Parturient paresis

Milk fever; Hypocalcemia

Definition:

A disease of cattle, sheep and goats occurring around the time of parturition and caused by hypocalcemia and characterized by weakness , recumbency and ultimately shock and dearth.

Parturient paresis in cows (Milk fever , Hypocalcemia) : is an acute to per acute , a febrile , flaccid paralysis of mature dairy cows that occurs most commonly at or soon after –parturition .

Parturient hypocalcemia (milk fever, parturient paresis): is an acute calcium deficiency condition that manifests with progressive loss of skeletal, cardiac, and smooth muscle function.

It is the most common metabolic disease of dairy cattle but also occurs in beef cattle infrequently.

It is manifested by changes in mentation, generalized paresis, and circulatory collapse.

Subclinical hypocalcemia is defined as total serum calcium concentration below 8.0 mg/dl in the absence of clinical signs of hypocalcemia. Cows with subclinical hypocalcemia are thought to be predisposed to lower intake and other secondary diseases, including LDA. Cows with subclinical hypocalcemia had higher NEFA concentrations compared with normocalcemic cows.

Etiology

The onset of lactation results in a sudden large demand on the calcium homeostasis.

At or near the time of parturition. The onset of lactation results in the sudden loss of calcium into milk.

A depression of the levels of ionized calcium in tissue fluids is the basic biochemical defect in milk fever.

A transient period of hypocalcemia occurs at the onset of lactation caused by an imbalance between calcium output in the colostrums and influx of calcium to the extra cellular pool from intestine and bone.

The loss of calcium in single milking is about nine times as much calcium as that present in the entire plasma calcium pool of the cow.

Calcium lost from the plasma pool must be replaced by increasing intestinal absorption and bone resorption of calcium.

Hypocalcemia occurs in spite of apparently adequate function of the parathyroid and vit D endocrine system and most cows adapt within 48 h. after calving by increases in plasma concentrations of parathyroid hormone and 1, 25 –(OH) 2 D vitamin at the onset of the hypocalcemia and mobilize calcium by increasing intestinal absorption and bone resorption

Epidemiology

Occurrence

Cattle :

The disease occurs most commonly in high – producing adult lactating dairy cattle. Lactating beef cows are affected but less commonly.

The disease may be seen in cows in any age, but is most common in high producing dairy cows > 5 year old.

The disease is present whenever higher producing dairy cattle are raised . generally , it does not occur before four years of age (third parturition) , but has been observed in first calf heifers and occasionally in mid – lactation in high producing cows .

Overall incidence of clinical hypocalcemia is approximated at 8% to 90%, but variation between herds is tremendous, ranging from none to greater than 60% prevalence. The incidence of milk fever has generally been reported to range from 5 to 10% .

Age:

Mature dairy cows are most commonly affected in the 5- 10 year age group, although rare cases have been observed at the first and second calving.

The hypocalcemia at calving is also age related and most marked in cows at their 3rd to 7th parturition ; it is infrequent at the first parturition .

Breed :

There are differences in susceptibility between the breeds

Jerseys are most susceptible . Ayrshire lactations , cows in higher producing herds were at increased risk of milk fever and ketosis .

The disease in beef cattle breeds occurs either in individual cows or in herd outbreaks .

Individuals cows:

Individual cows , and to some extent families of cows , are more susceptible than others , the disease tends to recur at successive parturitions.

The heritability of susceptibility to milk fever and hypocalcemia has been assessed as in significant .

Complete milking in the first 48 hrs after calving , as opposed to normal sucking by a calf , appear to be a precipitating factor.

Time of occurrence :

The disease most commonly occurs in high producing adult cattle within 48 hours of calving, although a small percentage of cases occur ante partum and between 48 and 72 hours after calving.

It usually occurs between 12 hours pre partum and 48 hours post partum with most cases occurring 6 to 24 hours post partum .

In cattle , milk fever occurs at three main stages in the lactation cycle .

Most pre partum cases occur in the last few days of pregnancy and during parturition but rare cases occur several weeks before calving .

