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Ketosis, Milk Fever and Grass Tetany: The 'Deadly Trio' Among Metabolic Diseases of Lactating Dairy Cows

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Abstract

Metabolic disorders are due to faulty feeding of the animals especially during stress conditions like lactation and parturition. Common metabolic diseases seen in lactating dairy cows in India are ketosis, milk fever and grass tetany. These three diseases cause severe economic losses to the farmers and are referred to as 'the deadly trio' of metabolic diseases.

This paper focuses on the etiology, causative factors, mechanism by which the disease occurs, clinical signs, biochemical changes, treatment and control, with special reference to the nutritional strategies adopted for prevention. Adoption of nutritional interventions such as phase feeding strategy, adequate dietary cation anion deficit (DCAD) and 'holding off pasture' in lactating dairy cows will help to prevent the incidence to ketosis, milk fever and grass tetany, respectively.

Keywords: Metabolic diseases, Ketosis, Milk Fever, Grass Tetany

1. Introduction

Metabolic disease refers to a group of conditions caused by deficiencies of certain essential nutrients resulting in disturbance of the animal's normal metabolic processes (Mulligan and Doherty, 2008). These conditions are multi factorial and commonly occur at times of high physiological stress or demand for these nutrients, with late pregnancy and early lactation being the key times (Block, 2010). The metabolic diseases in lactating dairy cows include ketosis, milk fever, grass tetany and fat cow syndrome. Among these, the most commonly seen ones in India are ketosis, milk fever and grass tetany (Bakshi *et al*., 2017). The annual economic losses due to these three metabolic disorders in cattle in India were Rs. 9.57 crores, in the year 2016 (DAHD, 2017). Since the economic losses caused to dairy farmers are huge, they are referred to as 'the deadly trio' of metabolic diseases.

Although the development of these diseases are largely related to production or management factors, the pathogenesis of each disease is primarily related to alterations in metabolism, viz., an increased demand for a specific nutrient that has become deficient under certain conditions. These three diseases are augmented by management practices directed toward improving and increasing production and are hence also referred to as production diseases (Block, 2010). However, they are also metabolic diseases because management of the animal is directed at production, which at its peak, is beyond the capacity of that animal's metabolic reserves to sustain a particular nutrient at physiologic concentrations (Roche *et al*., 2013).

The signs of these diseases can overlap and look similar and it is not uncommon for more than one of these diseases to occur at the same time further complicating the picture. For this reason it is important to understand the causes of these diseases, because the prevention and treatment are different. Moreover, it should be borne in mind that, all these diseases can produce an acute, temporary, but potentially fatal deficiency (Makkar, 2016). Hence, making suitable corrections in the diet of cows during the period from late pregnancy to peak lactation is crucial in preventing these diseases (Bakshi, *et al*., 2017).

2. Review of literature

The characteristic features of these three diseases are discussed hereunder:

2.1. Ketosis

Ketosis or 'acetonaemia' refers to an increase in 'ketone bodies' in blood of dairy cows until they spill over into the urine and (or) milk (Littledike *et al*., 1980). In dairy cows ketosis is a lactation disorder usually associated with intense milk production and negative energy balance (Huzzey *et al*., 2011). Ketosis is essentially a deficit in energy manifested as a fall in blood glucose at a time when the animal has an increased energy demand such as late pregnancy and early lactation (Janovic *et al*., 2011). If the animal cannot or does not eat enough to meet demand their demand they use other resources for energy, notably body fat and this leads to the production of large amounts of chemical byproducts called ketone bodies (Knegsel, *et al*., 2014).

2.1.1. Etiology

Knegsel *et al*. (2014) opined that the etiology of ketosis can be broadly classified into four:

2.1.1.1. Inadequate nutrient supply especially energy:

Milk production peaks four to six weeks after parturition, while dry matter intake (DMI) peaks only 8-12 weeks after parturition. Hence there is a time lag of 6 to 8 weeks, during which period the cow will be in negative energy balance (Janovic *et al*., 2011).

