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Topical Review

Reproductive Causes of Hypocalcemia

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A B S T R A C T

Reproductive causes of hypocalcemia include puerperal tetany (eclampsia) and mild hypocalcemia during whelping. This article reviews the pathophysiology, signalment, clinical signs, and treatment of eclampsia in the bitch and queen. The second part of the article focuses on the consequences and treatment of hypocalcemia prior to and during whelping in dogs and cats.

Eclampsia (Puerperal Tetany)

Eclampsia, or puerperal tetany, is an acute, life-threatening hypocalcemia that occurs in the periparturient period. Eclampsia is one of the most common causes of hypocalcemia in dogs and cats. [1] The clinical signs in small animals include muscle fasciculation and tetany, but not actual seizures; consciousness is maintained.[2] Hyperthermia and hypoglycemia can occur as a consequence. Hypomagnesemia and hypophosphatemia can occur simultaneously.[3] Eclampsia occurs most commonly during the first 4-weeks postpartum, but can also occur in the last few weeks of gestation. The condition occurs in bitches more frequently than queens, and can happen in any breed, but is most common in small breeds of dogs with large litter size.[4-7] The neonates are typically plump.[3] Hypocalcemia occurs if the total serum calcium concentration is less than 9 mg/dl in bitches or 8 mg/dl in adult queens, or the serum ionized calcium concentration is less than 1.0 mmol/L.[1]

Eclampsia is caused by a depletion of ionized calcium in the extracellular compartment. Inability of calcium homeostatic mechanisms (increased absorption in the gastrointestinal system, decreased excretion of calcium from the kidney, and increased osteolysis) to compensate for the loss of calcium in milk is thought to be the cause of lactation-associated hypocalcemia in dogs and cats.[8] Predisposing factors include improper perinatal nutrition, inappropriate calcium supplementation, and heavy lactational demands.[9] Excessive prenatal calcium supplementation can lead to the development of eclampsia by promoting parathyroid gland atrophy and inhibiting parathyroid hormone release, thus interfering with the normal physiological mechanisms to mobilize and conserve adequate calcium stores and utilize dietary calcium sources. Thyrocalcitonin secretion is stimulated. Metabolic conditions favoring protein binding of serum calcium can promote or exacerbate hypocalcemia, such as alkalosis resulting from prolonged hyperpnea during labor or dystocia. The equilibrium between ionized calcium and protein-bound calcium is affected by pH. Acidosis increases the ionized fraction and alkalosis decreases ionized calcium; total calcium concentration is not affected by changes in pH. An alkalotic animal may show signs of hypocalcemia yet have a calcium result that is within the reference range. The bicarbonate result and anion gap, as well as the albumin result, should be considered when interpreting the calcium result.[2,9]

The clinical signs of eclampsia are caused by hypocalcemia and include facial pruritus, panting, limb pain, trembling, muscle fasciculation, weakness, and ataxia. These early clinical signs quickly progress over a few hours to stiffness and tetany with tonic-clonic spasms and opisthotonos. Heart rate, respiratory rate, and rectal temperature are increased, especially during tetany. Clinical signs are rapidly progressive and may be fatal.[2,6] Therapeutic intervention usually should be initiated immediately upon recognition of the clinical signs of tetany, without waiting for laboratory results; a heparinized blood sample ideally should be acquired first for later biochemical confirmation. Immediate therapeutic intervention should be instituted with a slow intravenous infusion of 10% calcium gluconate (bitch 5-30 ml, queen 2-5 ml) given to effect.[3,6,7] Cardiac monitoring for bradycardia and arrhythmias should accompany administration, their occurrence warrants temporary discontinuation of the infusion and a slower subsequent rate. The response to treatment is dramatic, and clinical signs generally resolve during IV calcium administration. Because cerebral edema can occur from uncontrolled seizures, diazepam (1-5 mg intravenously) or barbiturates can be used to control persistent seizures once eucalcemia is attained. Mannitol may be indicated for cerebral inflammation and swelling. Corticosteroids are undesirable because they promote

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calciuria, decrease intestinal calcium absorption, and impair osteoclasia. Hypoglycemia should be corrected if present, and exogenous treatment for hyperthermia given if necessary.[10,11] Once the immediate neurologic signs are controlled, a subcutaneous infusion of an equal volume of calcium gluconate, diluted to 50% with saline, is given, repeated q 6-8 hours until the dam is stable and able to take oral supplementation.[1,10-12] Calcium gluconate or carbonate (10-30 mg/kg q 8 hours) should be instituted. Each 500 mg calcium carbonate tablet (TUMS) supplies 200 mg calcium.[10]

Efforts to diminish lactational demands on the dam and improve her plane of nutrition are indicated. If response to therapy has been prompt, once the dam is stable and eating, nursing can be gradually reinstituted until the neonates can be safely weaned, usually at a slightly early age (3 weeks). Concurrent supplementation of the nurslings with commercial bitch or queen milk replacement is encouraged; nursing time should be limited. If eclampsia recurs, the nurslings should be weaned.[2,3,12]

Prevention of eclampsia is based on proper perinatal nutrition. The use of a balanced growth (puppy/kitten) formula commercial feed without additional vitamin or mineral supplementation is optimal during the second half of gestation. This gestational diet should contain between 1.0% and 1.8% calcium and 0.8% and 1.6% phosphorus. Supplementation with cottage cheese during gestation should be avoided as it disrupts normal calcium-phosphorus-magnesium balance in the diet. The postpartum diet should be balanced for all life stages, including lactation, and contain at least 1.4% calcium, with a calcium:phosphorus ratio of 1:1.[3] The administration of supplemental calcium throughout lactation, but not gestation, may be attempted in dams with a history of recurrent eclampsia (calcium carbonate 500-4000 mg/dam/day divided). Supplemental bottlefeeding of the litter with milk replacer early in lactation and with solid food after 3-4 weeks of age may be helpful, especially for large litters.[2,6]

Hypocalcemia During Whelping and Queening

Calcium supplementation of bitches and queens during whelping and queening can improve the quality of labor. The administration of calcium increases the strength of myometrial contractions as determined by tocodynamometry. Conversely, calcium-channel blockers can be used as tocolytics to decrease myometrial irritability in pre term labor. Calcium administration is less likely to cause uterine rupture than oxytocin, but should still be used with caution if an obstructive dystocia is suspected. Calcium gluconate 10% solution with 0.465 mEq Ca++/ml (Fujisawa) is given SC at 1.0 ml/5.5 kg BW as indicated by the strength of uterine contractions, generally no more frequently than every 4-6 hours. Doses larger than 5 ml should be divided between 2 sites to avoid irritation. Most bitches or queens are eucalcemic, suggesting that the benefit of calcium administration is at a cellular or subcellular level.[10] Smooth muscle contractions are initiated by the calcium-activated phosphorylation of myosin. Contractions in vertebrate smooth muscle are initiated by agents that increase intracellular calcium. This is a process of depolarizing the sarcolemma and extracellular calcium entering through L-type calcium channels, and intracellular calcium release predominately from the sarcoplasmic reticulum.

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