Most case occur within the first 48 hr after calving and the danger period extends up to about the 10^{th} postpartum day .

Up to 20% of cases can occur subsequent to the 8^{th} day after calving .

In such cases the declines in serum calcium and phosphorus levels are smaller and the increases in serum magnesium levels are greater than in parturient cows .

The clinical signs are also less severe and there are fewer relapses after treatment .

Occasional cases occur 6-8 weeks after parturition (mid – lactation) . such cases are most often recurrences of the disease in highly susceptible cows which were affected at calving .

Undue fatigue and excitement may precipitate such attacks and there is a special susceptibility at estrus . in the latter case , the depression of appetite by the elevation of blood estrogen levels may be a significant factor .

Stressors :

Starvation for 48 h also causes severe depression of serum calcium levels and thus may be of importance in the production of hypocalcemic paresis in this species are the times other than in the post parturient period

Pregnant beef cattle may develop hypocalcemic paresis during the winter months when they are fed on poor – quality roughage .

The disease has also been recorded in beef cows affected with diarrhea of undetermined etiology .

As another explanation of the heightened susceptibility of cows at estrus , a possible depression of the degree of ionization of calcium under the influence of increased serum estrogen is suggested .

Subclinical hypocalcemia occurs in dairy cattle during the first few weeks of lactation .

Hypocalcemic syndromes in ruminants are also observed at time other than related to parturition . thus , it can be part of an early or mild overeating of fermentable carbohydrates .

The IV administration of certain aminoglycosides , especially neomycin dihydrostreptomycin and gentamicin , may cause a reduction in the degree of ionization of serum calcium and a syndrome similar to milk fever .

Pathogenesis

Hypocalcemia / hypomagnesemia / hypophosphatemia

Hypocalcemia :

Is the cause of the signs of typical milk fever. A tony of skeletal muscle and plain muscle are well – known . physiological effects of hypocalcemia

Hypophosphatemia and variations in levels of serum magnesium also occur and have secondary role . Serum calcium levels decline from a normal of 10- 12 mg dl, to 2.7 mg / dl.

Commonly, serum magnesium is increased, serum phosphorus is decreased and cows are hyperglycemic.

The normal blood calcium concentration in adult cows is between 8.5 and 10 mg /dl which translates into a total plasma pool of only about 3 g in a 600 kg individual .

It is evident that to meet the calcium needs of colostrums production , fetal maturation , and incipient lactation at the end of gestation (collectively these requirements may reach 30 mg / day) , adult cows will need to mobilized substantial amounts of calcium from bones and increase the efficiency of gastrointestinal tract absorption . intestinal absorption of calcium is heavily dependent on the production of 1, 25 dihydroxy vitamin D3 by the kidney in response to parathormone (PTH) secretion .

Hypomagnesemia

When hypomagnesemia coexists with hypocalcemia the clinical signs continue but with normal or higher than normal levels , relaxation , muscle weakness , depression and coma supervene.

It is likely that the hypocalcemic tetany is overcome by the relative hypermagnesemia (the ratio of ca; mg may change from 6: 1 to 2: 1) approximating the ratio at which magnesium narcosis develops .

There is normally a rise in serum magnesium levels at calving but in those cases of parturient paresis in which tetany is a feature serum magnesium levels are low.

Hypophosphatemia

Low serum phosphorus levels occur in , milk fever and contribute to the clinical signs .

Some case of milk fever may not respond to calcium injections even though the serum calcium levels return to normal but may appear to recover when the udder is inflated and serum phosphorus levels rise .

Field observations indicate sodium acid phosphate given orally or IV may result in recovery of cases not responding initially to calcium salts .

Sheep and goats

In sheep , the disease commonly occurs in outbreaks in groups of ewes exposed to forced exercise , long – distances transport , sudden deprivation of food , and grazing on oxalate – containing plants or green cereal crops . these circumstances commonly precipitate outbreaks of hypocalcemic paresis in sheep , mature ewes are the most susceptible , particularly in the period from 6 wks before to 10 weeks after lambing .

