Physiological and Metabolic Changes During the Transition Period and the Use of Calcium Propionate for Prevention or Treatment of Hypocalcemia and Ketosis in Periparturient Cows

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ABSTRACT

The transition from late gestation to early lactation is regarded as the most critical period of the production cycle in dairy cows. Most of metabolic disorders and infectious diseases occur during the transition period because of metabolic and physiological changes, metabolic stress of pregnancy, calving and lactation, a sudden and marked increase of nutrient requirements for milk production and a lack of dry matter intake. Milk fever, subclinical hypocalcemia, ketosis, fatty liver syndrome, retained fetal membranes, metritis, mastitis and displaced abomasum primarily affect dairy cows during this period. Calcium propionate, as a source of both calcium and energy, has been used for preventing or treating hypocalcemia and ketosis in dairy cows. In this review, different administration ways of calcium propionate in transition dairy cows were summarized and efficacy of calcium propionate in prevention or treatment of metabolic disorders was evaluated.

Key Words: Calcium Propionate, Hypocalcemia, Ketosis

Geçiş Dönemindeki Fizyolojik ve Metabolik Değişimler ile Doğum Sonrası Süt İneklerinde Hipokalseminin ve Ketozisin Engellenmesi veya Tedavisinde Kalsiyum Propiyonatın Kullanımı

ÖZET

Süt ineklerinin yaşam döngüsünde ileri gebelikten laktasyon dönemine geçiş en kritik dönem olarak görülmektedir. Metabolik ve fizyolojik değişimler, gebeliğin, buzağılamanın ve laktasyonun oluşturduğu stres, süt üretimi için besin maddesi gereksinimlerinin birden ve belirgin artışı ve kuru madde tüketimindeki yetersizlik sebebiyle metabolik rahatsızlıkların ve enfeksiyöz hastalıkların birçoğu bu geçiş dönemi sırasında meydana gelmektedir. Süt humması, subklinik hipokalsemi, ketozis, karaciğer yağlanması, retensiyo sekundinarum, metritis, mastitis ve abomazum deplasmanı, geçiş döneminde süt ineklerini etkileyen başlıca rahatsızlıklardır. Hem kalsiyum hem de bir enerji kaynağı olan kalsiyum propiyonat, süt ineklerinde hipokalsemi ve ketozisin engellenmesi veya tedavisi amacıyla kullanılmıştır. Bu derlemede, geçiş dönemindeki süt ineklerinde kalsiyum propiyonatın farklı uygulama yolları özetlenmiştir ve kalsiyum propiyonatın metabolik rahatsızlıkların engellenmesinde veya tedavisindeki etkinliği değerlendirilmiştir.

Anahtar Kelimeler: Kalsiyum Propiyonat, Hipokalsemi, Ketozis

INTRODUCTION

The transition period, from 3 weeks before to 3 weeks after parturition, is critically important for health, production and profitability of dairy cows (Grummer 1995, Drackley 1999). This period is characterized by tremendous metabolic and endocrine adjustments that the cows must experience from late gestation to the early lactation (Drackley et al. 2001, DeFrain et al. 2005). The most important physiological changes occurring during this period are the reduction in dry matter intake around parturition and a sudden increase in nutrients that the cows need for milk production (Drackley 1999, Ingvartsen and Andersen 2000).

During late pregnancy, the growing uterus occupies an increasing amount of the abdominal cavity and leads to the physical compression of the rumen, which reduces the volume of rumen. After calving, the uterus retracts back toward the pelvic inlet (Goff and Horst 1997, Ingvartsen and Andersen 2000).

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The concentration of plasma insulin continually declines in the transition period until calving while plasma somatotropin concentration rapidly rises during the period from the late stages of pregnancy to the first days of lactation. Progesterone is the dominant hormone of pregnancy. On the day before parturition, the concentration of plasma progesterone rapidly falls to nearly undetectable level. In addition, there is a transitory elevation in plasma estrogen and cortisol concentrations in the periparturient period. Estrogen and cortisol have their highest plasma concentrations at day 3 before parturition and parturition day, respectively, after which the concentrations decline to their normal postpartum levels within few days (Grummer 1995, Goff and Horst 1997, Ingvartsen and Andersen 2000).

The reduction in volume of rumen by the growing fetus and above-mentioned hormonal changes reduce dry matter intake of dairy cows around parturition (Grummer 1995, Ingvartsen and Andersen 2000). Physical and metabolic stress of pregnancy, calving and lactation contributes to a reduction in resistance of cows (Goff and Horst 1997, Melendez 2006). Milk fever, subclinical hypocalcemia, ketosis, fatty liver syndrome, retained fetal membranes, metritis, mastitis and displaced abomasum primarily affect dairy cows during the transition period (Drackley 1999, Melendez 2006).

