Treatment of metabolic disease

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JAMES ADAMS BVSc, MRCVS considers the issues around mineral deficiencies in cattle that practitioners are likely to meet in their clients' animals and suggests optimum treatments

IN the first part of this article (*VT*44.38), glucose deficiency and the consequences were discussed, with treatment options reviewed.

This second article talks about common macromineral deficiencies in cattle, normally in the periparturient period, that farm vets will encounter on their daily rounds.

Hypocalcaemia

Hypocalcaemia can be a primary problem, but also predisposes to secondary ketosis, hence the numerous products available that treat for both.

A dry cow may need 30g a day of calcium, but up to 80g a day once the animal is lactating, with the initial loss occurring as the udder fills in the 24 hours post-calving. A cow can lose half of its circulating calcium before disease is precipitated (DeGaris and Lean, 2007) although most cows have some degree of hypocalcaemia regardless of clinical signs, with gut stasis happening first. Calcium is needed throughout the body to help allow muscles and nerves to function properly.

The clinical signs of milk fever are due to the effect on contractility of the three types of muscle – skeletal, smooth and cardiac. At a neuromuscular junction, the amount of acetylcholine released is proportional to the extracellular calcium, hence muscle contractility decreases. A lack of smooth muscle function causes reduced gastrointestinal (GIT) movement and the distinctive

bloating and constipation. The cow is recumbent due to the skeletal muscle inactivity (Figure 1), with an “S-shaped neck”.

Tachycardia often arises due to a lack of strength of contraction in the heart. Loss of muscle tone in the gut and uterus and at the teat sphincter, along with the immunosuppressive effect of cortisol, predisposes the cows to displaced abomasums, metritis and mastitis.

The immediate need is to increase the extracellular fluid concentration of calcium. The treatment’s aim is to reverse depressed neuromuscular transmission, to correct paresis and to maintain the cow until normal calcium homeostasis can be re-established through increased absorption from the bone and intestine (Littledike et al, 1981). This process needs to be done quickly because a cow recumbent for as little as four hours may develop the “crush syndrome” effect.

Oral calcium supplementation is the best approach for hypocalcaemic cows that are still standing, such as cows in a hyper-excitable state or that have undetected subclinical hypocalcaemia (Oetzel, 2011). This may be as a bolus, or in a supplement to a drench. All fresh cow products contain a high level of calcium. Cows absorb an effective amount of calcium into the bloodstream within about 30 minutes of supplementation. Blood calcium concentrations are supported for only about four to six hours afterwards (Goff and Horst, 1993) for most forms of oral calcium supplementation.

In a recumbent cow with a simple uncomplicated hypocalcaemia, administration of a calcium salt bolus intravenously should be sufficient. This often takes the form of a 400ml bottle of 40 per cent calcium borogluconate. The most effective dose is 2g calcium/100kg bodyweight (Goff, 2008). The calcium should be administered at 1g/minute. Listening to the heart while administering the calcium is advised due to the potential danger of arrhythmias and potential cessation during systole (Goff, 2008).

The calcium given does not decrease the time it takes a cow to mobilise calcium; it simply sustains the cow for the two to three days it takes to stabilise blood calcium levels.

Subcutaneous calcium is commonly given by the farmer before arrival on the farm and, although this can be used to support blood calcium concentrations around calving, it has substantial limitations. Absorption of the subcutaneous calcium requires sufficient peripheral perfusion, a common problem in cows with milk fever. Tissue necrosis is also a risk.

Figure 2 shows the processes that occur when a cow is deficient in calcium, with parathyroid hormone (PTH) released. Magnesium is critical for the release of parathyroid hormone and in the synthesis of 1.25-dihydroxyvitamin D. In hypomagnesaemic states the kidney and bone are less responsive to PTH (Goff, 2000) and there is poor mobilisation of calcium. This shows the importance of magnesium supplementation in hypocalcaemic animals. A bolus of 400ml 25 per cent magnesium sulphate heptahydrate subcutaneously should be sufficient, although there are preparations available that incorporate both magnesium and calcium and can be given safely intravenously. It is

still imperative to auscultate the heart when administrating the fluid combination. Rude (1998) suggested magnesium therapy alone may restore the calcium concentration to normal.

