Iron deficiency anaemia in calves and lambs

Peter Plate, PGCertVetEd MRCVS, Royal Veterinary College, Regional Veterinary Centre – South of England, Stinsford Business Centre, Kingston Maurward College, Dorchester DT2 8PY, pplate@rvc.ac.uk

Abstract

While iron deficiency anaemia is a well recognised condition in piglets its importance for calves and lambs has recently been highlighted. In particular, housed lambs and calves fed on whole milk are prone to subclinical iron deficiency anaemia, with surveys showing prevalence figures from 20 % to more than 50 %. Many studies show reduced daily liveweight gain as a main clinical sign in both species; some also show health issues such as increased incidence risk of pneumonia and diarrhoea in calves and an increase in abomasal bloat risk in lambs. Iron supplementation trials consistently led to higher growth rates pre-weaning and to improved haemotological values. In the UK there are no injectable iron preparations licensed for calves or lambs, but preparations licensed for pigs can be used off label.

Key words: iron – haemoglobin – anaemia – calves – lambs – whole milk

Introduction

While iron deficiency anaemia is a well-established condition in neonatal piglets it has also been identified in calves and lambs for a long time, but more recent research in several countries has led to an increasing awareness of the condition in those species. This article gives an overview of the current knowledge.

Iron in the body and its regulation

Most of the iron in the body is stored in haemoglobin (60-70 %); other storages are haemosiderin (spleen, liver) and myoglobin. Some is transported in blood, bound to transferrin. Apart from its function in transporting oxygen in haemoglobin and storing oxygen in myoglobin it is an essential part of enzymes like peroxidases, catalases and cytochromes and also works as an anti-oxidant. Therefore, iron deficiency is not only associated with anaemia but also with oxidative stress (Rajabian et al. 2017) and a reduced immune response (Gygax et al., 1993). In piglets iron has been shown to directly promote intestinal development, (Pu et al. 2018), brain development (Leyshon et al. 2016) and spacial cognition (Rytych et al. 2012)

Iron homoeostasis is tightly regulated, with hepcidin, a peptide hormone produced in the liver, playing a central role. If the iron concentration in blood increases, or in the presence of inflammatory mediators, hepcidin down-regulates intestinal absorption and leads to more intra-cellular storage of iron in the reticuloendothelial system, monocytes and macrophages. This is important for two reasons:

- Excessive free iron and haeme (in haemolytic situations) can generate toxic free radicals, resulting in tissue damage
- Iron is also a nutrient for pathogens, and limitation of iron is a well-established mechanism to control infections. In another context this is strategy is well known in dry cows producing lactoferrin in the udder.

As a unique feature for iron, its regulation (via hepcidin) is not only influenced by its concentration but also by the host's infection status – hepcidin gene expression is upregulated in the presence of pathogens and cytokines, limiting the iron supply to bacteria and protozoa but also the potential for viruses to replicate (Drakesmith and Prentice 2012).

Iron content of whole milk and iron demand

Neonatal piglets, calves, lambs and kids are born with a finite iron store, leading to a rapid decline in haemoglobin levels in the first one to two weeks. Cows' milk contains around 0.5 mg of iron per kg (Ziegler 2011), while the iron demand of a six week old pre-weaned dairy calf is stated at around 135 mg (NRC 2001) – it is obvious that whole milk cannot supply the iron demand, and with more recent recommendations to increase the intensity of milk feeding and later weaning, this discrepancy may be exacerbated. Almost all commercial milk replacers are therefore supplemented with around 100 mg/kg dry matter of iron. A similar discrepancy is known in piglets and lambs. However, outdoor reared pigs root in the soil from an early age which contains high amounts of iron, so that the problem here is especially prominent in indoor reared pigs, although iron supplementation has been shown to be beneficial in outdoor reared piglets as well (Szabo and Bilkei 2002) but is practically more difficult.

Iron deficiency anaemia shows haematologically as a microcytotic, hypochromic anaemia (Joerling and Doll 2019).

Definitions and symptoms of subclinical iron deficiency anaemia in calves and lambs and diagnostic tools

While clinical anaemia is readily diagnosed following a physical examination, subclinical anaemia often remains un-noticed. Reduced growth rates have been established in calves (Allan et al. 2020) and lambs (Crilly and Plate 2022) in intervention studies. A higher frequency of neonatal disease like diarrhoea and pneumonia in calves (Bünger et al. 1986) and a higher frequency of abomasal bloat in lambs has also been described (Vatn and Torsteinbø 2000).

