Magnesium: some lesser-known effects of derangements

Alice Fraser, of SVS Laboratories in Hamilton, discusses two cases that highlight the diversity and complexity of Mg functions.

ONE OF THE divalent, predominantly intracellular cations, magnesium (Mg) is a cofactor in more than 300 enzymatic reactions in mammals (including ATP-driven energy providers) and is essential for normal cellular function and replication.

Mg has important roles in electrolyte balance and impulse generation/propagation in excitable tissues. Mg homeostasis is maintained by the balance between intake/absorption and renal excretion. There is no direct hormonal control in response to Mg levels, although intestinal absorption and renal excretion are affected by several hormones (eg PTH, ADH and aldosterone) (Stockham and Scott, 2008).

Younger animals are able to mobilise Mg from bone stores, but this facility decreases with age, such that adult mammals depend on a balance between GI tract absorption of Mg and its renal excretion (Goff, 2014).

Measurement of Mg, based on laboratory measurement of total serum Mg, includes protein-bound (about 30%), Mg-free ions (about 55%), plus phosphate and citrate complexes. Hence, knowledge of serum albumin level is essential in interpretation, together with a good clinical and nutritional history in order to make relevant correlations. Unlike other electrolytes, such as potassium, acid-base disturbances have little effect on the distribution of serum Mg.

Significant research has been done on the prevention of Mg derangements in the dairy cow, whose huge changes in mineral demands during the transition phase necessitate accurate and strategic supplementation. Owing to the role of Mg in calcium mobilisation, routine nutritional management of Mg in the prevention of both hypocalcaemia (milk fever) and clinical/acute hypomagnesaemia (grass staggers) is now commonplace. As a result, the less well-recognised subclinical/chronic hypomagnesaemia occurs infrequently. On the flipside, there is the potential for over-supplementation, causing effects related to hypermagnesaemia.

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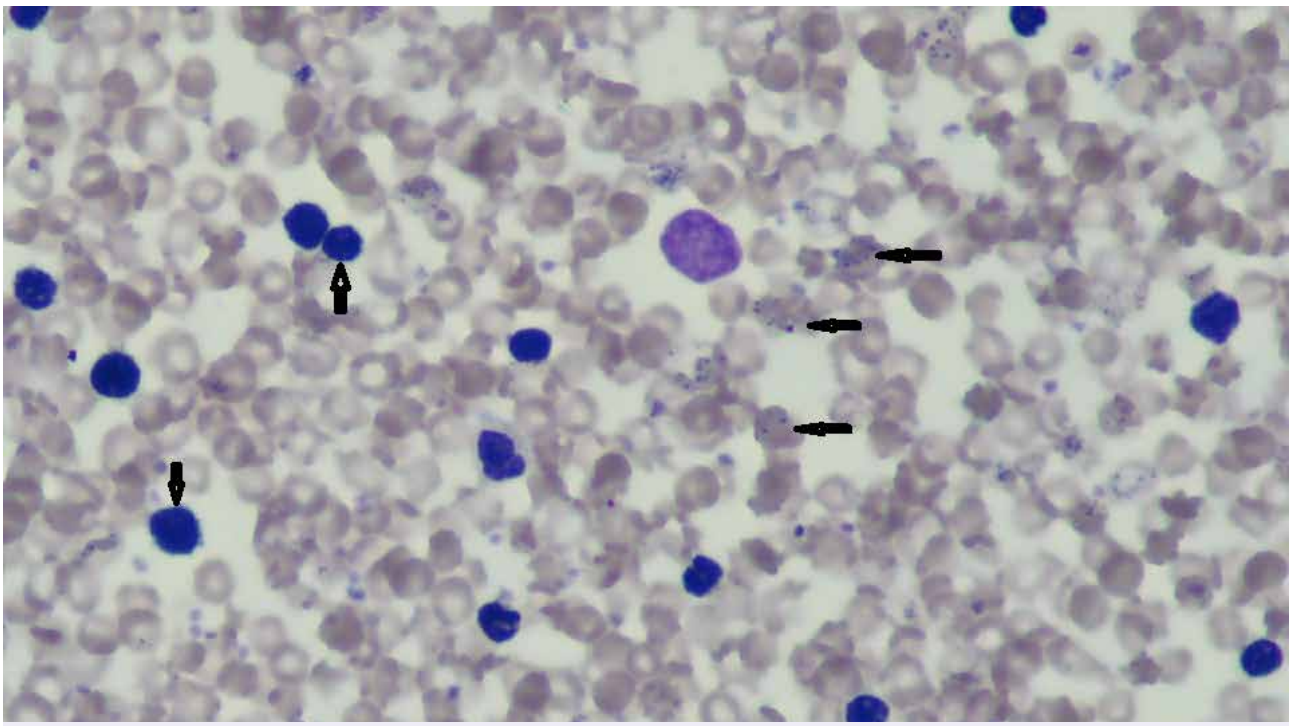