Up to 25% of the flock may be affected at one time .

The disease also occurs in young sheep up to about 1 year old , specially when they graze green oats , but also when pasture is short in winter and spring .

The disease is manifested by paresis but in the rest of the flock poor growth , lameness and bone fragility can be detected .

A sudden deprivation of feed or forced exercise of ewes can cause marked depression of the serum calcium levels.

Ewes are in a susceptible state in early lactation because they are in negative calcium balance . in late lactation state of positive balance is due to a low rate of bone resorption .

Hypocalcemia may occur in pregnant ewes fed a calcium – deficient diet over a prolonged period .

A high dietary level of magnesium in late pregnancy may also predispose to hypocalcemia in pregnant ewes .

In Goats :

A depression in serum levels of calcium and phosphorus occurs similar to that in cows but in ewes no such depression occurs art lambing

Milking goats become affected mostly during the 4- 6 year age group . cases occur before and after kidding , some later than 3 weeks after parturition .

Clinical syndromes are identical to those in cows , including the two stages of ataxia and recumbency .

Morbidity and case fatality

Annual morbidity of 3.5 and 8.8 % of susceptible adult cows have been recorded .

Generally the disease is sporadic but an individual farms the incidence may rarely reach 25-30% of high risk cows .

With early treated relatively few deaths occur in uncomplicated case but incidental losses due to aspiration pneumonia , mastitis and limb injury may occur .

From 75- 85% of uncomplicated cases respond to calcium therapy alone . a proportion of these animals requires more than one treatment , either because complete recovery is delayed or because relapse occurs .. the remaining 15-25% are either complicated by other conditions or incorrectly diagnosed .

Risk factors : major risk factors include :

1. Increasing age of cow
2. high – producing dairy cattle
3. dry period nutrition
4. housing

Animal risk factors :

Serum calcium levels decline in all adult cows at calving due to the onset of lactation .

Serum calcium levels decline to lower levels in some cows than in others and it is this difference which results in the varying susceptibility of animals to parturient paresis.

First - calf heifers rarely develop milk fever because while some degree of hypocalcemia occurs during the first few days of lactation , they are able to adopt rapidly to the high demands of calcium for lactation . with increasing age , this adaptation process is decreased and results in moderate – to – severe hypocalcemia in most adult cows .

The adaptation mechanism is directly related to the efficiency of intestinal absorption of calcium , which decreases with increasing age .

Regulation of calcium homeostasis

Within plasma levels that maintain critical muscular , nervous , and other cellular functions is achieved through

I. The action of PTH

The normal physiologic response to decreasing calcium levels is to produce PTH , which acts to increase osteoblastic bone resorption (Direct PTH effect) .

II. increase intestinal absorption (1,25 dihydroxy vit D3)

III. enhance renal tubular resorption of calcium .

PTH secretion is exquisitely sensitive to small decreases in plasma calcium , but the response can be blunted by hypomagnesemia , partly explaining the well – documented link between clinical hypomagnesemic tetany and hypocalcemia , even in non lactating cattle .

The role of acid- base status plays is an important factors that interferes with PTH activity .

Metabolic alkalosis predispose to both milk fever and subclinical hypocalcemia principally because it interferes with skeletal calcium resorption and intestinal absorption by conformationally altering the PTH – receptor interaction at the tissues levels .

Bu altering this interaction , downstream signally events that should results in increased plasma calcium do not occur despite PTH secretion.

So that practice of anionic salt supplementation to the diets of dry cows as a means by which milk fever and subclinical hypocalcemia rates can be reduced because of relative acidification of cattle in late gestation .

It is worth noting that strong univalent cations , such as potassium and sodium , probably influence the development of milk fever via their alkalinizing effects and subsequent diminished tissue responsiveness to PTH , far more than does calcium in the diet during the late dry and early lactational period .

With increasing age there is a reduced pool of calcium available for absorption from bone as a result of diminishing pool of calcium available for absorption from bone as a result of diminishing numbers of bone cells , and this is a reason why heifers in whom osteoblastic activity is high do not suffer from clinical milk fever .