Milk fever (parturient paresis) is a hypocalcemic disorder associated with the onset of lactation in dairy cows (Goff and Horst 1994, Goff and Horst 1997). Hypocalcemia may be clinical or subclinical (Goff and Horst 1997). Clinical hypocalcemia, also known as milk fever, is a particular concern in the newly calved cow. Most of cases of milk fever occur within 24 hours of calving (Goff 2008). Generally, cows with milk fever are recumbent and are unable to rise as a result of low blood Ca (Goff 1999), whereas cows with subclinical hypocalcemia have no clinical signs of hypocalcemia (Reinhardt et al. 2011). Hypocalcemia reduces dry matter intake, milk production and fertility and increases the risk of secondary diseases such as ketosis, retained fetal membranes, displaced abomasum and mastitis and the incidence of dystocia and uterine prolapse (Goff and Horst 1997, Mulligan et al. 2006a, Goff 2008). Prevention of hypocalcemia, not just milk fever, should be a major goal of dairy farms (Goff 2008).

Most dairy cows in the early lactation experience a period of negative energy balance due to the reduction in dry matter intake and a metabolic priority for milk production (Baird 1982, Mulligan et al. 2006b). As a result, the cows utilize body fat as a source of energy, which leads to excessive body fat mobilization. Ketosis is caused by negative energy balance and excessive body fat mobilization (Goff and Horst 1997, de Roos et al. 2007). Ketosis is defined as a metabolic disease characterized by high levels of ketone bodies in blood, milk and urine. The ketone bodies, acetone, acetoacetate and ß-hydroxybutyrate (BHBA), are formed in the liver during oxidation of fatty acids (nonesterified fatty acids-NEFA) (Goff and Horst 1997, Mandebvu et al. 2003, de Roos et al. 2007). There is a close relationship between ketosis and fatty liver syndrome. Extreme rates of body fat mobilization because of negative energy balance lead to increased triglyceride accumulation in the liver and if this fat infiltration becomes severe, fatty liver syndrome may result (Drackley 1999, Mulligan et al. 2006b).

Adaptation of rumen to lactation diet that is high in energy density, enhancing dry matter intake, maintenance of normocalcemia and maintenance of a strong immune system would greatly reduce the incidence of periparturient diseases in dairy cows (Goff and Horst 1997).

Oral administration of Ca salts prior to and at parturition has been suggested to prevent hypocalcemia in dairy cows (Goff and Horst 1994, Goff 2008). The use of a source of Ca that has no adverse effects, such as necrotic lesions in the abomasum, on the digestive tract is preferable. Large amounts of propionate produced in the rumen as a result of carbohydrate metabolism have no adverse effects. Therefore, calcium propionate might be expected to be a satisfactory source of Ca (Pehrson et al. 1998). Propionate is the major glucose precursor in ruminants that are in positive energy balance and is antiketogenic (Pehrson et al. 1998, Drackley 1999). Depressed dry matter intake during the transition period leads to a lack of propionate supplied for glucose synthesis in the liver (Drackley 1999, DeFrain et al. 2005). Nutritionally, propionate can be supplied orally in the form of calcium propionate (Mandebvu et al. 2003, Melendez 2006, Hernández et al. 2009). Calcium propionate is a white crystalline powder. Molecular formula, molecular weight, density and pH of calcium propionate are $C_6H_{10}CaO_4$, 186.22, 0.56 g/cm3 and 8.5 to 10, respectively (Kara 2009). Calcium propionate, as a source of both Ca and energy, has been administered to transition dairy cows for prevention and / or treatment of hypocalcemia and ketosis (Goff et al. 1996, Stokes and Goff 2001, Kara et al. 2009). Calcium propionate can be used by oral

drenching (Stokes and Goff 2001, Kara et al. 2009), adding to total mixed ration or concentrate mixture (Mandebvu et al. 2003, Liu et al. 2010) and in a paste or gel form (Goff et al. 1996, Higgins et al. 1996).

In this review, different administration ways of calcium propionate in dairy cows were summarized and efficacy of calcium propionate in prevention and treatment of metabolic disorders was evaluated.

MILK FEVER AND SUBCLINICAL HYPOCALCEMIA

As the sudden demand for Ca of colostrum and milk production cannot be met by dietary Ca absorption, bone Ca mobilization and renal Ca resorption, most dairy cows have some degree of hypocalcemia (milk fever or subclinical) during the early postpartum (Penner et al. 2008, DeGaris and Lean 2009). Hypocalcemia occurs because Ca leaves the extracellular fluid pool to enter the mammary gland faster than it can be replaced by intestinal Ca absorption, bone Ca mobilization and renal Ca resorption (Goff and Horst 1997, DeGaris and Lean 2009).

Blood Ca in the adult cows is maintained between 8.5 and 10 mg/dl (2.0 and 2.5 mmol/L) (Goff 2008). Maintenance of blood Ca within the acceptable range is a balancing act between the Ca demand of milk production and the cow's homeostatic mechanisms to maintain blood Ca (Taylor et al. 2008). Clinical signs of milk fever (clinical hypocalcemia, parturient paresis) often are not seen until serum Ca concentration is about 4 mg/dl (Goff and Horst 1997). Subclinical hypocalcemia is defined as <7.5mg/dl serum Ca concentration (Goff et al. 1996, Oetzel 1996).