Barton et al (1984) demonstrated a pre-calving diet high in phosphorus can have a negative impact on calcium homeostasis. Diets high in phosphorus prevent the absorption of calcium so phosphorus supplementation is not recommended initially, although this may be a problem consequently as the PTH causes the phosphorus to be excreted from the kidney. When the phosphorus concentration is around 2mmol/L, phosphate has a direct inhibitory effect on the renal enzyme, converting 25-hydroxyvitamin D to 1.25-dihydroxyvitamin D; therefore, even if PTH is released, high phosphorus levels will prevent uptake of calcium for the intestine.

Even if PTH has been activated and the cow is able to absorb calcium via the intestine, it must have sufficient calcium to be absorbed. By dosing the animal with large amounts of very soluble calcium it is possible to force calcium across the intestinal tract by means of passive diffusion, not across the epithelial cells (Goff, 2006). The cow needs between 50g/calcium to 125g/calcium per treatment. Be aware that doses greater than 250g/cow given in one dose may be toxic and can cause death (Goff et al, 2002).

Calcium propionate should ideally be given as this will have the added benefit of introducing a gluconeogenic precursor. Calcium chloride solutions increase blood calcium concentrations faster than calcium propionate, but the action of calcium propionate lasts longer (Goff and Horst, 1994). Drenching the cows was the most effective way for the cow to absorb the calcium. Goff and Horst also established giving calcium salts per rectum has no benefit, and giving sufficient calcium chloride or calcium propionate rectally at a dose for it to be effective would cause haemorrhage or necrosis of the rectum.

From the author’s research, vitamin D has no benefits to be given in the treatment of hypocalcaemia, with the levels needed to be effective actually being deleterious to the cow’s health as they prevent the production of PTH and may trigger hypocalcaemia.

Hypomagnesaemia

Pregnant and lactating cows are more prone to hypomagnesaemia due to the extra routes by which the magnesium can be lost via the milk and the placenta to the foetus. Magnesium is a major intracellular cation necessary for enzymatic reactions vital to every metabolic pathway, and extracellular magnesium is needed for nerve conduction and muscle function.

Once levels are below 0.8mmol/L (Goff, 2006) then the cow is susceptible to the effect of hypomagnesaemia, which may present as hypocalcaemia for reasons discussed before. Therefore, this may only be diagnosed by running blood biochemistry. Clinical signs such as recumbency, convulsions and nystagmus will ensue once blood levels are sub 0.4mmol/L (Goff, 2006).

Magnesium cannot be mobilised from the bone, so the cow obtains nearly all its magnesium from the diet. Absorption from the GIT is affected by many things, such as potassium and ammonia levels in the rumen. Magnesium absorption from the rumen is dependent on the concentration of magnesium in solution in the rumen fluid and the integrity of the magnesium transport mechanism, which is a sodium-linked active transport process (Martens and Gabel, 1986).

Treatment protocols have remained unchanged over the past 30-plus years, and relatively little has been published on this recently. The author suspects this is due to the decreasing clinical incidence as cows tend to have their diets supplemented and intraruminal magnesium boluses are used. Hypomagnesaemia is an emergency and the cow needs to raise the cerebrospinal fluid (CSF) magnesium levels as soon as possible; up to 30 per cent of cases die despite treatment (Littledike and Cox, 1979), with the extent of haemorrhage, oedema, vascular lesions and deposition of calcium salts affecting prognosis.

Magnesium can be given intravenously, with several preparations available. It is important to never give a 25 per cent magnesium sulphate solution intravenously as this will cause death. The common practice is to use a bottle of 40 per cent calcium and remove one-quarter of it, replacing it with one-quarter 25 per cent magnesium sulphate. After thorough mixing, the solution is given intravenously over 10 to 15 minutes. The rest of the magnesium solution can then be given subcutaneously. Radostits et al (2007) recommend giving 100ml of 10 per cent magnesium sulphate as a short-term treatment, but this is not curative.

