The relationship between trace elements status and health in calves

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SUMMARY

This paper reviews the present knowledge on the relationship between selected trace element nutrition of cows or calves and the health in calves. Trace elements deficiencies can lead to specific diseases relating to specific nutritional functions; myopathy for selenium, goitre or thyroid dysfunction for iodine, anaemia for iron. Insufficient status of copper, zinc and mainly selenium can lead to a decrease of defences, mediated in the newborn calves by a low transfer of immunoglobulin from the colostrum, and in older calves by a depressed acquisition of immunity. These effects on immunity have more often been demonstrated experimentally on biological markers of immune defences than on the incidence of diseases. However, large scale survey can evidence an increased risk of diseases, mainly diarrhoea, in calves immune defences than on the incidence of diseases. However, large scale surveys may evidence an increased risk of diseases, mainly diarrhoea, in calves. Moderate deficiencies mainly result in non-specific clinical signs, some of them being specific enough to provide a diagnostic relative to one trace-element deficiency. Such specific effects are usually observed only with strong deficiencies. Moderate deficiencies mainly result in non-specific disorders, decreasing growth or affecting health, mainly via depressed immune defences.

Introduction

The objective of this paper is to review information concerning the influence of trace elements nutrition of cows and calves on the health of calves. In calves, the effects of trace element deficiencies can be observed in newborn animals, whose trace-elements stores are in relation with maternal nutrition. Indeed, the trace elements status of newborn calves depends on maternal transfer via the placenta, the colostrum or the milk. For this reason, maternal nutrition can be considered as a major determinant of the status of young calves, affecting directly their health. Deficiencies can also be observed in older calves but they are then due to an insufficient supply in their diet.

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Evidencing the effects of trace element deficiencies on animals can be made via experiments, mainly based on the effects of trace element supplementation, or via large scale surveys in commercial herds. In a recent retrospective study [13], based on a data set of analysis in 2080 dairy and beef cattle herds in France and Belgium, copper, zinc and selenium status of herds were investigated as risk factors for health problems in calves. Available data were:

- health problems in dams and calves in the herd,
- individual trace-element status of adult cows assessed by plasma copper, plasma zinc and erythrocyte glutathione peroxidase activity. Herd statuses were classified as deficient, marginal, low-adequate or high-adequate, based on the lower tercile of individual values. Table I shows the main relationships observed in this survey between trace-element status of adult cows and major health disorders of calves, calculated as odd-ratios comparing case herds and control (without health abnormalities) herds. This table shows that all three trace elements can be involved as risk factors for health problems in calves.

Mots clés : Veau, oligo-éléments, cuivre, zinc, sélénium, iode, fer.
Copper status

Copper deficiency can be either primary, due to low copper content in forage, or secondary to an excess of antagonists, mainly sulphur and molybdenum. In France and Belgium, most forage has low concentrations of copper and molybdenum [25, 44] so that copper deficiencies are mainly primary.

In the neonatal calf, copper mainly originates from liver stores accumulated during pregnancy. The foetus has priority upon the dam organism [19], so that only a strong deficiency can result in low liver stores in the neonate. A maternal diet with half the usual copper recommendation, results in calves with lower liver stores than in dams fed with a normal copper status as assessed by plasma copper [12]. In spite of this priority, deficient copper herd status had no modification of sickness in calves. WARD et al [48] showed in 30 days old calves that copper deficiency tended to negatively affect serum immunoglobulin M and antibodies against Pasteurella hemolytica but not rhinotracheitis virus after exposure to aerosols of these pathogens. However, copper supplementation did not reduce clinical signs. Humoral response was also addressed by GENGLBACH and SPEARS [17]: after injection of porcine erythrocytes to 98 days old dairy calves receiving strongly copper deficient milk without or with a copper supplementation, they observed a trend toward higher serum specific antibodies in copper-supplemented calves.