A further age – related change is the reduction in PTH receptors un peripheral tissues of older cattle .

Calcium homeostasis

Three factors affected calcium homeostasis and variations in one or more of them may be important in causing the disease in any individual :

1.excessive loss of calcium in the colostrums beyond the capacity of absorption from the intestines and mobilization from the bones to replace . variations un the susceptibility between cows should be due to variations in the concentration of calcium in the milk and the volume of milk secreted .

2. impairment of absorption of calcium from the intestine at parturition .

3. Mobilization of calcium from storage in the skeleton may not be sufficiently rapid to maintain normal serum levels.

The calcium mobilization rate and the immediately available calcium reserves are sufficiently reduced in cows in later pregnancy to render them in capable of withstanding the expected loss of calcium in the milk.

In older cows , bone resorption makes only minor contribution to the total rate of calcium mobilization at parturition and is therefore of minor importance for the prevention of periparturient hypocalcemia .

Osteoblasts are the only type of bone cell to express the 1,25 (OH) 2 D receptor protein , and the decrease in the numbers osteoblasts with increasing age could delay the ability of bone to contribute calcium to the plasma calcium pool .

Tissue 1, 25 – dihydroxy vitamin D receptor concentrations decline with age , which renders older cows less able to respond to 1,25 dihydroxy vitamin D.

The intestinal 1,25 (OH)2 D receptor numbers decline with age in the cow and thus the older cow is less able to respond to the hormone and will take longer to adapt intestinal calcium absorption mechanisms to meet lactational demands for calcium .

Aperplexing situation in dairy practice is the recently calved cow with peracute coliform mastitis which may also be mildly hypocalcemic and have some of the clinical signs of milk fever .

The escherchia coli endotoxin given IV depresses serum calcium and phosphate levels so that coliform mastitis may contribute to a degree of hypocalcemia in individual cows.

Dietary and environmental; risk factors

Several dietary factors of the pregnant cow during the pre partum period (last 4 weeks) can influence the incidence of milk fever in cattle .

Dietary calcium

Feeding more than 100 g of calcium daily during the dry period is associated with and increased incidence of milk fever . cows daily requirement (31 g of calcium) in late gestation , can be met almost entirely by passive absorption of dietary calcium .

The active transport of calcium from the diet and bone calcium resorption mechanisms are homeostatically depressed and become quiescent .

As a consequence , at calving the cow is unable to use bone calcium stores or intestinal calcium absorption mechanisms and is susceptible to sever hypocalcemia until these mechanisms can be activated which may take several days .

In sheep

Hypocalcemia may occur in pregnant ewes fed a calcium – deficient diet over a prolonged period .

A high dietary level of magnesium in late pregnancy may also predispose to hypocalcemia in pregnant ewes .

Dietary phosphorus

Prepartum diets high in phosphorus (>80 g of phosphorus / d) also increase the incidence of milk fever and the severity of hypocalcemias.

High dietary levels of phosphorus increase the serum level of phosphorus which is inhibitory to the renal enzymes that catalyze production of 1,25(OH)2 D , which when decreased reduce the intestinal calcium absorption mechanisms prepartum .

Economic importance

Losses are due to complicati0ns

There is a highly significant relationship between milk fever and dystocia , retained fetal membrane , ketosis sand mastitis ,.

Cows which recover from ,ilk fever are more likely to develop ketosis and mastitis compared to those which do not have milk fever .

Milk fever in dairy cattle is a risk factor for several reproductive diseases such as dystocia , retained placenta , metritis and uterine prolapsed .

Some studies have found that mil fever directly increased to likelihood of developing hypomagnesemia, abomasal disease and ketosis.

The overall net effect is that an incident of milk fever potentially reduces the mean productive life of a dairy cow by about 3 years.

