jersey cows are being more susceptible than Holstein

Friesian [13] [14]. At this time to insufficient blood calcium levels at the onset lactation, depending on the extent of dropped blood calcium, the animals exhibit a range of clinical symptoms [15]. In clinical hypocalcemia the blood calcium level drops below 1.4 mmol/L, while in subclinical hypocalcemia the total blood calcium level drops into 1.4 – 2.00 mmol/L [11]. The cows that are once affected with parturient paresis are more susceptible to several metabolic disorders such as ketosis, retained placenta, displaced abomasum and muscle weakness [11] [13] [16] [17].

Overall, the study conducted in USA, indicated that the prevalence of milk fever and subclinical hypocalcemia are more common in Jersey cows; due to their higher milk production per unit body weight. In general, dairy cattle exhibit a delay in calcium resorption from bone resulted in manifestation of milk fever [13].

### **3. Prevention Strategies of Milk Fever**

#### **3.1. Feeding of Low-Calcium Diets**

Conventionally, it was known that feeding with low calcium diets during dry period is one of milk fever prevention strategy. This was achieved through feeding the cows with less than 50 g per day. Therefore, to do so, high calcium forages such as alfalfa, have to be eliminated from animal's diet. Forages such as corn silage and grass hay have to be routinely used in dry from to reduce calcium composition within it [9].

Calcium requirements for the non-lactating cow are as minimal as 41 grams/day for a 1400lb cow [18], being necessary only for maintenance and fetal skeletal development. Hence, when calcium requirements are met through dietary feed, the metabolic processes of calcium mobilization from bone will be inactivated. However, upon parturition and onset of lactation, there is an immediate demand for large amounts of calcium for colostrum

production. At this time, the dietary calcium could not be met the sudden demand of calcium, normally, due to dry matter intake decreases a few weeks before parturition. Therefore, calcium must be mobilized from bone in order to meet this sudden demand of calcium. However, since calcium requirement during dry period being met from diet, the mobilization of calcium from bone is very minimal, so that the cows experience milk fever [9].

In contrary, underfeeding of calcium during dry period promotes calcium mobilization from bone and ensures calcium homeostasis during parturition. In addition, calcium absorption from small intestine is proportionally higher when the cow fed lower calcium during dry period. Thus, a low-calcium diet will promote efficient resorption of calcium from bone, as well as calcium absorption from small intestine [9].

#### **3.2. Feeding of Anionic Salts**

The anionic salts are simply minerals that possess high proportion of anions. Anions are ions that are negatively charged and cations are ions that are positively charged. The tissues of living being maintain a balance of cations and anions, so that they remain neutral. So that, in order to not interfere with anionic and cationic balance, their net sum in the feeds of the animals should be near neutral. However, certain cations and anions, such as sodium, potassium, chloride and sulfur have significant effects on acid-base balance of the body. Therefore, quantifying these major cations and anions in animal diet are very important. The quantification is done by calculating the dietary cation-anion difference (DCAD); which is achieved by a subtracting a sum of dietary cations (i.e. sodium and potassium) from anions (i.e. chloride and sulfur) [9].

A negative DCAD, diet contains more equivalents of anions than cations, a zero

DCAD diet contains equal equivalents, and a positive DCAD diet contains more cation equivalents. This was used to estimate the influence of cation and anions in the diet on acid-base status of animals. Hence, the anionic diet (negative DCAD) will induce metabolic acidosis and lower blood pH [7]. The induced metabolic acidosis, was therefore, suggested to increase tissue responsiveness to parathyroid hormone, in resorption of calcium from bone [19] [20]. The desired effect of feeding anionic salts is to decrease blood pH, which is highly correlated with reduced urine pH and increased blood calcium. Thus, urine pH is used as indicator for blood pH. Thus, an anionic diet, a negative DCAD diet, induces a mild metabolic acidosis, normal blood calcium and a urine pH between 6.5 and 5.5 in close up cows [7]. Urine pH can be monitored on the farm using pH paper or a pH meter, thus when urine pH is greater than 7.0, it should be considered to supplement anionic salts. But, when urine pH is less than 5.5, the anionic salts salt intake is very high, so that consider anionic salts intake reduction [19].

