METABOLIC DISEASES IN SHEEP – DEVELOPMENTS AND TREATMENT

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LOUISE SILK discusses the most common of these diseases in sheep, looking at the associated risk factors, as well as the available novel therapies

THE three most common metabolic diseases of sheep, namely hypocalcaemia, hypomagnesaemia and pregnancy toxaemia, occur in and around the periparturient period and are caused by the failure of animals to have their nutritional requirements met during late pregnancy and/ or early lactation (Brozos et al, 2011).

This is usually linked to a decreased supply of the nutrient (caused by lack of nutrient availability or reduced intakes) combined with increased demand for the nutrient.

This article will describe later developments in the treatment of these three diseases as well as any husbandry changes necessary to prevent further cases within a flock. The success of a treatment will depend firstly on an accurate diagnosis. Hypocalcaemia and pregnancy toxaemia often coexist and differential diagnosis between the two diseases is difficult on a farm level (Brozos et al, 2011). A summary of the clinical presentations of the three diseases is given in [Table 1](#).

The only true way to accurately diagnose these conditions is by the measurement of calcium, magnesium and â-hydroxybutyrate levels in the blood. In practice, however, the clinician will tend to rely on clinical signs and a good history, followed by assessment of response to treatment, to obtain the correct diagnosis.

Hypocalcaemia

Hypocalcaemia condition can occur at any stage from a few weeks before lambing, or until several weeks after, and is the result of a mismatch between supply and demand of calcium in the ewe. It is around lambing that the maternal calcium demands are maximal due to fetal skeletal mineralisation in the last few weeks of pregnancy, followed by the onset of milk production in early lactation. While this condition is predominantly seen pre-lambing, calcium concentration in ewes' milk is almost double that in cows' milk (Moreno-Rojas et al, 1994), and Polychroniadou et al (1985) found production can increase to more than three litres of milk per day in some individuals, resulting in a high and prolonged demand for calcium during the first stage of lactation.

• Risk factors associated with hypocalcaemia

• Dietary intakes of calcium are extremely important when it comes to meeting calcium demands and any interruption to this, through incorrect feeding or husbandry changes, could precipitate an outbreak of hypocalcaemia in a group of periparturient ewes.

• In the spring in particular, rapidly growing grass and lush pastures have low calcium levels and this coincides with maximal calcium demands on the ewe.

• The calcium: phosphate ratio is also important in a pregnant ewe and an excess of phosphates on the pasture will reduce the available calcium and predispose to hypocalcaemia.

• Cereal-based diets are low in calcium (Brozos, 2011).

• Feeds containing high amounts of oxalates, which precipitate the formation of non-absorbent compounds with calcium, will reduce the calcium availability in the diet. Such feeds include beets, rhubarb and sorrel.

• Irrespective of dietary intakes, ewes are unable to absorb enough dietary calcium through the gut wall in late pregnancy and early lactation to completely meet their high demands, resulting in the mobilisation of skeletal stores to make up the deficit. If too much calcium is delivered in the diet during the pregnancy, however, this will inhibit calcium mobilisation in late pregnancy and early lactation, which can precipitate clinical hypocalcaemia.

• The mobilisation of skeletal calcium in late gestation and early lactation results in a skeletal deficit in calcium that must be replaced. Ewes respond to periods of calcium deficiency by increasing absorption from the diet to a high level when calcium is again plentiful. Failure to provide adequate nutrition to allow the ewes to replenish the reserves when absorption is high in later lactation will result in poor skeletal reserves for the following year and subsequent problems.

• Treatment of hypocalcaemia

Treatment of acute cases of this condition involves calcium administration to make up the deficit, combined with a reduction in the factors that predispose to disease, which include stressors such as handling and housing. As with all metabolic disease, the earlier the problem is diagnosed, the greater the chance of a successful outcome.

Scott (1995) describes uncomplicated hypocalcaemia that will respond within minutes to intravenous calcium in the form of 30ml to 60ml of 20 per cent calcium borogluconate solution. The solution should be warmed to 35°C to 40°C prior to administration and must be given slowly over five to seven minutes, while the animal's heart rate is continually monitored. Administration should be stopped at once if there is evidence of arrhythmia (Brozos et al, 2011).

A further 60ml divided over two separate sites should be given subcutaneously and may be repeated 24 hours later to reduce the likelihood of relapse. An alternative solution of calcium, magnesium and glucose monohydrate solution can be administered subcutaneously. If no response is evident, the diagnosis should be reevaluated (Roger, 2009).