Clinical signs :

Cattle :

Three stages of milk fever in cattle are commonly recognized and described

Stage I

In the first stage the cow is still standing . this is also brief stage of excitement and tetany with hypersensitivity and muscle tremor of the head and limbs .The animal is disinclined to move and does not eat.

There may be a slight shaking of the head , protrusion of the tongue and grinding of the teeth .

The rectal temperature is usually normal to slightly above normal . stiffness of the hind legs is apparent . the animal is ataxic and falls easily and , on going down , the hind legs are stack out stiffly.

Earlier stage than the first stage can be observed by owner and clinician .

It is characterized by anorexia , agalactia , rumen status , scant feces and a normal temperature , heart rate and respiration .

Affected cows may remain in this prodromal stage for several hours.

Stage 2:

The second stage is prolonged sterna recumbency . depressed consciousness , the cow has a drowsy appearance in sterna recumbency usually with lateral kink in the neck or the head turned into the flank .

When approach , some of these cows will open their mouths , extend their head and neck and protrude their tongues which may be an expression of apprehension and fear in an animal unable to stand .

The tetany of the limbs present in the first stage is not present and the cow is unable to stand .

The muzzle is dry , the skin and extremities cool , and the rectal temperature subnormal (36- 38oc) .

There is a marked decreased in the absolute intensity of the heart sounds and an increase in rate (about 80 bpm).

The arterial pulse is weak and the venous pressure is also low , making it difficult to raise the jugular veins .

The respirations are not markedly affected , although a mild forced expiratory grunt or groan is sometimes audible .

The eyes are usually dry and staring . the papillary light reflex is incomplete or absent and the diameter of the pupil varies from normal to maximum dilatation .

Ruminal stases and secondary bloat are common and constipation is characteristics . there is also relaxation of the anus and loss of the anal reflex.

Examination of reproductive tract usually reveals a fully dilated cervix and normal presentation of the fetus.

Prolapse of the uterus is a common complication of milk fever and often the calcium levels are lower than in parturient cows without uterine prolapsed .

Stage -3-

The third stage is lateral recumbency . the cow is almost comatose and although the limbs may be stuck out there is complete flaccidity on passive movement and the cow cannot assume sterna recumbency on its own.

in general , the depression of temperature and the cardiovascular system are more marked .

The heart sounds are almost in audible and the rate increased to up to 120 bpm .

The pulse is almost impalpable and it may be impossible to raise the jugular veins .

Bloat is usual because of lateral recumbency.

Without treatment , a few animal remain unchanged for several hours but most become progressively worse during a period of several hours and dye quietly from shock in a state of complete collapse.

Concurrent hypomagenesemia :

Mild to moderate tetany and hyperesthesia persisting beyond the first stage suggests a concurrent hypomsagnesemia .

There is excitement and fibrilltary twitching of the eyelids , and titanic convulsions are readily precipitated by sound or touch .

Trimsmus may be present .

The heart and respiratory rates are increased and the heart sounds are much louder than normal .

Without treatment death occurs during a convulsion .

Aconcurrent hypophosphatemia

With a concurrent hyypopphosphatemia , the clinical findings are typical of milk fever which responds to calcium therapy in all respects except that the cow is unable to stand after treatment .

Sheep and goats

The disease in pastured ewes is similar to that in cattle .

The early signs include a stililty , proppy gait and tremor of the shoulder muscles .

Recumbency follows , sometimes with tetany of the limbs but the proportion of ewes with hypocalcemia which are recumbent in the early stages is much less than in cattle .

A similar generalization applies to female goats .

The characteristic posture is sternal recumbency , with the legs under the body or stretched out behind.

Ruminal movements are absent , the head is rested on the ground , there may be an accumulation of mucus exudates in the nostrils and the respiratory rates is increased .

The venous blood pressure is low and the pulse impalpable .

Mental depression is evidenced by a drowsy appearance and depression of the corneal reflex.

Constipation is usual .

Response to parenteral treatment with calcium salts is rapid , there is normal 30 minutes after a SC injection.