In contrast, Lorenz et al. (2021) found iron supplementation at birth a risk factor for neonatal diarrhoea in calves, but did not distinguish between oral and parenteral supplementation. This apparent paradox is discussed below.

While serum iron concentration and ferritin have been discussed as potential parameters to evaluate the iron status, both have methodological difficulties. Serum iron shows considerable circadian variation and is also affected by inflammatory processes (it is also part of haptoglobin), while ferritin is species specific and therefore not available in routine veterinary diagnostics. The correlation between serum iron and haemoglobin is weak (r=0.35, Doll, 2018). The haemoglobin concentration, however, is most frequently used to define anaemia, although its suitability has also been questioned (Joerling and Doll 2019). It is the basis of most animal welfare legislation, e.g. regarding veal calves. There is, however, no generally agreed reference range for haemoglobin levels in calves, different authors and sources state different lower levels to define anaemia. EU and UK law (Welfare of Farmed Animals Regulations 2007) and the UK Welfare Code (DEFRA 2013) both require diets leading to a minimum of 4.5 mmol/l Hb, while German regulation (as a group average) and RSPCA accreditation require 6 mmol/l.

Prevalence of iron deficiency anaemia

Calves

Doll (2018) surveyed 128 calves on 23 German farms, 18 dairies and 5 beef suckler herds and found the majority of dairy calves (sampled up to three months of age) to be anaemic when using the cut-off point of 6 mmol/l Hb (Fig. 1). Only seven of the 18 dairy farms surveyed fed their calves on whole milk, only one dairy gave oral iron supplementation at birth.

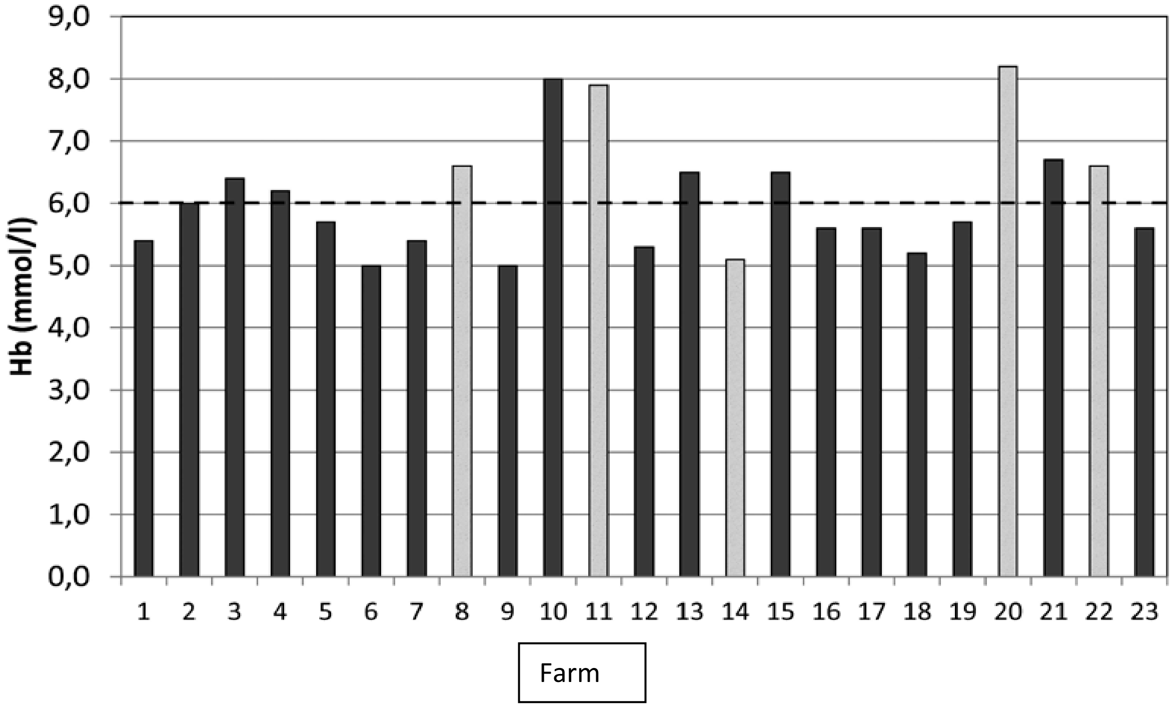

Fig 1: Survey of 128 calves on 23 German farms, lightly shaded farms are beef suckler farms, displayed values are means per individual farm (Doll, 2018)

In a separate German study Joerling and Doll (2019) found 8 out of 40 calves (20 %) of different feeding regimes anaemic, using a cut-off point of 5.6 mmol/l.