Intestinal Ca absorption and bone Ca resorption are controlled by parathyroid hormone, which is secreted by the parathyroid glands, and 1,25-dihydroxyvitamin D, which is produced in the kidney (Horst et al. 1994). As there is a decline in blood Ca concentration, parathyroid hormone concentration is increased. When blood Ca is within the normal range, parathyroid hormone secretion is decreased (Goff 2008, Taylor et al. 2008). Parathyroid hormone initiates renal production of 1,25-dihydroxyvitamin D to permit Ca homeostasis (Goff et al. 2004). In addition, renal resorption of Ca is enhanced by parathyroid hormone (Goff 2008, Taylor et al. 2008).

Metabolic alkalosis blunts the response of the cow to parathyroid hormone and predisposes dairy cows to milk fever and subclinical hypocalcemia. Metabolic alkalosis largely occurs as the result of diets high in cations, especially sodium and potassium, and low in anions, especially chlorine and sulfur. Precalving diets high in anions and low in cations or containing anionic salts such as ammonium sulfate, magnesium sulfate and ammonium chloride can decrease the occurrence of hypocalcemia (Goff 2008, DeGaris and Lean 2009). In addition, many strategies including feeding a precalving diet containing a low Ca concentration, administration of vitamin D at approximately 1 week before calving and supplementation of Ca at calving have been used for the prevention of hypocalcemia (Roche et al. 2003).

Cows in first lactation almost never experience milk fever. They may have some degree of hypocalcemia during the first days of lactation. Their intestine and bone rapidly adapt to the Ca demand of lactation. As cows age, Ca homeostatic mechanisms react more slowly to the Ca demand of lactation (Horst et al. 1994).

Hypocalcemia reduces smooth muscle contraction, which results in reduced ruminal and abomasal motility leading to reduced dry matter intake and displaced abomasum (Jorgensen et al. 1998, Goff 2008). The reduction in dry matter intake at the first days of lactation is exacerbated by hypocalcemia, which increases the energy deficit of the cow and the risk of ketosis and fatty liver (Goff and Horst 1997, Stokes and Goff 2001). In addition, tissue uptake of glucose is inhibited since hypocalcemia prevents the secretion of insulin. Reduced glucose uptake would exacerbate lipid mobilization during the early lactation, thus increasing the risk of ketosis (Goff and Horst 1997).

Milk fever or subclinical hypocalcemia has been related to dystocia, uterine prolapse and retained fetal membranes (Mulligan et al. 2006a, b). The loss of muscle tone in the uterus due to hypocalcemia increases the incidence of dystocia, uterine prolapse and retained fetal membranes (Stokes and Goff 2001, Mulligan et al. 2006b). Dystocia is a risk factor for retained fetal membranes. Retained fetal membranes predispose dairy cows to metritis (Mulligan et al. 2006a, Melendez 2006). The clear links between hypocalcemia, dystocia and retained fetal membranes, together with the link between hypocalcemia and periparturient immunosuppression, provide a

strong basis for the association between hypocalcemia and metritis (Kimura et al. 2006). Hypocalcemia reduces contraction of the teat sphincter muscle responsible for closure of the teat orifice after milking and may exacerbate the immunosuppression ordinarily present at calving, which increases the risk of mastitis (Goff and Horst 1997, Kimura et al. 2006, Goff 2008).

KETOSIS

During the early lactation, dairy cows experience a typical negative energy balance characterized by mobilization of NEFA from adipose tissue (Herdt 2000), which is explained by low dry matter intake around parturition and a slower increase in dry matter intake than in milk production during the early lactation. Energy required for maintenance and milk production exceeds the amount of energy that dairy cows can obtain from dietary sources (Goff and Horst 1997, Mulligan et al. 2006b, Oliveira et al. 2004). The lowest dry matter intake occurs at calving. Milk production typically peaks between week 5 to 7 postpartum while maximum dry matter intake is reached between week 8 and 22 after calving. The rate of an increase in dry matter intake after calving are affected by the diet fed during lactation, prepartum feeding and body condition score of periparturient cows (Ingvartsen and Andersen 2000).

Depressed dry matter intake during the early lactation leads to a lack of ruminal propionate supply to the liver (Drackley 1999, DeFrain et al. 2005). Propionate produced in the rumen after fermentation of carbohydrates is the major glucogenic volatile fatty acid (DeFrain et al. 2005). Propionate stimulates insulin secretion, which suppresses NEFA mobilization (Pehrson et al. 1998, Drackley 1999). After propionate is absorbed by the rumen epithelial wall, it is transported via the portal vein to the liver. Propionate is incorporated into the tricarboxylic acid cycle through succinyl coenzyme A and is converted to glucose via pyruvate and oxaloacetate by the liver (Melendez 2006, Allen et al. 2009). Propionate deficiency due to low dry matter intake and increased lactational demand for energy leads to a lack of oxaloacetate which is used to convert acetate, butyrate and NEFA to energy in the tricarboxylic acid cycle. As a result, the acetyl-coenzyme A synthesized from acetate, butyrate and NEFA cannot enter into the tricarboxylic acid cycle and is converted to ketone bodies (acetone, acetoacetate and BHBA) (Goff and Horst 1997, Kara 2009).