In spite of the foetus priority, and because milk only contains a low amount of copper (0.15 mg/l [58]), copper deficiency can arise in calves after a few weeks. The implication of copper deficiency in inflammatory response involves ceruloplasmin, which is an acute-phase protein. Ceruloplasmin oxidises ferrous iron to ferric iron, facilitating incorporation of iron to ferritin [52] and inhibiting microbe iron uptake. Moreover, another copper dependent enzyme, superoxide dismutase, has an antioxidant function that can be important during phagocytose [3]. After an experimental challenge with bovine herpesvirus in heifers, plasma ceruloplasmin remained low in heifers made copper deficient by a molybdenum supplementation, but increased in control heifers [3], which could lead to decreased defences of copper-deficient animals. Bactericidal activity of neutrophils has been shown to be higher in copper than molybden (a copper antagonist) supplemented calves [18], but no modification of superoxide dismutase activity in neutrophils was observed in this experiment. Moreover, copper-supplemented calves exhibited higher rectal temperature and lower feed intake than molybden-supplemented calves after an intratracheal administration of Pasteurella hemolytica. This could be interpreted as a better response in copper-supplemented calves, but could also be seen as potentially detrimental for performance.

Copper deficiency can also negatively affect humoral response. STABEL et al [55] showed in 30 days old calves that copper deficiency tended to negatively affect serum immunoglobulin M and antibodies against Pasteurella hemolytica but not rhinotracheitis virus after exposure to aerosols of these pathogens. However, copper supplementation did not reduce clinical signs. Humoral response was also addressed by GENGLBACH and SPEARS [17]: after injection of porcine erythrocytes to 98 days old dairy calves receiving strongly copper deficient milk without or with a copper supplementation, they observed a trend toward higher serum specific antibodies in copper-supplemented calves.

Zinc status

Zinc deficiency is primary, contents in forages being very variable but less systematically deficient than those of copper in France (Table II). The main negative interaction affecting zinc absorption is excess of copper, which is not usual in ruminant nutrition. Zinc is efficiently transferred from the
than the recommended amount in the diets (Table II).

Very low: contents of some forages are under 10 times less than the usual recommendation for ruminants (28). Zinc stores are relatively less available than copper stores [29], making the risk of deficiency greater.

In the survey of ENJALBERT et al. [13], marginal or deficient zinc statuses were associated with increased mortinatality or increased frequency of diarrhoea.

Zinc-deficient calves with a genetic abnormality preventing zinc absorption have lowered lymphocyte activities after 3 weeks of age, when they become zinc-deficient [45]. In genetically normal animals, KINCAID et al. [28], supplementing milk-consuming calves with different sources and amount of zinc, did not observe any effect on different in vitro measurements of immune function. However, their control diet contained 60 mg of zinc per kg of dry matter, which is over the usual recommendation for ruminants (Table II). ENGLE et al. [12] demonstrated that zinc supplementation of weaned zinc-deficient calves (17 mg of zinc per kg of dry matter) improved cell-mediated immune response to phytohemagglutinin. PRASAD and KUNDU [48] found, after an antigenic challenge performed at 35 and 65 days of age, that calves receiving zinc-supplemented milk had stronger immunoglobulin G and immunoglobulin M responses than unsupplemented or copper-supplemented calves. Both these experiments related to calf acquired immunity, which is not involved in perinatal mortality or neonatal diarrhoea, but a similar decrease of antibody synthesis in cows could have impaired colostral concentration of immunoglobulins.

In spite of these experimental data, limited evidence of practical relationship between zinc status and immune response has been published, so that SPEARS [54] outlined that, as a whole, studies on the effects of marginal zinc deficiency in ruminants do not carry definitive conclusions regarding immunity.

### Selenium status

Selenium deficiency is primary, contents of forages being very low: contents of some forages are under 10 times less than the recommended amount in the diets (Table II).

In the survey of ENJALBERT et al. [14], selenium status showed a stronger relationship with calf health than did copper or zinc. Selenium deficiency was associated with perinatal mortality, neonatal diarrhoea, vaccination failure, heart failure, and was very strongly associated with myopathy. Marginal selenium status of dams also was associated, to a lesser extent, with these health disorders.

The relationship between selenium deficiency and muscular degeneration, including myocardial necrosis, has been known for a long time [40]. This disorder mainly occurs when calves turn out to pasture, due to the high content of polyunsaturated fatty acids in this feedstuff, which promotes free-radical damage in the tissues. Selenium is a major component of an antioxidant enzyme, the glutathione peroxidase, which catalyses the reduction of hydroperoxides to hydroxyacids, preventing tissue damage. Only strong deficiencies are classically involved in this trouble, so that this disease is unusual in dairy calves.

