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Parturient Paresis (Milk Fever) (حمّى الحليب) الخذل الولادي

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Summary:

Hypocalcemic condition occurs just before, around, or after parturition particularly in dairy cows.

Etiology

- Hypocalcemia just before, around, or after parturition.
- A certain degree of hypocalcemia around parturition is unavoidable due to the sudden imbalance of Calcium homeostasis at the onset of lactation.
    - Calcium requirements of a cow in late gestation are minimal at about 30 g/d.
    - A transient subclinical hypocalcemia occurs at the onset of lactation:
        - caused by an imbalance between calcium influx to the extracellular pool from gut and bone and output in colostrum and milk.
        - total plasma calcium [Ca] 1.4 to 2.0 mmol/L or 8 mg/dL.
    - The sudden increase of Calcium losses through the mammary gland at the onset of lactation:
        - Calcium ≈ 2 g / kg milk
        - Calcium ≈ 2.3 g / kg colostrum
    - Calcium lost from the extracellular pool must be replaced by increasing intestinal absorption and bone resorption of calcium.
        - Most cows adapt within 48 hours after calving by increases in plasma concentrations of parathyroid hormone (PTH) and the biologically active form of vitamin D3 (the 1,25-dihydroxyvitamin D).
- **Factors contributing to development of clinical disease in any individual cow:**
    1. Excessive loss of calcium in the colostrum beyond the capacity of absorption from the intestines and mobilization from the bones to replace it.
    2. Impairment of absorption of calcium from the intestine at parturition.
    3. Reduction of calcium mobilization from storage in the skeleton to maintain normal plasma calcium levels.

Parathyroid hormone maintains serum calcium level:

- **Directly**
  - **on bones**
    - increases the rate of skeletal remodeling and net rate of bone resorption.
    - increases osteolysis and the number of osteoclasts on bone surfaces.
  - **on kidney**
    - increases reabsorption of calcium.
    - accelerates formation of active form of vitamin D (1, 25 dihydroxcholecalciferol).

Indirectly → at the intestine → Increases the active form of vitamin D from kidney leading to increase calcium intake from intestine.

Epidemiology

- **Occurrence**
  - Most commonly in high producing lactating multiparous dairy cattle (3rd to 7th lactation).
    - First-calf heifers rarely develop the disease because they are able to adapt more effectively to the high Calcium demand at the onset of lactation than older cows due to the efficiency of intestinal absorption of Calcium decreases with increasing age.
  - More frequently in Jersey than Holstein–Friesian cows (due to higher milk Ca concentration).
  - It tends to recur at successive parturitions (individual variation).
  - Most cases occur within the first 48 hours after calving, up to about the 10th postpartum day.
  - Milking goats (4- to 6-year-old age) before and after kidding (some later than 3 weeks).
  - Overall clinical disease is sporadic.

- **Risk Factors**
  - Complete milking in the first 48 hours after calving rather than normal sucking by a calf.
  - Diarrhea of undetermined etiology.
  - Medications that reduce the ionization of serum calcium (e.g., neomycin and gentamicin), or reduce serum levels of calcium (e.g., oral doses of zinc oxide).
  - In sheep: long-distance transport, sudden feed deprivation, and grazing on oxalate-containing plants or green cereal crops.
  - High body condition score increases the risk of milk fever.
  - Supplying calcium more than the daily requirements.
    - The active absorption of Ca from the digestive tract and mobilization from bone are homeostatically depressed.
    - Feeding prepartum diets with a calcium concentration low enough induces a negative calcium balance before calving can prevent milk fever by activating