Excessive body fat mobilization occurring as a result of negative energy balance leads to increased amount of NEFA oxidized by the liver or exported from liver as very low density lipoprotein (Goff and Horst 1997, Drackley 1999, Liu et al. 2010). However, there is a limit to the amount of NEFA that can be oxidized to completion by the tricarboxylic acid cycle of the liver or exported from the liver. When the limited capacity of liver is reached, triglycerides accumulate within the hepatocytes and impairing their function (Goff and Horst 1997, Liu et al. 2010).

Ketosis is a typical metabolic disease explained by low dry matter intake, a low level of glucose, negative energy balance and a high level of fat mobilization in early postpartum cows (Herdt 2000, Guo et al. 2008). Dairy cows are susceptible to ketosis during especially the first 6 to 8 weeks after calving. High producing cows are more susceptible to ketosis than low producing ones (Melendez 2006, de Roos et al. 2007, Guo et al. 2008). Although increased concentrations of plasma ketone bodies are normal around calving, abnormally increased concentrations can lead to clinical or subclinical ketosis (Duffield et al. 2009, Goldhawk et al. 2009). Subclinical ketosis is defined as serum BHBA concentration above 1.0 mmol/L (Duffield 2000, Goldhawk et al. 2009). Clinical ketosis may start at serum BHBA concentration above 2.6 mmol/L (Duffield 2000). In addition, serum NEFA concentration is generally higher than 1.0 mmol/L in the cows having ketosis and fatty liver (Grummer 1993, Herdt and Gerloff 1999). However, these levels are extremely variable among animals (Duffield 2000).

Body condition score at calving is a measure of adipose tissue reserves that can be used during lactation to supply energy and precursors for milk fat. Excessive body condition at calving increases losses in body condition during the lactation and decreases dry matter intake and milk production (Roche et al. 2009). Fat cows are in a greater negative energy balance and have higher plasma concentration of NEFA (Melendez et al. 2003). Excessive body condition at calving contributes to the development of metabolic diseases such as fat cow syndrome, mastitis and metritis (Roche et al. 2009).

Increased plasma NEFA concentrations during the last 7 days before calving are associated with greater incidence of ketosis, displaced abomasum and retained fetal membranes (Grummer 1995, Ospina et al. 2010). High plasma concentration of NEFA may lead to mastitis due to its negative effect on the immune system (Lacetera et al. 2005, Melendez et al. 2009). Ketosis characterized by increased NEFA and BHBA concentrations leads to a loss in milk production, a greater incidence of cystic ovaries, increased days open and increased culling (Melendez et al. 2003, Melendez 2006).

USE OF CALCIUM PROPIONATE IN DAIRY COWS

The studies with calcium propionate in dairy cows were presented in a chronological order.

Goff and Horst (1994) tested the effect of a water soluble carrier (propylene glycol) versus a water insoluble carrier (soybean oil) on the ability of a single oral dose of calcium chloride and calcium propionate to increase plasma Ca concentration in nonpregnant and nonlactating Jersey cows. A paste was made by adding 300 ml of either propylene glycol or soybean oil to 75 g of Ca as either the chloride or propionate salt. 208 g of calcium chloride containing 36 % Ca and 349 g of calcium propionate containing 21.5 % Ca provided 75 g of elemental Ca. The paste of calcium chloride made in propylene glycol increased plasma Ca concentration more rapidly than did the paste of calcium propionate made in propylene glycol. However, the increase in plasma Ca was sustained longer with calcium propionate. For cows treated with Ca salts administered in soybean oil, plasma Ca concentrations were not statistically increased over pretreatment concentrations. Goff and Horst (1994) reported that a water insoluble carrier (soybean oil) decreased the availability of the Ca for absorption, which was likely because insoluble Ca soaps were formed. The amount of Ca absorbed after oral administration of various Ca salts depended on the solubility of Ca salt in water (Goff and Horst 1994). Goff and Horst (1994) suggested that propylene glycol can be used to form a paste that is readily soluble in water. At the same study, Ca salts were also rectal1y administered to nonpregnant Jersey cows. The cow receiving 97 g of Ca as calcium propionate (463 g) in 4 L of water exhibited a rapid and sustained increase in plasma Ca concentration. Goff and Horst (1994) observed blood-tinged feces at 6 hours after rectal administration of calcium propionate and the cow exhibited tenesmus. Mean plasma Ca concentrations of three cows receiving 116 g of calcium propionate (25 g of Ca) dissolved in 500 ml of water were not significantly increased. No signs of hemorrhage or necrosis were evident in these cows.

Goff et al. (1996) administered the paste of calcium propionate containing 74 g of Ca and 268 g of propionate at calving and again 12 hours after calving to Holstein cows. Treating the cows with calcium propionate significantly decreased the number of cows with subclinical hypocalcemia at 12 and 24 hours after calving. However, administration of calcium propionate had no significant effect on plasma Ca, NEFA and BHBA concentrations. In the same study, calcium propionate administered to Jersey cows increased plasma Ca concentration and decreased the incidences of subclinical hypocalcemia and milk fever, plasma NEFA and BHBA concentrations at 24 hours after calving.