Placental transfer of selenium to the foetus is important in cows, and the foetus has higher selenium concentrations in liver than the dam [1, 30, 59]. Due to this efficient transfer, supplementation of deficient dams during late gestation improves selenium status of calves at least until 6 weeks of age [1]. Selenium supplementation of cows also can increase the selenium content of colostrum [1]. In an experiment on deficient beef cows, ENJALBERT et al. [15] showed that a 15 days prepartum selenium supplementation of cows efficiently improved erythrocyte glutathione peroxidase activity in 15 days old calves. Erythrocyte glutathione peroxidase is a long term indicator of selenium status, due to the several months life span of erythrocytes. The improvement increased linearly with the interval between the beginning of supplementation and calving when 13 or 32.5 mg of selenium were supplemented daily. This improvement was more important and did not depend on this interval when 45.5 mg of selenium were supplemented daily. In the same experiment, it was shown that maternal supplementation after calving resulted in lower effects on calf status than prepartum supplementation, suggesting that milk transfer is less efficient than placental transfer.

Selenium is strongly involved in immunological defences [16, 49, 61], which explains the relationship observed by ENJALBERT et al. [13] between selenium status and diarrhoea or vaccination failure. Depressed immune defences can occur, even with marginal deficiencies. The concentration of immunoglobulins in the colostrum can be improved

<table>
<thead>
<tr>
<th>Copper</th>
<th>Zinc</th>
<th>Selenium</th>
<th>Iodine</th>
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<tbody>
<tr>
<td>12 - 18</td>
<td>21 - 30</td>
<td>0.3</td>
<td>0.4-0.5</td>
</tr>
<tr>
<td>11</td>
<td>43 - 55</td>
<td>0.3</td>
<td>0.4 - 0.6</td>
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Table II: Dietary recommendations, range of concentrations in forages and maximum allowed content of copper, zinc, selenium and iodine for late pregnancy dairy cows [25, 34, 41, 51].
by selenium supplementation of deficient beef cows: distribution of a selenium supplemented (120 mg/kg) free-access mineral complement during the second half of gestation improved immunoglobulin G concentration in the colostrum and in the serum of calves [57]. This result was confirmed later by AWADEH et al. [6] with a shorter supplementation (90 days): compared to 20 mg of selenium /kg of mineral supplement, 60 or 120 mg resulted in higher colostrum immunoglobulin G and higher plasma immunoglobulin G in both cows and their calves. Colostrum concentration of immunoglobulin M was not significantly affected in these experiments, and serum concentration of immunoglobulin M in calves was improved by selenium supplementation in the experiment of AWADEH et al. [6] but not in the experiment of SWECKER et al. [57]. In some experiments, the effects of selenium supplementation have been studied together with those of vitamin E, another major biological antioxidant. LACETERA et al. [31] observed a higher colostrum yield associated with a higher secretion of total immunoglobulins in cows which received two parenteral administrations of vitamin E + selenium 3 and 1.5 weeks before calving. However, the concentration of immunoglobulins in the plasma of calves was not affected by the supplementation, and neither supplemented nor unsupplemented calves exhibited diarrhoea or pneumonia, preventing any comparison of sickness incidence.

Additionally, the concentration of selenium in the colostrum can modulate the absorption of immunoglobulin G by the newborn calf, as demonstrated by KAMADA et al. [26] by addition of 1 to 3 mg of selenium / kg of colostrum. However, this supplementation is to be considered as supra-nutritional: 1 mg of selenium / kg of colostrum is far beyond the natural concentration (around 0.05 mg/l, [1]), and far beyond the maximal incorporation level allowed by the regulation of feed additives in the European Union (Table II).

In the survey of ENJALBERT et al. [13], vaccination failure in selenium deficient herds could have been due to a lower synthesis of immunoglobulin in dams. Actually, PANOUSIS et al. [42] found a significantly improved production of antibodies after a vaccination against Escherichia coli in selenium-injected cows than in control cows or cows injected with only vitamin E. Such a low synthesis of immunoglobulin in deficient cows can be expected to result in a lower protection of newborn calves against the risk of diarrhoea, because immunoglobulin G originating from colostral transfer can be transferred from serum back into the gut contributing to the protection of intestinal mucosa, as demonstrated by PARRENO et al. [43] after oral inoculation with bovine rotavirus.