Mild hypomagnesaemia will increase the risk of and severity of hypocalcaemia by reducing the secretion and tissue sensitivity to parathyroid hormone, which controls calcium up regulation ([Figure 1]). Treatment in cases complicated by subclinical hypomagnesaemia (such as cases in early lactation) should, therefore, include administration of magnesium subcutaneously. Furthermore, if pregnancy toxaemia is suspected alongside the hypocalcaemia, the calcium should only be administered by the subcutaneous route, as calcium can be fatal to animals with poor liver function.

Hypomagnesaemia

Hypomagnesaemia can occur in ewes two to eight weeks post-lambing, particularly in animals rearing multiple lambs, and is most often seen in animals grazing young, rapidly growing pastures, especially during the spring.

This is because rapidly growing spring grass is relatively low in magnesium, which must be taken in from the diet every day – there is very little magnesium stored in the body to draw from in times of shortage. Clinical cases of hypomagnesaemia tend to occur as a result of poor dietary intakes or a reduction in the ability of the animal to absorb the magnesium available.

• **Risk factors associated with hypomagnesaemia**

• High potassium levels at pasture (due to K fertiliser usage) may predispose to hypomagnesaemia by having an inhibitory effect on the absorption of magnesium from the rumen.

• Low sodium levels found in spring grass result in increased secretion of the hormone aldosterone, which increases potassium secretion by the salivary glands, increasing the potassium in the fore-stomachs and then the circulation. This increased potassium level has an inhibitory

effect on magnesium absorption in the gut.

• Lush pasture also has a high moisture content, which results in rapid passage of forage through the GI tract and decreased time for magnesium absorption.

• Feeding rapidly fermentable carbohydrates in the diet (for example, grains and so on) can increase the production of short chain fatty acids, resulting in a drop in rumen pH that changes the rumen papillae and decreases magnesium absorption.

• **Treatment of hypomagnesaemia**

Unfortunately, the most common clinical sign of hypomagnesaemia is sudden death, therefore the opportunities for treatment of affected animals are sometimes few and far between. The success rate for treatment of this condition is also low. However, if caught in time, administration of magnesium and calcium salts, separately or as a combined solution, is the recommended treatment (Foster, 2007) – 10ml of a solution containing four to five per cent magnesium hypophosphite and 20 per cent calcium borogluconate should be given by slow intravenous injection, followed by 40ml to 50ml of 25 per cent magnesium sulphate solution given subcutaneously.

Too rapid administration of magnesium solutions can result in cardiac dysfunction and respiratory failure (Foster et al, 2007). Sedation may be necessary to control tetany and it is important to handle affected animals quietly to prevent aggravation of their condition (Foster et al, 2007). Some animals will recover rapidly following treatment, but unfortunately for animals that relapse or remain recumbent for several hours after treatment, the prognosis is very poor (Foster et al, 2007).

If clinical cases of hypomagnesaemia are diagnosed within a flock, it is prudent to supplement magnesium in the remaining animals via bolus administration or in feed or water supplementation, to prevent further cases. The dose rate advised by the National Research Council 1985 was 7g/animal/day orally of magnesium oxide. In future years, it is worth considering how the predisposing risk factors could be reduced on the affected farm and, if this is not possible, how preventive strategies could be put in place to reduce the incidence of disease.

Options for prevention include improved pasture management, such as top dressing pasture, changes to the timing of potassium fertilisation strategies, feeding concentrates supplemented with magnesium to "at risk" groups or bolus administration.

Ovine pregnancy toxaemia

While the full aetiology is not fully understood, pregnancy toxaemia is essentially a severe form of ketosis characterised by low circulating blood glucose and high ketone body levels (Andrews, 1997). The disease usually occurs in animals carrying multiple foetuses, but can be seen in single-

bearing ewes that have undergone considerable nutritional stress. This disease tends to occur in the last six weeks of pregnancy, as this is the time when nutritional intakes are limited and fetal growth, and therefore energy demands, on the ewe are maximal.

A mismatch in energy supply and demand at this time results in a net energy deficiency. At first, the body uses up glycogen stores in the liver to produce glucose, but then switches to mobilising increasing amounts of body fat reserves to make up the deficit, resulting in the production of ketone bodies. Ketone bodies can then be used as an alternative energy supply to glucose, but as ketone levels increase in the body and glucose levels fall, clinical signs (described in **Box 1**) become evident. These clinical signs are primarily the result of the brain tissue's preference for glucose and inability to use ketones for metabolism.

• Risk factors associated with pregnancy toxaemia

Predisposing factors for the onset of disease include a dietary change, even if that is of improved nutritional quality, as this may result in temporary inappetence; severe weather conditions or disease in the ewes – such as a high parasite burden or a broken mouth – that may compromise nutrition. Both thin and fat ewes can be affected as thin ewes have less body reserve to draw on, while over-fat ewes tend to become inappetent as lambing approaches and they have less abdominal capacity for food.