Pehrson et al. (1998) conducted a comparative study of the effectiveness of calcium propionate and calcium chloride for the prevention of milk fever in Swedish Red and White and Swedish Friesian cows. The cows in experimental group received 6 boluses of calcium propionate (each containing 20 g Ca and about 85 g propionate) between 24 hours before and 24 hours after calving. The cows in control group received 4 doses of calcium chloride (each containing 54 g of Ca) during the same period. Pehrson et al. (1998) reported that calcium propionate might be a satisfactory alternative to calcium chloride for the prevention of milk fever.

Calcium chloride is slightly more effective and takes up less volume than calcium propionate. It also is an acidifying agent (Goff and Horst 1993, Goff and Horst 1994). A mild metabolic acidosis can help enhance Ca homeostasis. However, a severe metabolic acidosis can occur when repeated treatments of calcium chloride are administered. In addition, calcium chloride is very irritating to mucous membranes and lesions can be caused in the upper digestive tract. Since calcium propionate does not induce metabolic acidosis, larger amounts of Ca can be given (Goff and Horst 1994, Goff 2008). Oral treatments of calcium propionate can increase plasma Ca concentration within 30 to 60 minutes of administration and plasma Ca concentration remains elevated for about 6 hours (Goff 1999, Melendez 2006).

Jonsson et al. (1998) investigated the effect of drenching with 349 g of calcium propionate in 200 ml molasses on plasma Ca and glucose concentrations in lactating and nonlactating Jersey cows. Drenching with calcium propionate increased plasma Ca concentration by 10 % for periods less than 7 hours and plasma glucose concentration was also elevated by 11 % for less than 3 hours after the treatment with calcium propionate in molasses.

Stokes and Goff (2001) reported that 680 g of calcium propionate administered orally to Holstein cows as two doses at calving and again 24 hours after calving had no significant effect on plasma Ca, glucose, NEFA and BHBA concentrations and milk production. However, drenching with calcium propionate significantly decreased the incidence of metritis in this study. Stokes and Goff (2001) observed that the number of cows with displaced abomasum was more in the group receiving calcium propionate in comparison to control group. Propionate within the abomasum inhibits contractility of abomasum, thus increasing the risk of displaced abomasum. In this study, the increased incidence of displaced abomasum was not related to administrations of calcium propionate (per drench containing 146 g Ca and 7.3 moles glucose precursor) since possible deleterious effects of propionate in the abomasum could be offset by the beneficial effects of Ca entering the blood to maintain abomasal motility (2001).

Mandebvu et al. (2003) observed that 110 g/day of calcium propionate (78.43 % propionate and 21.36 % Ca) added into total mixed ration for last 3 weeks prepartum and first 3 weeks postpartum decreased subclinical ketonuria during week 1 and 2 postpartum in Holstein cows. In this study, Feeding total mixed ration containing calcium propionate lowered milk fat percentage during weeks 1 to 3 postpartum and tended to decrease serum NEFA concentration during week 1 postpartum. Lowered milk fat percentage in the cows receiving calcium propionate can be explained by the reduction in circulating NEFA utilized for milk fat synthesis by mammary gland. Mandebvu et al. (2003) reported that supplementation of calcium propionate did not affect milk production and variation of body condition score.

Melendez et al. (2003) administered a single oral dose of 510 g calcium propionate, containing 110 g Ca, plus 400 g propylene glycol within 6 hours after calving to dairy cows fed anionic diets (-80 mEq/kg dry matter) during 21 days before expected calving time. The treatment with calcium propionate plus propylene glycol was not effective in reducing the incidence of calving-related disorders such as milk fever, ketosis, fatty liver, retained fetal membranes, metritis and displaced abomasum. Pregnancy rate, calving to conception interval and services per conception were not also affected by the treatment. In addition, administration of calcium propionate plus propylene glycol did not improve milk production and body condition score.

In the study conducted by Oliveira et al. (2004), daily oral administration of 500 g calcium propionate, from 11 days before the estimated calving date until 51 days postpartum, did not affect plasma NEFA concentration, variation of body condition score and the number of days to first postpartum estrus in Holstein cows.

McNamara and Valdez (2005) investigated the effects of 125 g/day of calcium propionate and chromium propionate to supply 10 mg of chromium/day on dry matter intake, milk production and composition, serum glucose and NEFA concentrations in Holstein cows treated from 21 days prepartum to 35 days postpartum. Propionate salts (calcium propionate, chromium propionate and calcium propionate plus chromium propionate) added into total mixed ration had no effect on milk production, body condition score, serum glucose and NEFA concentrations. Milk fat percentage was lower in the groups with calcium propionate and chromium propionate. Treating cows with calcium propionate tended to increase dry matter intake in both prepartum and postpartum period. In this study, addition of either calcium propionate or chromium propionate did not increase rates of lipogenesis during 21 days prepartum. After calving, all cows had a large drop in lipogenesis. However, rates of lipogenesis in the cows treated with calcium propionate and chromium propionate were much greater than in control cows at 14, 28, and 56 days postpartum.