FIGURE 1: Vertical arrows: nucleated RBCs (metarubricytes). Horizontal arrows: RBC stippling.

CASE 1: SUBCLINICAL/CHRONIC HYPOMAGNESAEMIA

This is manifested as an anaemia, hence its colloquial name 'Taranaki anaemia', and also called 'leather bag' due to the often concomitant udder oedema (Anon., 1975). With the high incidence of theileria cases in cattle in the Waikato region, blood samples from anaemic cows are usually submitted for the more cost-effective theileria screen (as below). In this case, a blood sample was submitted from a two-year-old Ayrshire dairy cow who had been milking well until about five days before veterinary examination, at which point she was clinically anaemic but did not show the udder oedema. As theileriosis had been previously diagnosed on the farm, samples were submitted for a theileria screen. Results:

HCT: 0.19L/L (ref. range 0.24-0.40).
Hb: 60g/L (85-130g/L).
Theileria: None seen on blood smear.

On examination of the blood smear, there was RBC stippling with increased nucleated RBCs.

As a result of the unusual RBC nuclear morphology, serum Mg was tested. It was decreased at 0.22mmol/L (ref. range Mg: 0.49-1.15mmol/L), with a normal albumin of 35g/L (ref. range 25-40g/L). The cows had not received in-feed Mg supplementation during the dry or peak lactation period (but there was no history of potassium fertiliser applications, which could interfere with Mg GI tract absorption). However, there were no recent cases on the farm of either grass staggers or milk fever. This likely reflected the chronic marginally negative Mg balance, as the serum and CSF concentrations are supported by Mg from other tissue pools during a gradual Mg deficiency (a shift from intracellular to extracellular compartments), compared with acute decreases in serum Mg that manifest as acute neurological signs.

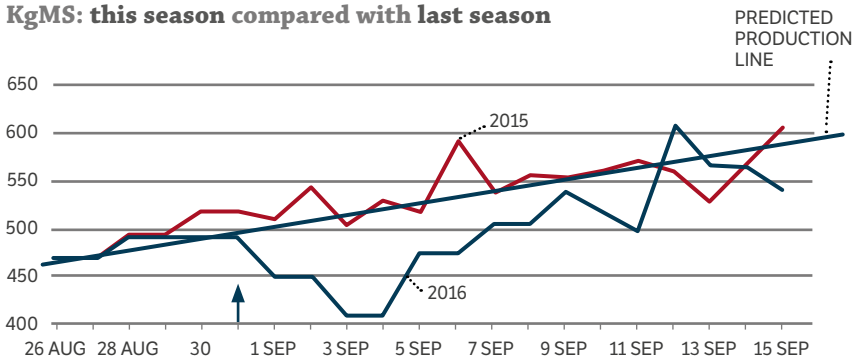
Little is published about the effect of chronically low Mg on the RBCs of cattle, and most affiliated erythrocyte/Mg research has been carried out in humans, particularly in geriatric patients with Mg-poor diets (although, comparative pathology aside, this dairy cow was only two years old). Since Mg is predominantly an intracellular cation, research has been done on erythrocyte Mg levels as a more accurate indicator of Mg deficiency (Ulger et al., 2010).