Finally, the effect of selenium status on health of calves is not limited to effects on neonatal calves mediated by colostral transfer of maternal immunoglobulin. YOSHITAKA et al. [62] explored both non-specific and specific immunity in 5-weeks old calves born from control cows or cows supplemented with selenium. Non-specific immunity was affected since the oxidative reactions associated with phagocytosis in neutrophils happened earlier in calves from selenium-supplemented cows than in controls. Defective function of neutrophils in selenium deficient animals are due to a lack of glutathione peroxidase activity, this enzyme preventing the destruction of neutrophils by their own free radicals produced for killing phagocyted bacteria [4]. In the experiment of YOSHITAKA et al. [62], the response of lymphocytes to a stimulation with concanavalin was significantly higher in calves from supplemented cows. These changes in non-specific and specific immune responses were associated with higher serum selenium concentrations.

The effect of selenium status on specific acquired immunity has been explored in several other experiments. POLLOCK et al. [47] demonstrated that selenium supplementation in 7 months old calves increased the lymphocyte response to an immunisation with hemocyanin, in interaction with vitamin E. After an intranasal inoculation of weaned calves with the virus of infectious bovine rhinotracheitis, the serum immunoglobulin M concentration was higher in selenium supplemented than in selenium depleted calves, and this change was associated with higher blood and plasma glutathione peroxidase activities [50]. STABEL et al. [56] also observed on weaned calves a slightly higher total immunoglobulin M response in selenium supplemented calves after inoculation with Pasteurella hemolytica, but lower anti-P. hemolytica titers.

In these two experiments [50, 56], selenium supplementation did not result in any effect on the monitored clinical sign which was rectal temperature. Similarly, in a survey on housed calves, PHILIPPO et al. [46] found that selenium status of calves assessed by blood glutathione peroxidase activity was not associated with the incidence of pneumonia, and found that a selenium treatment of newborn calves failed to decrease the incidence of pneumonia. However, HALL [23] explained that the selenium supplementation in the experiment of PHILIPPO et al. [46] was not sufficient to obtain a normal selenium status in deficient herds, and that some herds in the survey had an initial normal status, so that lack of effect could be expected. Moreover, he outlined his own field observations of decreased clinical cases of scours and pneumonia in selenium-supplemented herds. Similarly, BONOMI et al. [9] reported that switching from 0.2 to 0.3 or 0.4 mg of selenium per kg of milk for veal calves positively affected health status, strengthening resistance to respiratory and digestive diseases.

Perinatal mortality has often been described as the "weak calf syndrome", and was strongly associated with selenium deficiency in the survey of ENJALBERT et al. [13]. However the relationship between selenium and a high incidence of perinatal mortality remains unclear, since several supplementation studies failed to show a reduction of the weak calf syndrome [37].

Beyond single effects of selenium, AWADEH et al. [6] showed that a free-choice mineral supplement with 120 mg of selenium /kg improved the triiodothyronin / thyroxin ratio in newborn calves, outlining the involvement of selenium in the deiodination of thyroxin to triiodothyronin [5]. AWADEH et al. [6] concluded that, due this interaction with thyroid hormones, selenium intake could influence heat transfer from brown adipose tissue, and be important in weak calf disorder, in relation with iodine.
Iodine status

Although some goitrogens may be found in ruminant diets, thyroid dysfunction in ruminants is mainly associated with iodine deficiency, and most forage in France cannot meet the recommendations (Table II). The transfer of iodine from the cow to the calf both involves elemental iodine and maternal thyroxin [24].

The main effects of iodine deficiency in pregnant cows are abortion and goitre in newborn calves, which can be observed in iodine deficient areas when an adequate supplementation is not used. McCOY et al. [35] demonstrated that calves born from iodine deficient (0,13 mg of iodine / kg of dietary dry matter) but selenium adequate heifers had a moderate or severe thyroid hyperplasia but were born clinically normal, without stillbirth or weak calf syndrome. In a survey on 357 calves stillborn or dead soon after birth, abnormal thyroid gland was associated with uninfiliated lungs and a high risk of pneumonia [53]. However, these abnormalities were also associated with lower selenium concentration in the kidneys than in calves with a normal thyroid, so that the relative involvements of iodine and selenium deficiency on these abnormalities were unclear. Iodine deficiency without selenium deficiency results in a 10 to 12 fold increase of thyroid-deiodinase activity in the thyroid gland, which could maintain circulating triiodothyronin at a normal level [63].