Kara et al. (2009) reported that drenching with 680 g of calcium propionate (per drench containing 143 g of Ca) did not affect dry matter intake, body condition score, milk production, the incidence of retained fetal membranes, serum NEFA and glucose concentrations in lactating Holstein cows. Kara et al. (2009) observed that two drenches of calcium propionate at calving and 24 hours after calving were beneficial in treating milk fever.

In the same study, three drenches of calcium propionate at calving, 24 hours after calving and 7 days after calving significantly decreased the incidence of metritis.

Liu et al. (2010) observed that different amounts of calcium propionate (100 g/day, 200 g/day and 300 g/day) added into total mixed ration during first 63 days of lactation were not affected on dry matter intake, milk production and composition in Holstein cows. In this study, feeding all supplementation levels of calcium propionate tended to increase body weight at a higher rate relative to feeding control diet (no calcium propionate). Increasing supplementation of calcium propionate improved energy status, as indicated by the levels of higher blood glucose, lower blood BHBA and NEFA and lower urine ketones. Liu et al. (2010) reported that the optimum dose of calcium propionate was approximately 200 g/day/cow and further increase to 300 g/day/cow was not beneficial to improve concentration of urine ketones.

Peralta et al. (2011) administered a mixture of calcium propionate, propylene glycol and minerals as a drench in water within 12 hours after calving and at 30 days in milk to Holstein cows. Drenching with the mixture containing 375 g of calcium propionate and 400 g of propylene glycol increased plasma Ca concentration but was not effective in reducing plasma NEFA concentration. In addition, Peralta et al. (2011) reported that administration of the drenches had no significant effect on milk production and milk component, conception rate, days to first ovulation, days to first estrus, days to first service and services per conception.

Feeding calcium propionate requires less labor in comparison with oral administration of calcium propionate as a drench or paste and reduces stress. However, the amount of calcium propionate added into total mixed ration or concentrate mixture is limited since it is unpalatable. Oral administration of calcium propionate as a drench or paste provides greater amounts of Ca and propionate at once compared with feeding calcium propionate. To prepare an oral drench, calcium propionate is mixed with warm water (Kara et al. 2009) or molasses (molasses + water) (Jonsson et al. 1998) and then this solution is delivered into the esophagus via an esophageal feeder tube. Oral paste of calcium propionate is prepared by mixing with less water in comparison to preparing drench (Goff et al. 1996) or mixing with propylene glycol or soybean oil (Goff and Horst 1994) and is packaged into the tube designed for delivery with a caulking gun.

Ca absorption in the rumen is less efficient than in the intestine because the volume of fluid in rumen will rapidly dilute Ca concentration to a value less than 6 mmol/L required for passive absorption. Pastes reduce the amount of Ca likely to bypass the rumen. Thus, more Ca must be administered by paste to reach the rise in plasma Ca concentration obtained by an oral Ca drench. Drenches can lead to severe aspiration pneumonia since some cows can aspirate the solution (Jonsson et al. 1998, Melendez 2006).

CONCLUSIONS

Nutrition and management of dairy cows during the transition period have received tremendous interest in recent years because of the increased risk of metabolic disorders such as hypocalcemia and ketosis during this critical period. Hypocalcemia and ketosis have an etiological role in the reduction in dry matter intake and milk production, the development of reproductive disorders, fertility problems and infectious diseases. Thus, these metabolic disorders should be prevented or treated immediately. Calcium propionate has been used for the prevention and treatment of hypocalcemia and ketosis in dairy cows. The effects of calcium propionate in dairy cows have been variable due to different breed, body condition, physiological state, milk production and parity of dairy cows used in the studies, the ratio of concentrate to forage in the diet, the amounts and absorption rates of Ca and propionate administered as calcium propionate and the quality of calcium propionate product used. According to the results of studies summarized in this review, administration of calcium propionate mostly had no significant effect on plasma NEFA and glucose concentrations, milk production, dry matter intake, body condition score and reproductive parameters. However, calcium propionate was beneficial in increasing plasma Ca concentration and preventing or treating milk fever and subclinical hypocalcemia.

REFERENCES

Allen M.S, Bradford B.J and Oba M (2009). The hepatic oxidation theory of the control of feed intake and its application to ruminants. J. Anim. Sci., 87: 3317–3334.

Baird D.G (1982). Primary ketosis in the high producing dairy cow: Clinical and subclinical disorders, treatment, prevention and outlook. J. Dairy Sci., 65: 1–10.

DeFrain J.M, Hippen A.R, Kalscheur K.F and Patton R.S (2005). Effects of feeding propionate and calcium salts of long-chain fatty acids on transition dairy cow performance. J. Dairy Sci., 88: 983–993.

DeGaris P.J and Lean I.J (2009). Milk fever in dairy cows: A review of pathophysiology and control principles. Vet. J., 176: 58–69.

de Roos A.P.W, van den Bijgaart H.J.C.M, Hørlyk J and de Jong G (2007). Screening for subclinical ketosis in dairy cattle by fourier transform infrared spectrometry. J Dairy Sci., 90: 1761–1766.