Death often occurs within 6-12 hr if treatment is not administered ,

The syndrome is usually more severe in pregnant than in lactating ewes , possibly because of the simultaneous occurrence of pregnancy toxemia or hypomagnesemia .

Fat late pregnant ewes on high grain diets indoors or in feedlots show a similar syndrome accompanied by prolapse of the vagina and intestine.

Diagnosis

Determination of low plasma or serum ca concentration is diagnostic

History and presenting clinical signs m, in conjunction with rapid response to ca therapy , are more typically used in diagnosis .

In addition to hypocalcaemia , clinical chemistry abnormalities observed in uncomplicated cases include hypophosphatemia (< 3 mg \dl) , hypermagnesemia (> 3 mg \dl) and hyperglycemia (> 100 mg \dl).

Elevated PTH concentrations associated with hypocalcemia may account for observed hypophospatemia , due to increased renal excretion , and hypermagnesemia , a result of increased renal reabsorption.

Elevated cortisol levels associated with parturition and other stress factors could account for observed hypoglycemia .

Depending on duration and bedding conditions of a recumbent hypocalcemic cows , muscle enzymes , creatine kinase (CK) and asprtate transferase (AST) may be elevated .

Clinical pathology :

Total serum calcium levels are reduced to below 8 mg \ dl (2.0 mmol \L) , usually to below 5 mg (1.2 mmol\L) and sometimes to as low as 2 mg (0.5 mmol\L) . The reduction is usually , but not always , proportional to the severity of the clinical syndrome .

Serum magnesium level are usually moderately elevated to 4-5 mg \dl but in some areas low levels may be encountered , especially in cows at pasture .

Serum inorganic phosphate levels are usually depressed to 1.l5 – 3 mg \dl

Blood glucose levels , normal

Higher than normal blood glucose levels are likely to occur in cases of long duration .,

Serum muscle enzymes :

prolonged recumbency results in ischemic muscle necrosis and increases in the serum muscle enzymes creatine phosphokinase (cpk) and aspartate aminotransferase

Hemogram

Leucocyte count changes include eosinopenia ; neutrophilia ; lymphopenia ; suggestive of adrenal cortical hyperactivity .

High plasma cortisol levels and packed cell volume occur in cows with milk fever.

Differential diagnosis :

A diagnosis of milk fever is based on the occurrence of paresis and depression of consciousness in animals following parturition .

The diagnosis is supported by a favorable response3 to treatment with parenteral injections of calcium solution and by biochemical examination of the blood .

In ewes , the history usually contains some reference to recent physical stress and the disease is more common in the period preceeding lambing .

In the immediate post partum period , there are several diseases which cause recumbency in cows .

1.other metabolic diseases

2. diseases associated with toxemia and shock

3. injuries to pelvis and pelvic limbs .

4.degenerative myopathy

5. downer cow syndrome .

Toxic mastitis

Toxic metritis

Other systemic toxic conditions

Traumatic injury (e.g. stifle injury , coxofemoral luxation , fractured pelvis , spinal compression).

calving paralysis syndrome (damage) to the L6 lumbar roots of sciatic and obturator nerves . Or compartment syndrome .

Treatment

Cows found in lateral recumbency should be placed in sternal recumbency until treatment is available .

This will reduce the chances of aspiration if the cow regurgitates

Calcium borogluconate at 100- 200 g is the treatment of choice

Dose 8- 10 g (calcium borogluconate is 8.3% calcium).for cattle 400- 800 ml of 25% solution is the usual dose .

Calcium salts have a toxic effects when given IV

Initial dose (cow 540- 590 kg) requires 800- 1000 ml of 25% solution and small cow (320- 360 kg) 400- 500 ml .

Under dosing increases the chances of incomplete response ,with in ability to rise of relapse .

In sheep and goats 150-0 29 g IV with an optional 5- 10 g SC

Typical response to calcium borogluconate

Belching

Muscle tremor , particularly of the flanks and often extending to the whole body

showing and improvement in the amplitude and pressure of the pulse.

Increase in the intensity of the heart sounds

Sweating of the muzzle

Defecation .