Studies in people and laboratory animals show that Mg enters the erythrocytes only during erythropoiesis and is lost progressively during the life of RBC in the peripheral blood. In rats on an Mg-deficient diet, the bone marrow is able to produce erythrocytes with normal Mg concentrations, but as the cells age in an Mg-deficient environment there is a shortened RBC survival and development of erythrocyte ultra-structural membrane defects. However, it is clear from the literature (or lack thereof) that, as yet, we do not fully understand the pathogenesis of chronic Mg deficiency anaemia in the dairy cow.

GRAPH 1:

Daily production (26 August – 15 September 2016)

KgMS: this season compared with last season



Graph indicating marked drop in milk solids production at onset of feeding of over-supplemented MgO (arrow).

AS WITH ALL THINGS HOMEOSTATIC, **EXCESS MG CAN BE AS PROBLEMATIC AS DEFICIENCY.**

CASE 2: THE EFFECT OF EXCESS SUPPLEMENTATION – HYPERMAGNESAEMIA

As with all things homeostatic, excess Mg can be as problematic as deficiency. We have seen two cases of excess in-feed Mg supplementation in dairy cows during the recent winter and spring.

The most severe case was a feed production error in which a tenfold increase of magnesium oxide (MgO) had been erroneously added to the palm kernel extract feed, such that each cow was receiving 400g/day MgO instead of 40g/day. A large number of cows across the mobs (including milkers, colostrum cows and springers) were showing clinical signs, including recumbency (three cows, of which two died), abdominal pain, gut stasis, bloat and green scour. The milder cases were lethargic with green scour.

Graph 1 shows a sharp decrease in milk production from the date of the excess in-feed MgO compared with predicted and usual seasonal farm production levels. Blood samples (serum) for biochemistry from affected (non-recumbent) cows showed eight out of 10 cows had hypermagnesaemia (ranging from 1.28 to 1.61mmol/L, ref. 0.49-1.15mmol/L).

Biochemistry from the more severely affected (milking) downer cows (one and two) revealed Mg concentrations of 2.83 and 3.23mmol/L respectively (ref. 0.49-1.15mmol/L), in the face of albumin values of 43 and 40g/L respectively (ref. 25-40g/L). The minimal increase in albumin in cow one indicated some dehydration, but this level was considered unlikely to account wholly for the disproportionate increase in Mg, particularly since cow two had an even higher serum Mg in the face of albumin within the reference range (albeit the high end of normal). In addition, the cows had a severe hyperphosphataemia (3.86 and 6.08mmol/L), severe metabolic alkalosis and marked chloride losses. Cow two, the more severely affected cow, died.

Treatment consisted of increasing the serum calcium with Calpro and supportive NSAID therapy (Metacam) to the downers. For the non-downer cows, calcium was increased with lime flour on forage, and increased/ad-lib access to fresh pasture was provided. No further deaths ensued.

Hypermagnesaemic metabolic alkalosis has been previously reported in downer dry cows (Orbell, 2015) but there is little in the literature pertaining to lactating cows. Much of the research into the mechanism of ileus has been carried out in the human field. The marked excess in absorbed Mg rapidly acts as a non-specific calcium channel blocker (Lloyd, 1984) in the smooth muscle, before it can be excreted by the kidney, leading to ileus, pooling of chloride with subsequent metabolic alkalosis and dehydration. This further decreases the glomerular filtration rate, perpetuating the poor renal clearance of the excess Mg.

These cases highlight the diversity and complexity of Mg functions and some of the implications when homeostasis is lost through chronic deficiency or acute excess. Information gathering has highlighted that there are still gaps in our understanding of the effects of Mg derangements. In fact, for some time Mg was considered the 'forgotten cation'. VS

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