Drackley J.K (1999). Biology of dairy cows during the transition period: the final frontier. J. Dairy Sci., 82: 2259–2273.

Drackley J.K, Overton T.R and Douglas G.N (2001). Adaptations of glucose and long-chain fatty acid metabolism in liver of dairy cows during the periparturient period. J. Dairy Sci., 84 (Suppl E): 100–112.

Duffield T.F (2000). Subclinical ketosis in lactating dairy cattle. Vet. Clin. North Am. Food Anim. Pract., 16: 231–253.

Duffield T.F, Lissemore K.D, McBride B.W and Leslie K.E (2009). Impact of hyperketonemia in early lactation dairy cows on health and production J. Dairy Sci., 92: 571–580.

Goff J.P and Horst R.L (1993). Oral administration of calcium salts for treatment of hypocalcemia in cattle. J. Dairy Sci., 76: 101–108.

Goff J.P and Horst R.L (1994). Calcium salts for treating hypocalcemia: carrier effects, acid-base balance, and oral versus rectal administration. J. Dairy Sci., 77: 1451–1456.

Goff J.P, Horst R.L, Jardon P.W, Borelli C and Wedam J (1996). Field trials of an oral calcium propionate paste as an aid to prevent milk fever in periparturient dairy cows. J. Dairy Sci., 79: 378–383.

Goff J.P and Horst R.L (1997). Physiological changes at parturition and their relationship to metabolic disorders. J. Dairy Sci., 80: 1260–1268.

Goff J.P (1999). Treatment of calcium, phosphorus, and magnesium balance disorders. Vet. Cl. North Amer. Food. Anim. Pract., 15: 619–639.

Goff J.P, Ruiz R and Horst R.L (2004). Relative acidifying activity of anionic salts commonly used to prevent milk fever. J. Dairy Sci., 87: 1245–1255.

Goff J.P 2008. The monitoring, prevention, and treatment of milk fever and subclinical hypocalcemia in dairy cows. Vet. J., 176: 50–57.

Goldhawk C, Chapinal N, Veira D.M, Weary D.M and von Keyserlingk M.A.G (2009). Prepartum feeding behavior is an early indicator of subclinical ketosis. J. Dairy Sci., 92: 4971–4977.

Grummer R.R (1993). Etiology of lipid-related metabolic disorders in periparturient dairy cows. J. Dairy Sci., 76: 3882–3896.

Grummer R.R (1995). Impact of changes in organic nutrient metabolism on feeding the transition dairy cow. J. Anim. Sci., 73: 2820–2833.

Guo J, Peters R.R and Kohn R.A (2008). Evaluation of a mechanistic model of glucose and lipid metabolism in periparturient cows. J. Dairy Sci., 91: 4293–4300.

Herdt T.H and Gerloff B.J (1999). Ketosis. In: Current veterinary therapy 4: food animal practice (Eds.: J. Howard and R. Smith). WB Saunders Company, Philadelphia, USA, pp: 226–230.

Herdt T.H (2000). Ruminant adaptation to negative energy balance. Influences on the etiology of ketosis and fatty liver. Vet. Clin. North Am. Food Anim. Pract., 16: 215–230.

Hernández E.G.S, Bouda J, García J.A and Hernández J.A.N (2009). Effect of postpartum administration of calcium salts and glucose precursors on serum calcium and ketone bodies in dairy cows. Vet. Méx., 40: 17-26.

Higgins J.J, Sanchez W.K and Guy M.A (1996). An oral gel of calcium propionate plus propylene glycol is effective in elevating calcium and glucose levels in periparturient dairy cows. J. Dairy Sci., 79 (Suppl. 1): 130 (Abstr.).

Horst R.L, Goff J.P and Reinhardt T.A (1994). Calcium and vitamin D metabolism in the dairy cow. J. Dairy Sci., 77: 1936–1951.

Ingvartsen K.L and Andersen J.B (2000). Integration of metabolism and intake regulation: a review focusing on periparturient animals. J. Dairy Sci., 83: 1573–1597.

Jonsson N.N, Daniel R.C.V, Mayer D and Verrall R (1998). Effects of oral dosing with calcium propionate on total calcium and glucose concentrations in the plasma of the cow. J. Vet. Med., 45: 127–136.

Jorgensen R.J, Nyengaard N.R, Hara S, Enemark J.M and Andersen P.H (1998). Rumen motility during induced hyper- and hypocalcaemia. Acta. Vet. Scand., 39: 331–338.

Kara Ç (2009). Süt sığırlarının geçiş dönemlerinde kalsiyum propiyonat katkısının süt verimi ve bileşimi ile ketozis, hipokalsemi ve bazı döl verimi parametrelerine etkileri. The Degree of Doctor of Philosophy Thesis, U. Ü. Veteriner Fakültesi, Bursa, Turkey.

Kara Ç, Orman A, Udum D, Yavuz H.M and Kovanlıkaya A (2009). Effects of calcium propionate by different numbers of applications in first week postpartum of dairy cows on hypocalcemia, milk production and reproductive disorders Ital. J. Anim. Sci., 8: 259-270.