In the UK, Allan et al. (2020) found 40 out of 117 untreated dairy calves (34 %), all fed on whole milk, with Hb levels of under 5.6 mmol/l (9 g/dl) at around six weeks of age.

Lambs

Green et al. (1997) found 25 % of untreated lambs with a haemoglobin concentration below 8.7 g/dl (5.4 mmol/l). Crilly and Plate (2022) looked at haemoglobin levels in lambs and goat kids under different feeding and management strategies and found 45 % of goat kids and 80 % of lambs anaemic (Hb below 8 g/dl – 5 mmol/l) when reared indoors on maternal milk, while outdoor and/or milk replacer fed animals showed a lower percentage of anaemia (Table 1).

Table 1: Mean haemoglobin levels and % animals below 8 mg/dl Hb of lambs and kids reared under different feeding and management strategies. Each group contains 20 animals. (Crilly and Plate 2022)

Group	Species	Environment	Diet	Mean [Hb] (g/dl)	95% CI	% [Hb] <Ref. Range
1	Goat	Indoors	Milk replacer	9.65	9.07–10.23	5%
2	Goat	Indoors	Suckling	7.73	7.21–8.24	45%
3	Sheep	Indoors	Milk replacer	10.13	9.37–10.89	5%
4	Sheep	Indoors	Suckling	6.8	6.14–7.46	80%
5	Sheep	Outdoors	Suckling	9.08	8.49–9.66	20%

Effects of iron supplementation

Calves

Iron deficiency anaemia in calves and supplementation trials have been described since the middle of the 20th century (Hibbs et al. 1963).

Bünger et al. (1986) carried out extensive research in the former East Germany in the 1980s. In one study 195 male calves from four source farms on rearing unit were divided into three groups – no iron substitution, daily oral and twice parenteral iron substitution. Calves were sourced and treated from about three weeks of age, the trial period lasted eight weeks. Iron-substituted calves had significantly lower treatment rates both for diarrhoea and pneumonia. The authors point out that the effect on disease rates was observed before the anaemia was corrected, suggesting a direct immunological effect of iron.

Heidarpour Bami et al. (2008) supplemented neonatal dairy calves in Iran with 1000 mg iron as iron dextrane parenterally and found 40g difference in daily liveweight gain (320 v 280 g) in supplemented calves, but no effects on calf health.

Allan et al. (2020) carried out a supplementation trial on six UK dairy farms feeding whole milk. Of 237 enrolled calves 120 were injected with 1000 mg iron as iron dextrane on day 2-10. Between enrolment and six weeks injected calves grew on average 78 g per day faster than control calves. The effect did not continue from 6 to 12 weeks, so although the 0-12 week daily liveweight gain was significantly different, this is purely due to the difference in the first six weeks.

Haemoglobin levels were measured at enrolment and at six weeks – control calves dropped on average by 12.1 g/l while supplemented ones gained on average 3.4 g/l, making the difference at 6 weeks 15.3 g/l. 40 animals in the control group and six in the supplemented group were considered anaemic at six weeks (Hb under 90 g/l). Health data was not collected in this study. The growth response to iron supplementation on individual farms in this study was not linked to the haemoglobin concentrations of untreated animals, so although the effect was consistent between farms its magnitude currently cannot be predicted.

Lorenz et al. (2021), in contradiction to earlier studies, investigated risk factors for neonatal diarrhoea on Bavarian dairy farms and found "iron supplementation after birth" a significant factor. They compared 59 farms with a diarrhoea problem with 18 control farms, so this was a retrospective analysis, not an intervention trial, and the exact timing and way of supplementation (oral versus parenteral) was not stated on the farms. While there is the possibility that problem farms were more likely to supplement, other preventive measures were not carried out at higher frequency. The authors discuss the possibility that in some circumstances iron may favour pathogens, as iron depletion (e.g. via intracellular storage, triggered by hepcidin) is a recognised pathway of the unspecific defence mechanism (Drakesmith and Prentice 2012). However, they state that further research is needed to validate the advantages and disadvantages of iron supplementation and different timings and means of administration.