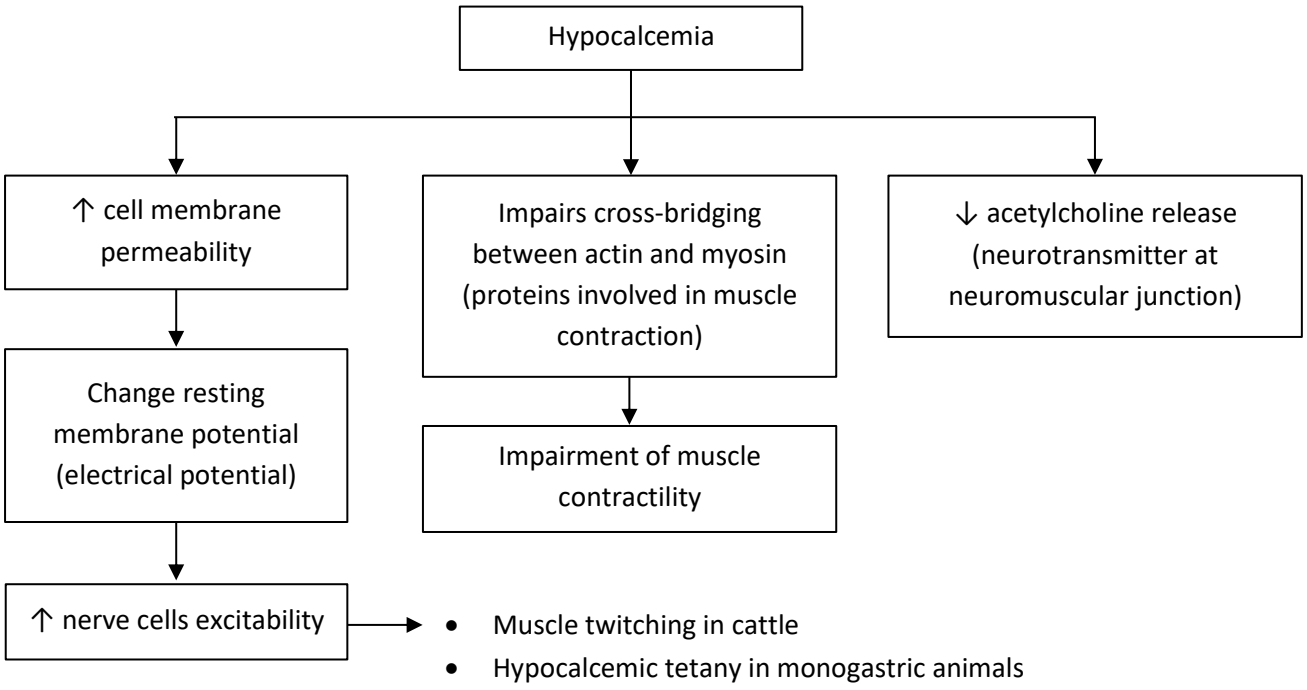
calcium transport mechanisms in the intestine and bone before parturition, thus allowing the animal to adapt more rapidly to the lactational drain of calcium.

- High potassium concentrations in the ration last weeks of gestation can increase the incidence of periparturient hypocalcemia.
  - Most forages, such as legumes and grasses, are high in potassium and are alkaline.
  - Potassium is a cation (positively charged electrolytes "K^+") that alkalizes the blood impairing the function of PTH hormone, and thus decreases mobilization of the calcium from the bones.
- Magnesium deficiency during late gestation is a major risk factor for periparturient hypocalcemia because magnesium is required for the release of PTH from the parathyroid glands and furthermore influences the tissue sensitivity to PTH.

- **Economic Importance**
  - Costs of medications and veterinary intervention.
  - Complications, such as the downer cow syndrome, dystocia, retained placenta, metritis, mastitis, and displacement of abomasum.
  - Culling.

Pathogenesis

- The plasma Ca concentration is normally maintained between 2.1 and 2.6 mmol/L (8.4 to 10.4 mg/dL).



- Disturbed muscle fiber contractility and neurotransmitter release are considered the basis of the flaccid paresis observed in advanced stages of milk fever in ruminants.
- Atony of skeletal muscle and plain muscle are well-known physiologic effects of hypocalcemia in ruminants.

Clinical Signs

- **In Cattle:**
- Characterized by three stages:

Stage 1	▪ Standing cow, with brief nervousness, excitement, and tetany with hypersensitivity. ▪ Muscle tremor of the head and limbs. ▪ The animal is disinclined to move with a decreased or no feed intake. ▪ Slight shaking of the head, protrusion of the tongue, and grinding of the teeth. ▪ The rectal temperature is normal to slightly above normal. ▪ The animal appears ataxic, with a stiff and insecure gait, and falls easily. ▪ Close examination: rumen stasis, and scant feces. ▪ Mild to moderate tetany and hyperesthesia persisting beyond the first stage suggests a concurrent hypomagnesemia.
Stage 2	▪ Sternal recumbency with depressed consciousness (drowsy appearance). ▪ Lateral kink in the neck or the head turned into the flank ▪ When approached, some cows will open their mouths, extend the head and neck, and protrude their tongues, which may be an expression of apprehension and fear. ▪ The muzzle is dry, the skin and extremities cool with subnormal rectal temperature. ▪ Decrease in the heart intensity with increased rate. ▪ Ruminal stasis and secondary bloat are common with constipation. ▪ Relaxation of the anus and loss of the anal reflex.
Stage 3	▪ Lateral recumbency (the cow cannot assume sternal recumbency on its own) ▪ Complete flaccidity and on passive movement. ▪ Depression of temperature and the cardiovascular system. ▪ Bloat is common because of prolonged rumen stasis and lateral recumbency.

- **In Sheep and Goats:**
  - The disease in ewes is similar to that in cattle.
  - Female goats show sternal recumbency, with the legs under the body or stretched out behind, while the head is rested on the ground
  - Mental depression is evidenced by a drowsy appearance.
  - The syndrome is usually more severe in pregnant than in lactating ewes, possibly because of the simultaneous occurrence of pregnancy toxemia or hypomagnesemia.