• Treatment of pregnancy toxaemia

Treatment of this disease, therefore, primarily revolves around increasing glucose levels in the body. Success of therapy relies on the ability to raise cerebrospinal fluid glucose concentrations, before irreversible changes occur in the brain (Sargison, 2008). This can be achieved in several ways: by administering gluconeogenic substances, by prompting the body into restarting its own gluconeogenic processes and by removing the energy drains on the body.

It is important, as with all the metabolic diseases discussed in this article, to identify the problem during the early stages of disease to increase the chances of a successful outcome. The aim of treating this disease is to return the animal to its normal appetite as quickly as possible and early detection of a problem is critical to achieving this outcome.

Unfortunately, the prognosis for ewes with pregnancy toxaemia is very difficult to establish – animals with apparently very severe signs will sometimes recover, while those with mild illness may rapidly deteriorate (Andrews, 1997). Death of the fetuses within the ewe will almost always result in a poor outcome, despite treatment. The ability to establish this prior to treatment may aid the decision of whether to attempt treatment or euthanise the animal. Sargison (2008) reports that despite a full course of treatment only one third of affected animals are likely to survive.

• Administer gluconeogenic substances

– Intravenous administration of 50ml to 100ml of a 40 per cent dextrose solution that can be repeated after a few hours.

– Oral administration of 50ml of propylene glycol or glycerol. This can be repeated twice daily and continued for several days as the ewe's appetite gradually returns.

– Oral administration of rehydration therapy would also be indicated.

– Offer palatable, energy rich, high-density feedstuffs and clean water.

• Prompt the body to restart its own gluconeogenic pathways/ improve use of glucose within the body

– Intramuscular insulin injections in the form of 20 IU to 40 IU/animal daily, every two days until recovery, of protamine zinc insulin have been tried to aid cellular uptake of glucose as an adjunct to the energy treatments described above (Rook, 2000).

– Vitamin B injections and transfaunation with healthy rumen liquor to ensure availability of glucose for energy metabolism and stimulate appetite.

– Recombinant bovine somatotrophin (RBS), administered in a slow release formulation at a rate of 160mg/kg BW subcutaneously, is advocated by some clinicians to improve the efficiency of glucose and ketone body usage at cellular level (although the mechanisms are incompletely understood) and thus reduce the mortality rates of affected ewes and their fetuses. In a study undertaken by Scott et al in 1998, a higher recovery rate was found in ewes (and their lambs) treated for pregnancy toxaemia with RBS alongside oral dextrose and electrolyte solution, but the effects were not statistically significant.

– Corticosteroids given by injection, in the form of 16mg of dexamethasone or betamethasone, are thought to assist gluconeogenesis and improve appetite.

• Remove energy drains on the body

– Corticosteroids (as above) can be used to induce abortion in affected ewes from 135 days of gestation. The effectiveness of this strategy may be extremely variable as plasma cortisol levels are already very high in clinically affected animals. Plasma cortisol levels are also raised in clinical cases of hypocalcaemia, a condition that commonly occurs alongside pregnancy toxaemia. In both conditions, the levels of stress endured by the animal are sufficient to result in an increased concentration of circulating endogenous cortisol, thus desensitising the individual to the drug treatment given (Andrews, 1997).

– An injection of 0.375mg of cloprostenol alongside the cortisol injection may increase the efficacy

of the induction treatment (Brozos, 2011).

– An alternative to induced abortion would be to remove the fetuses by elective caesarean section. This strategy needs to be attempted early in the course of disease and while it may result in improved survival rates in the ewe, it will often result in the death of the lambs if not carried out within a couple of days of the natural due date.

– The ewe should be brought inside or provided with sufficient shelter to reduce the energy demands on its already stressed body. It should also be removed from the flock to a pen to eliminate any competition for food and water.

Summary

With the prognosis of this disease relatively poor despite treatment, it is essential we consider how to prevent clinical cases occurring for the healthy ewes within the flock in the current and future seasons. Good management is key when it comes to preventing this disease and strategies such as ensuring the ewes are in the correct body condition at all stages of the annual cycle, as well as maintaining good nutrition and minimising stressful events in the weeks running up to lambing, are essential.

Unfortunately, despite best efforts, the prognosis for individuals affected by the three diseases discussed above is often poor and euthanasia on welfare grounds should always be considered an option on a case by case basis.

The most important point to remember when it comes to metabolic diseases in sheep is they are readily preventable through good animal husbandry and flock management. If treatment is necessary, the outcome is more likely to be successful if the correct diagnosis is made and treatment is instigated early in the course of disease.