Traditionally, cows have been sedated before treatment to ensure the veterinarian’s safety and to minimise the effects of the grass staggers. Xylazine is the only licensed product. It is used to induce muscle relaxation, and reduce the respiratory and heart rates. Xylazine induces a transient change in the conductivity of the cardiac muscle, which may oppose the effects of hypomagnesaemia, reducing the current required to cause contraction in the heart (Todd and Horvath, 1970).

Once the animal is standing it must then eat to provide magnesium that can be absorbed from the rumen and meet the needs of the animal. The farmer needs to provide feed such as haylage, which is both palatable and magnesium rich. The cow must continue to take in magnesium every day so food given with both a high magnesium content and a high dry matter content are essential. Magnesium can be driven across the rumen wall when concentrations exceed 4mmol/L (Ram et al, 1998), with the diet needing to supply at least 3.5g/kg dry matter. This passive process is not affected by the levels of potassium in the rumen so supplementing the cows with magnesium boluses is recommended.

Hypophosphataemia

Phosphorus deficiency is commonly known as the “happy downer” or “creeper” cow syndrome. Phosphorus is needed for the release of ATP and so these cows present as weak and in extreme

cases there may be haemolysis. The problem is often secondary to hypocalcaemia, caused by a combination of lack of feed intake and because the PTH released due to the hypocalcaemia causes phosphorus to be excreted via the kidney and saliva (Figure 2). Intestinal inactivity means much of the phosphorus is not reabsorbed and is instead excreted via the faeces. Phosphorus is also excreted via the udder. Insulin triggers an intracellular shift of phosphorus so giving a cow dextrose intravenously may precipitate a deficiency (Grunberg, 2014). A blood measurement is accurate of an acute phosphorus deficiency, but not a chronic one (Grunberg, 2014).

Administration of calcium generally causes resumption of GIT activity, allowing absorption of dietary phosphorus (Goff, 1998) and preventing the urinary loss by decreasing PTH levels.

Goff (2006) suggests oral treatment with 50g of phosphorus, or 6g phosphorus given intravenously, with Grunberg (2014) suggesting 7g to 12g per cow intravenously. Be wary of far exceeding this dose as the phosphorus may precipitate with calcium or magnesium, thus decreasing their concentrations. Excessive phosphorus will be excreted by the kidneys so for a long- term benefit, oral phosphorus must also be given.

Cheng et al (1998) suggest administering phosphorus orally has longer lasting effects, with Grunberg (2014) suggesting doses of 150g to 230g per cow being sufficient to replace the intracellular phosphorus lost. This dose may need to be repeated eight to 12 hours later. The danger is giving phosphorus orally may prevent the uptake of calcium and precipitate magnesium in the rumen, thus reducing its availability for absorption. Dosing phosphorus little and often may be the best course of action.

The pathogenesis in some cases is not clearly understood, but by ensuring the cow does not suffer hypocalcaemia and has sufficient food intake, the chances of hypophosphataemia are greatly reduced.

It is important to follow up these cases in the days post-treatment by contacting the farmer. The longer a cow is recumbent, the less likely it is to rise. In time these cows may become a welfare issue needing daily care, so the farmer needs to be aware of this. Take a blood sample from the cow before treatment so biochemistry can be run if the animal is non-responsive. This will definitively tell you if a metabolic issue is present and, if so, whether the treatment plan needs altering.

After the animal has been treated specifically and has shown signs of recovery, it is important to realise the role of food intake post-treatment in preventing recurrence.

The animal needs to be able to take in sufficient calcium, magnesium, phosphorus and energy for its needs. Food should be plentiful, palatable, and the animal should feel safe to eat it. Farmers need to avoid pushing their cows further and allow their homeostatic mechanisms to be re-established by taking precautions such as reducing the milk taken from the animal.

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Figure 1. A cow suffering from hypocalcaemia. Note the position of its neck.

IMAGE: N J Bell, RVC.