Clinical Pathology

- Serum Ca levels are reduced to below 2.0 mmol/L (8 mg/dL), usually < 1.2 mmol/L (5 mg/dL).
- Serum magnesium levels are moderately elevated to 1.65 to 2.06 mmol/L (4 to 5 mg/dL).

Differential Diagnosis

- Other metabolic diseases.
- Acute carbohydrate engorgement.
- Diseases associated with toxemia and shock (e.g., acute diffuse peritonitis, coliform mastitis).
- Injuries to the pelvis and pelvic limbs.
- Myopathy.
- Downer-cow syndrome.

Diagnostic confirmation

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

Treatment

- Calcium borogluconate IV, oral calcium salts.
    - Calcium gluconate (8 to 12 g Ca/cow IV or SC as single dose), or:
    - Calcium borogluconate (8 to 12 g Ca/cow IV or SC as single dose), or:
    - Calcium chloride (8 to 12 g Ca/ cow IV as single dose), or:
    - Calcium chloride (50 g Ca/cow) PO every 12h for 48h.
    - Calcium propionate (50 g Ca/cow) PO every 12h for 48h.

- Calcium gluconate is more common in human medicine.
- calcium borogluconate is primarily used in veterinary settings.

- The IV route is preferred because the response is rapid and obvious.
- The heart should be auscultated throughout the IV administration for evidence of arrhythmia, bradycardia, and tachycardia.
    - Bradycardia is a normal response to Ca administration, but the IV administration should be interrupted if arrhythmia or tachycardia is noticed.
- Recovery can be expected in 75% of cases within 2 hours.

Typical Response to Intravenous Ca-Borogluconate

- Belching.
- Muscle tremor, particularly of the flanks and often extending to the whole body.
- Slowing and improvement in the amplitude and pressures of the pulse,
- Decrease of the heart rate and increase in the intensity of the heart sounds.

- Sweating of the muzzle.
- Defecation.
- Urination usually does not follow until the cow stands.

Unfavorable Response to Intravenous Ca-Borogluconate

- Marked increase in heart rate.
- Sudden death may also occur after calcium injections if the cow is excited or frightened, which may be the result of an increased sensitivity to epinephrine.
- Heatstroke may occur when affected cows are exposed to the sun or a hot, humid atmosphere.
    - Attempt should be made to reduce the temperature to below 39.5° C (103° F) before the calcium is administered.

Overdosage may occur when:

- standard dose is administered to quickly.
- excessive dose is administered.
- repeated doses are administered in excess of requirements.
- in individual with increased sensitivity to Ca

Toxicity can occur:

- when farmers treat cases unsuccessfully by multiple SC injections and these are followed by an IV dose.
    - When the peripheral circulation is poor, it is probable that the calcium administered subcutaneously is not absorbed until the circulation improves following the IV injection, and the large doses of Ca then absorbed cause acute toxicity.

SC route

- Commonly used by farmers.
- Used by veterinarians when the effects of IV administration of Ca are uncertain or if an unusual response occurs during IV administration.
- The amount of Ca administered per injection site should be limited to 50 to 75 mL.
- Administration of 500 mL over 10 injection sites can increase plasma Ca concentration of over 15% within 30 minutes.

Oral administration

- Low cost and small volume is required to administer.
- Concentrated formula may cause severe damage of the digestive tract mucosa
- Repeated treatment with Calcium chloride may result in uncompensated metabolic acidosis.
- Ca-propionate formulas are less injurious to tissue and do not alter the acid–base equilibrium.

General management and clinical care procedures

- If the cow is recumbent for any length of time, she must be kept in sternal recumbency not lateral recumbency, which may result in tympany, regurgitation, and aspiration pneumonia.
- The cow should be rolled from side to side every few hours with adequate bedding.
- If a cow is recumbent for more than 48 hours, occasional assisted lifting using appropriate cow lifters should be considered.

Control

- Dietary management to reduce dietary potassium intake prepartum to increase the content of anions in the ration.
    - Induction of mild to moderate acidosis during the last weeks of gestation.
- Reduce dietary calcium content below requirements prepartum to prepare the organism for a negative calcium balance.
- Oral administration of calcium salts immediately before, at, and after calving.
    - It does not disturb mechanisms regulating the Ca homeostasis, but rather supports them by providing oral Ca while intestinal Ca absorption has been upregulated.
- Oral or parenteral vitamin D before calving.

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References:

- Constable PD, Hinchcliff KW, Done SH, et al. (2017). Veterinary Medicine: A Textbook of the Diseases of Cattle, Horses, Sheep, Pigs, and Goats. 11th ed. Elsevier, St. Louis, Missouri, USA.