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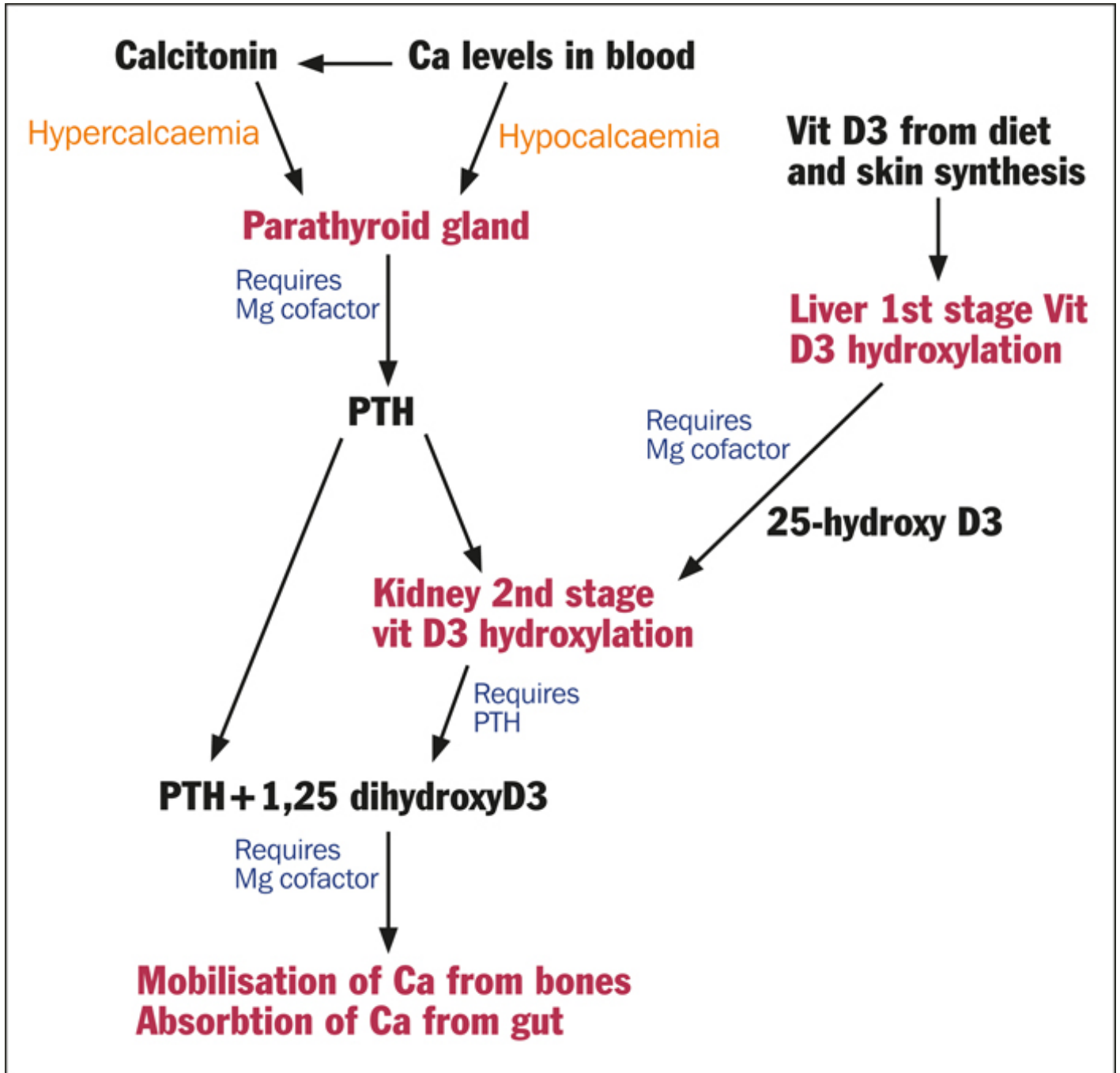
Figure 1. Diagram of the role of magnesium and parathyroid hormone in calcium mobilisation (Kelly, 1988).

The success of treatment depends on an accurate diagnosis.

Ovine pregnancy toxaemia
Separation from the rest of the flock
Dull and depressed
Poor body condition and udder development, but increased abdominal distension
Lack of menace response
Wide-based stance and loss of proprioceptive reflexes
Star-gazing, increased salivation, head pressing and bruxism can be seen
Progresses to recumbency with legs extended out behind the ewe within 24-48 hours
Urine staining at perineum
Muscle fasiculations around the face
Hypocalcaemia
Isolation from the flock
Slow to rise, progressing to recumbency within two to six hours
Cold ears, constipation
Disorientation and panting, progressing to head on the ground in an unresponsive stupor
Passive reflux may result in ruminal contents appearing around nose and mouth
Hypomagnesaemia
Sudden death
Sometimes proceeded by lateral recumbency and fitting

TABLE 1. Clinical signs (Scott, 1995).