Lambs

Green et al. (1997) found housed lambs treated with 300 mg iron as iron dextran 1 kg heavier at weaning than untreated controls, with a trend in lower mortality. Haematological parameters at 12 and 24 days of age were also significantly improved. Vatn and Torsteinbø (2000) in Norway found reduced serum iron concentrations in housed lambs which developed abomasal bloat, compared to those who did not develop the condition, and subsequently significantly reduced the incidence by supplementing iron (300 mg of iron as iron dextrane subcutaneously in the first week of life). Supplemented animals also had a daily liveweight gain increase by 17 grams in the first spring and an overall average liveweight gain increase of 7 grams per day from birth to slaughter.

Crilly and Plate (2022) also found increased liveweight gains in treated lambs in the UK, but the difference to control animals was only significant for twin lambs, the overall difference here was 23 grams per day. Again, a significant difference in haemoglobin levels was observed at one month of age.

Key points and conclusions for practitioners:

Iron deficiency anaemia is common in housed calves and lambs fed on whole milk, and studies on the effects of iron supplementation on growth rates and haemoglobin levels favour supplementation. Some studies have shown health benefits (reduced incidence of pneumonia and diarrhoea in calves, reduced incidence of abomasal bloat in lambs), but some did not determine any health or mortality effect, and one retrospective analysis of risk factors for neonatal calf diarrhoea questions iron supplementation. Further studies are needed to establish optimum timing and means of administration. In practice, iron deficiency anaemia should be a risk factor to be considered when investigating the conditions described, and haemoglobin levels at 2-6 weeks of age may indicate the severity of a problem. Unlike in other European countries, there is no licensed parenteral iron injection for calves and lambs in the UK, so if this route of administration is chosen any treatment will have to be given off label, using a preparation licensed for pigs. The recent literature is consistent in using 1000 mg iron for calves and 300 mg for lambs once soon after birth, so these doses can be recommended. Increased iron supplementation of dams during pregnancy has not shown any significant effects in pigs or cattle.

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CPD questions:

1. The main reservoir of iron in the body is
   a. The bone marrow
   b. The liver
   c. The spleen
   d. Haemoglobin in red blood cells
   e. Myoglobin in muscle cells

2. Iron deficiency anaemia is generated mainly due to
   a. Iron deficiency in the dam during pregnancy
   b. The low iron content of whole milk
   c. The low iron content of starter pellets
   d. Insufficient iron content in milk replacers

3. The prevalence of iron deficiency anaemia is highest in pre-weaned calves and lambs which are
   a. Outdoor reared on maternal milk
   b. Outdoor reared on milk replacer
   c. Indoor reared on maternal milk
   d. Indoor reared on milk replacer

4. Symptoms associated with iron deficiency anaemia are
   a. Lameness
   b. Reduced growth rates
   c. Increased incidence of diarrhoea
   d. Increased incidence of pneumonia
   e. Increased incidence of abomasal bloat in lambs

5. Which of the following is true about iron regulation in the body?
   a. There is no regulation, iron status depends solely on supply
   b. Iron uptake is regulated depending solely on the body's iron status
   c. Iron uptake is regulated depending on the body's iron status and infectious/inflammatory status
   d. Iron status is regulated mainly by iron excretion via urine

6. Iron deficiency anaemia can be prevented by
   a. Nutritionally supplementing the dams during pregnancy

b. Injecting veterinary iron preparations at 1000 mg for calves and 300 mg for lambs in the first week of life
c. Injecting veterinary iron preparations to the dams in late pregnancy to increase the iron content of colostrum
d. Feeding iron supplemented milk replacer
e. Offering starter pellets from day 1

7. Reducing the iron availability in the body by reducing the uptake and increasing intracellular storage is a mechanism which is
    a. An evolutionary defect leading to iron deficiency anaemia
    b. A recognised strategy in the defence against pathogens
    c. A protection mechanism against iron toxicity
    d. Of no known relevance to the body