Kimura K, Reinhardt T.A and Goff J.P (2006). Parturition and hypocalcaemia blunts calcium signals and immune cells of dairy cattle. J. Dairy Sci., 89: 2588–2595.

Lacetera N, Scalia D, Bernabucci U, Ronchi B, Pirazzi D and Nardone A (2005). Lymphocyte functions in overconditioned cows around parturition. J. Dairy Sci., 88: 2010–2016.

Liu Q, Wang C, Yang W.Z, Guo G, Yang X.M, He D.C, Dong K.H and Huang Y.X (2010). Effects of calcium propionate supplementation on lactation performance, energy balance and blood metabolites in early lactation dairy cows. J. Anim. Physiol. Anim. Nutr., 94: 605–614.

Mandebvu P, Ballard C.S, Sniffen C.J, Tsang D.S, Valdez F, Miyoshi S and Schlatter L (2003). Effect of feeding an energy supplement prepartum and postpartum on milk yield and composition, and incidence of ketosis in dairy cows. Anim. Feed. Sci. Tech., 105: 81–93.

McNamara J.P and Valdez F (2005). Adipose tissue metabolism and production responses to calcium propionate and chromium propionate. J. Dairy Sci., 88: 2498–2507.

Melendez P, Donovan G.A, Risco C.A, Littell R and Goff J.P (2003). Effect of calcium-energy supplements on calving-related disorders, fertility and milk yield during the transition period in cows fed anionic diets. Theriogenology, 60: 843–854.

Melendez P (2006). Nutritional management of the transition period to optimize fertility in dairy cattle. In: Proceedings 3rd Florida and Georgia Dairy Road Show Conference, Tifton, GA, USA, March 7, pp: 1–50.

Melendez P, Marin M.P, Robles J, Rios C, Duchens M and Archbald L (2009). Relationship between serum nonesterified fatty acids at calving and the incidence of periparturient diseases in Holstein dairy cows. Theriogenology, 72: 826–833.

Mulligan F.J, O'Grady L, Rice D and Doherty M (2006a). Production diseases of the transition cow: Milk fever and subclinical hypocalcaemia. Irish Vet. J., 59: 697-702.

Mulligan F.J, O'Grady L, Rice D and Doherty M (2006b). A herd health approach to dairy cow nutrition and production diseases of the transition cow. Anim. Reprod. Sci., 96: 331–353.

Oetzel G.R (1996). Effect of calcium chloride gel treatment in dairy cows on incidence of periparturient diseases. J. Am. Vet. Med. Assoc., 209: 958–961.

Oliveira P.G, Pires A.V, Meyer P.M, Susin I, Villarreta E.T, Rodrigues P.H.M and Santos F.A.P (2004). Gluconeogenic supplements do not affect production, reproductive traits and blood metabolite of Holstein cows during the transition period. Scientia Agricola (Piracicaba, Braz), 61: 376–385.

Ospina P.A, Nydam D.V, Stokol T and Overton T.R (2010). Evaluation of nonesterified fatty acids and betahydroxybutyrate in transition dairy cattle in the northeastern United States: Critical thresholds for prediction of clinical diseases. J. Dairy Sci., 93: 546-554.

Pehrson B, Svensson C and Jonsson M (1998). A Comparative study of the effectiveness of calcium propionate and calcium chloride for the prevention of parturient paresis in dairy cows. J. Dairy Sci., 81: 2011–2016.

Penner G.B, Tremblay G.F, Dow T and Oba M (2008). Timothy hay with a low dietary cation-anion difference improves calcium homeostasis in periparturient Holstein cows. J. Dairy Sci., 91: 1959–1968.

Peralta O.A, Duchens D.M, Moraga L and Nebe R.L (2011). Supplementing transition cows with calcium propionate-propylene glycol drenching or organic trace minerals: implications on reproductive and lactation performances. Arch. Med. Vet., 43: 65-71.

Reinhardt T.A, Lippolis J.D, McCluskey B.J, Goff J.P and Horst R.L (2011). Prevalence of subclinical hypocalcemia in dairy herds. Vet. J., 188: 122–124.

Roche J.R, Dalley D, Moate P, Grainger C, Rath M and O'Mara F (2003). A low dietary cation-anion difference precalving and calcium supplementation postcalving increase plasma calcium but not milk production in a pasture-based system. J. Dairy Sci., 86: 2658-2666.

Roche J.R, Friggens N.C, Kay J.K, Fisher M.W, Stafford K.J and Berry D.P (2009). Body condition score and its association with dairy cow productivity, health, and welfare. J. Dairy Sci., 92: 5769–5801.

Stokes R.S and Goff J.P (2001). Case study: evaluation of calcium propionate and propylene glycol administrated in to esophagus of dairy cattle at calving. Prof. Anim. Sci., 17: 115–122.

Taylor M.S, Knowlton K.F, McGilliard M.L, Seymour W.M and Herbein J.H (2008). Blood mineral, hormone, and osteocalcin responses of multiparous Jersey cows to an oral dose of 25-hydroxyvitamin D3 or vitamin D3 before parturition. J. Dairy Sci., 91: 2408–2416.