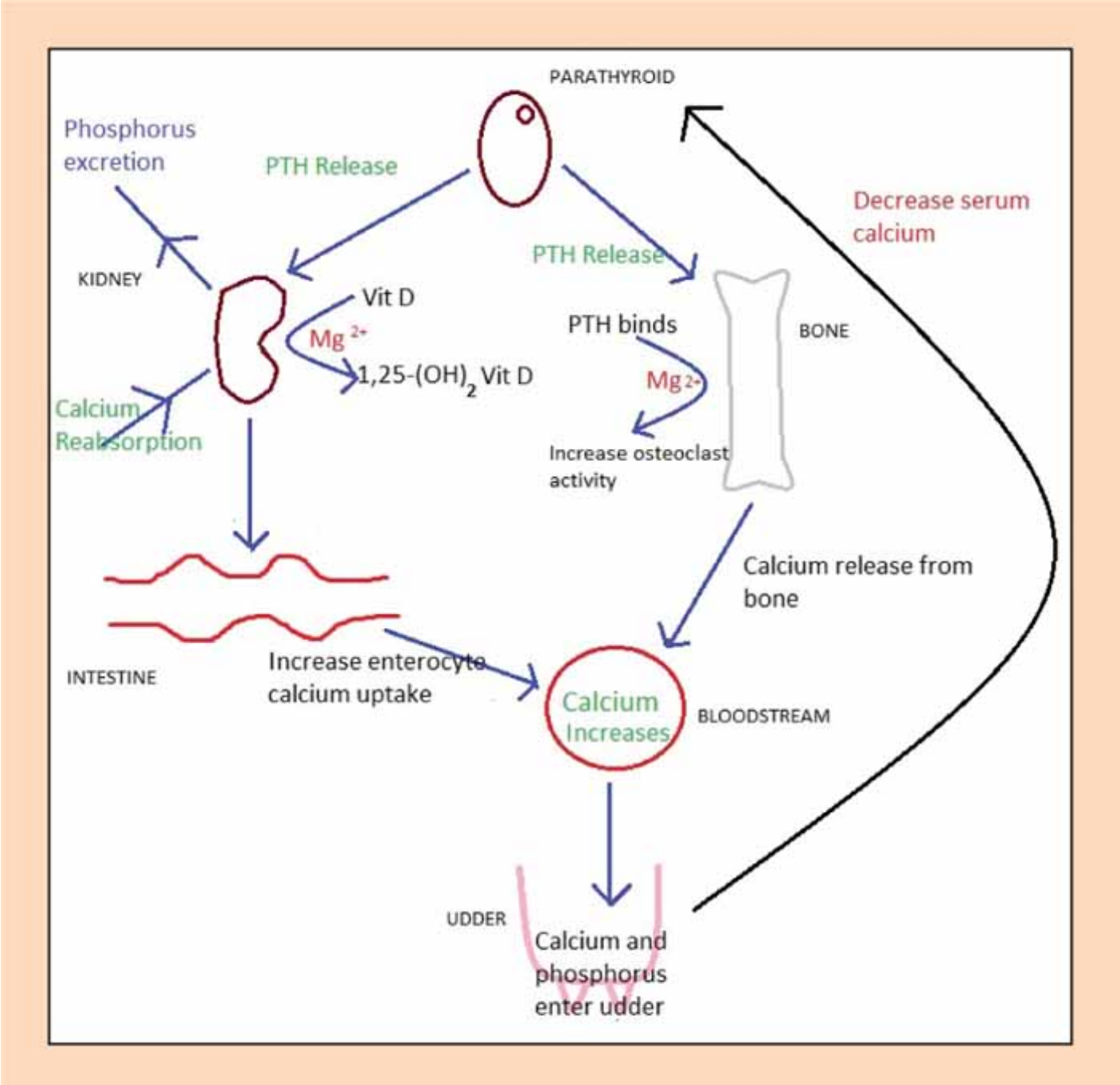

Figure 2. Calcium homeostasis in response to falling calcium levels.