In contrary, excessive anionic salts in the diet are usually, associated with reduced feed intake, displaced abomasum and kidney overload. However, the addition of anionic salts such as magnesium sulfate, calcium sulfate, ammonium sulfate, calcium chloride and magnesium chloride are the only means of achieving a negative DCAD [21]. Although supplementing close-up dry cow with the diets of anionic salts can reduce the incidence of milk fever, but excessive intake of anionic salts can cause potential problems to dairy cows. For instance, it can cause severe reduction in dry matter intake. Further, the severe reduction in dry matter intake near parturition can predispose animals to metabolic disorders such as displaced abomasum, milk fever and ketosis, it is necessary to closely monitor in close-up

cow, not to feed excessive level of anionic salts [9].

### **3.3. Management of Body Condition Score (BCS)**

Management of body condition score during dry period and calving is another important means of achieving milk fever. The research finding reported that, the dairy cows that are over-conditioned at calving are up to four times more likely to develop milk fever [22]. It is uncertain that why this case is happening, but several hypotheses have been suggested that firstly, dairy cows with higher BCS at calving have higher Ca output in milk, which makes them more prone to milk fever. Secondly, it has been widely appreciated that over-conditioned dairy cattle have a reduced feed intake relative to thinner cows, in the last 7 – 10 days of pre-calving. This may result in reduction of Ca and Mg intake and predisposing the animals to the development of hypocalcemia [3].

### **3.4. The Intravenous Infusion of Serotonin**

Obviously, colostrum and milk synthesis rapidly deplete Ca from the maternal circulation and therefore, Ca must be mobilized from maternal bone to maintain adequate circulating Ca concentrations become dip below the animal's minimal threshold for Ca, via a classic negative feedback loop [23]. Circulating Ca concentrations are tightly regulated and controlled by one of the parathyroid hormones related-protein (PTHrP) hormones. Recently, the research experiments demonstrated that mammary serotonin (5-hydroxytryptamine) regulates induction of PTHrP. Thus, the manipulation (injection) of serotonin, induces PTHrP synthesis near the end of the pregnancy period that could be critical in preventing the onset of hypocalcemia during the early lactation period [24].

However, though the overall circulating serotonin concentration are not constant within the course of given lactation period, its average is approximated at 1700ng/mL. Thus, it decreases around the time of calving period (from 0 to 2 days) and bounce back by ten days into lactation [25]. Therefore, according to Hernandez [26], the intravenous infusion of 5-HTP in lactating, non-pregnant, multiparous Holstein dairy cows have shown, a significant increase in circulating serotonin concentrations and altered Ca dynamics and it can be used to prevent hypercalcemia in high yielding dairy cows.

#### **4. Predisposing Factors for Hypocalcemia**

According to reports of several authors [27] [28] [29] [30] [31] [32], the factors contributing to milk fever and which influence its incidence and degree of severity are quite numerous. Therefore, these factors include: age parity of cows, breeds differences, body condition score, dietary factors, potassium supplementation and pathophysiology.

##### **4.1. Age and Parity of Cows**

The incidence of developing milk fever is increased with age cow [14][33]. Obviously, milk yield in dairy cows, from third lactation onwards, start to increase, which lead to high calcium demand for milk production. In addition to increase in milk production, increase in age also results in diminishing of the capability of mobilizing calcium from bone and declining of active transportation of calcium from intestine, which was resulted in increased risks milk fever incidence [34]. Thus, hypocalcemia is usually highly frequent from third to seventh calving due to reduced adaptation capacity of cows during calving [35]. The hypocalcemia at calving is age related and most marked in cows from third to seventh parturition; it is

infrequent at the first parturition. This is because while some degree of hypocalcemia occurs during the first few days of lactation, they are able to adapt rapidly to the high demands of calcium for lactation [36].

##### **4.2. Breed**

Certain breeds of dairy cows have shown more susceptibility to milk fever than other breeds. Specifically, cross breed or temperate breeds are more susceptible to milk fever than tropical zebu breeds. This could be attributed to their high milk yield and low ability to maintain their calcium homeostasis of cross breed and temperate breed [38]. The other important reason of higher susceptibility to milk fever is lower number of intestinal receptors for 1, 25-(OH) D, which responsible intestinal calcium absorption and bone calcium resorption [37].