Limited literature data indicate that iodine deficiency could be involved in colostral immunoglobulin dysfunction and neonatal diarrhoea [37].

Excess iodine has been shown to have immunosuppressive effects in calves [22]: a daily supplementation with 50 mg of iodine or more for 6 months on calves weighing 120 kg at the beginning of the experiment decreased both phagocytic activity of white blood cells and persistency of antigens. More recently, a series of experiments showed a depressed plasma immunoglobulin G concentration in lambs from ewes access- ing a free-choice mineral block, and this decreased concentra- tion was due to a decreased immunoglobulin absorption [7, 11]. This effect was showed to be due to iodine excess when 40 mg where given daily, compared to a 0.7 mg requirement [8], and to around 15 mg as the maximum allowed by the european legislation (Table II) for a late-pregnancy ewe.

Iron status

Iron deficiency in calves is due to the low amount of iron in milk resulting in a depletion of stores when milk is the main feedstuff for a long time. The usual production of veal calves strives to produce white meat, obtained via a controlled anaemia in animals. In France, the regulation on veal calves well-being [2] indicates that mean hemoglobinemia has to be maintained over 4.5 mmol/litre of blood (7.2 g/100 ml). GYGAX et al. [21], showed that iron deficiency (10 mg of iron / kg of milk replacer, compared to 50) in veal calves altered the number of neutrophils with phagocytic capacity, cell-mediated immunity and blood serum immunoglobulin G concentration. Blood haemoglobin decreased under 7.2 g/100 ml after 7 weeks of experiment, and negative effects were only observed later, which suggests that the level of anaemia allowed by the legislation prevents negative health effects.

General discussion

Most experiments described above for studying the effects of trace element deficiencies on calves have been performed on beef cows and calves rather than in dairy herds. Actually, trace element deficiencies are much more likely to occur in beef herds due to a less systematic complementation. It is very likely that the effects of trace element status are identical in dairy calves to those observed in beef calves, but it is obvious that marginal or deficient status are less frequent in dairy herds.

Most experiments studying the effects of a trace-mineral supplementation have demonstrated effects on the biological markers of immune status, but most experiments failed to evidence effects on clinical signs of diseases. Several reasons could explain this apparent discrepancy:

- in most conditions, forages contain an insufficient amount of several trace elements (see table II), so that when the mineral supplementation is absent of insufficient, ani- mals suffer from several deficiencies. Supplementing only one trace element in such conditions cannot be expected to result in a significant improvement of the health of animals. Unfortunately, authors experimenting the effects of one trace element usually do not indicate the detailed mineral status of animals before and after supplementation.

Large scale surveys can overcome these limits of experi- mental data, because the large number of animals and herds makes it possible to evidence moderate modifications of sickness incidence, and because multifactorial analysis makes it possible to take into account in the same database the effects of several trace elements.

Management in practice

Managing the risks due to trace elements deficiencies in calves first needs an assessment of the trace mineral status of the herds, and because the trace element status of the dams strongly influences the mineral status of the newborn and colostral transfer of passive immunity, this assessment must be performed on the cows. Two ways of assessment are possible:

- the determination of the dietary supply; if the mineral supplement does not provide all or nearly all the trace ele- ments that are required by the animals, a knowledge on the
trace elements contents of other feedstuffs will be necessary. Because of very large variations according to the soil, table values are not reliable in a particular herd.

- an assessment of the trace elements status of the animals based on blood analysis [20, 27], which can reveal both primary and secondary deficiencies.

When the status of dams is inadequate, or when the dietary supply is under recommendations, the status needs to be rapidly restored by oral or parenteral supplementation [32, 36], especially in late pregnancy cows, and then maintained by a regular supplementation. Oversupplementation and imbalances must be avoided due to the risk of negative interactions between trace elements, or the risk of direct negative effects.

Conclusions

Inadequate trace-mineral nutrition of either cows or their calves is a risk factor for poor health in calves. Among involved trace-minerals, selenium plays a major role, but copper, zinc and iodine deficiencies also can affect the health of calves. For copper, zinc and selenium deficiencies, impaired colostral transfer of immunoglobulin is the major reason of this decreased resistance of calves, mainly resulting in perinatal mortality and diarrhea. Additionally, trace element deficiencies can also impair acquired immunity in older calves.

References