##### **4.3. Body Condition Score**

According to Ostergard et al., [22], a high body condition score of dairy cows can raise the risk of milk fever. The dairy cows that are over conditioned at calving are four times greater in developing milk fever than skinny cows. This is due to, the dairy cows with higher BCS at calving have higher calcium output in milk and reduced feed intake due to loss of appetite. Hence, a combined effect of calcium loss through milk and reduced feed intake predispose high yielding dairy cows to parturient paresis [39]. Furthermore, Bewley and Schultz [39], suggested that the cows with over conditioned during calving and/or excessive weight loss just after calving demonstrated increased risks of dystocia, retained placenta, metritis, milk fever, cystic ovaries, lameness, mastitis, ketosis and metabolic disorders.

##### **4.4. Dietary factors**

Boda and Cole [39], indicated that providing a diet with high daily calcium

intake to non-lactating cows are associated with increased incidence of parturient paresis. Primarily, during the dry period, the maintenance requirement of calcium can be predominantly, met by passive absorption since active absorption of dietary calcium and bone resorption are then suppressed. The cows in this condition are not able to quickly place blood calcium lost in milk and become severely hypocalcemia. Excessive dietary phosphorus intake (>80g/day) during late gestation can also induce milk fever and the severity of hypocalcemia by raising blood phosphorus concentrations to the point that can inhibit renal synthesis of 1, 25 – (OH)<sub>2</sub>D<sub>3</sub>, which then reduces intestinal calcium absorption [41]. Generally, the pre-partum diets high in cations like sodium and potassium are associated with increasing incidence of milk fever, while the diets with high in anion such as chlorides and sulfides results in decreased milk fever incidence. The addition of anions to dairy cow's diet prior to parturition are claimed effective in reducing the incidences of milk fever by inducing metabolic acidosis, calcium bone resorption [42].

#### **4.5. Potassium Supplementation**

High potassium forages have been highly associated with milk fever in high yielding dairy cows. Usually, Alfalfa has long been considered as high potassium contents and leads to milk fever. Hence, in perspective high potassium levels may have been the cause of milk fever, in association with alfalfa-based dry cow diets. Grass hay can have lower level of potassium, but over-fertilizing with potassium on hay fields increases, both soil and hay potassium levels. High soil potassium often occur in the fields where manures have been applied for many years. But, harvesting of forages from such fields and separately feeding dry cows are recommended, since potassium

level drops as plants mature and get dried [9].

#### **4.6. Pathophysiology**

During the dry period, calcium demand is relatively low. Thus, the activity of intestinal and/or bone resorption of calcium is relatively sluggish during this time. The onset of lactation at the time of parturition results in sudden loss of calcium into milk. However, at this time when the calcium homeostasis is unable to meet the demand of calcium for milk production, the cow develops milk fever [43]. This fall in blood calcium level stimulates the calcium homeostatic mechanism to improve intestinal calcium absorption and increase bone resorption. Approximately 24 hours of elevated 1, 25 dihydroxy vitamin D<sub>3</sub> is required to improve intestinal transport of calcium and an increased rate of bone resorption requires 48-hours of PTH stimulation. But, when these compensatory mechanisms are prolonged for more than 48-hours, then the cows develop clinical hypocalcemia. Consequently, most of the cows with clinical hypocalcemia have shown higher level of PTH and 1, 25 dihydroxy vitamin D<sub>3</sub> [44] [45].

#### **5. Conclusion**

Milk fever and subclinical hypocalcemia are the most important macro mineral disorders of the transitioning cows. Since, it is highly correlated with several production diseases and reproductive complication milk fever was one of economically important disease among most of highly yielding dairy herds. Milk fever and subclinical hypocalcemia to large extent can be prevented through good dietary management of cows during dry period. The dietary calcium levels must be low in the weeks leading up to calving in order to minimize the risk of milk fever. Anionic salt feeding, body condition

management, feeding low calcium and the recent outcome of serotonin infusion to high yielding dairy cows are among the most important mechanisms of controlling milk fever.

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