2.1.1.2. Excessive fat mobilisation:

To meet the increased energy demand, consequent on lactation, body fat will be mobilised, manifested as drop in body weight during the first two to three months of lactation (Koltes and Spurloc, 2011). The end product of fat metabolism is acetate. For energy to be produced from acetate, it has to combine with oxaloacetate and form citrate and then enter the tricarboxylic (TCA)/ citric acid cycle (Bakshi *et al*., 2017).

2.1.1.3. Oxaloacetate deficiency

However, the oxaloacetate required for the utilisation of acetate, should come from carbohydrate metabolism (Maynard *et al*., 1985). The end product of carbohydrate metabolism is pyruvate, which is further metabolised to oxaloacetate and finally to glucose in the gluconeogenetic pathway (McDonald *et al*., 1995). If the animal is not getting adequate amount of soluble carbohydrate, oxaloacetate will not be produced in the body (Block 2010). Concentrate feeds like grains, oil cakes and compounded cattle feed are rich in soluble carbohydrate. That is, if adequate concentrate feed is not provided; or if the animal is not able to consume concentrate feed, as much as is required, deficiency of oxaloacetate can result (Knegsel, *et al*., 2014).

2.1.1.4. Hormone deficiency/ excess

1. Decreased production of adreno-cortico-tropic hormone (ACTH) leads to decreased cortisol: Cortisol provides the body with glucose by tapping into protein stores via gluconeogenesis in the liver. Absence of glucose can lead to subsequent oxaloacetate deficiency (Huzzey *et al*., 2011).

2. Decreased insulin and increased somatotropin production: Insulin acts by regulating ketone-body metabolism at three sites, viz., adipose tissue, the liver itself and the periphery. In adipose tissue lipolysis is inhibited and re-esterification is enhanced with consequent decrease of fatty acid release to the liver. In the liver, insulin increases the simultaneous formation of malonyl coenzyme A, which in turn inhibits the acylcarnitine transferase system and thereby decreases the transport of fatty acids into mitochondria and hence fatty acid oxidation and ketogenesis are decreased. In the periphery, insulin also has a small stimulatory effect on extrahepatic ketone body utilization. The net result of all these is that in the presence of adequate amounts of insulin, ketogenesis is decreased and vice versa (Huzzey *et al*., 2011).

Huderson *et al*. (2011) observed that somatotropin or growth hormone, has little effect in the presence of insulin, but can enhance ketogenesis in insulin deficiency, although the mechanism is unknown.

2.1.2. Pathogenesis:

In response to negative energy balance and low serum concentration of glucose, the cows will mobilise adipose tissue with consequent increase in serum concentrations of non esterified fatty acids (Leblanc, 2010). Moreover, there will be deficiency of oxaloacetate caused by carbohydrate deficiency, as mentioned above, as a result of which the Acetyl CoA produced in body (from fat or from acetate) cannot enter Kreb cycle (McArt *et al*., 2013a). Therefore, by an alternate pathway the Acetyl CoA molecules condense among themselves, get converted into ketone bodies resulting in ketonemia (presence of ketone bodies in blood) and ultimately ketonuria (presence of ketone bodies in urine). The characteristic clinical signs of ketosis are due to hypoglycaemia and hyperketonaemia, meaning, increase in ketone bodies in blood (McArt *et al*., 2013b).

2.1.2.1. Types of ketosis:

According to Duffield (2009), depending upon the presence or absence of rise in body temperature, there are two types of ketosis: viz:

1. Primary: where there is no rise in temperature
2. Secondary: where there can be rise in temperature

Examples for secondary ketosis are diseases like mastitis, metritis, displaced abomasum, indigestion, ROP, nephritis, TRP (hardware disease) and extended milk fever, all of which can result in decreased feed intake and subsequent ketosis (Leblanc, 2010).

2.1.3. Clinical signs

Janovic *et al*. (2011) observed that there are two forms for the disease, based upon the characteristic clinical manifestations: viz:

2.1.3.1. Wasting Form:

1. The animal first shows signs of loss of appetite
2. The animal picks at her feed and leaves behind some grain
3. The disease progresses to the animal leaving most of the grain and some of the silage to the stage of:
4. Eating only small amounts of hay and preferring to eat bedding
5. Further the ketosis develops, greater is the chance of development of perverted appetite
6. Milk production decreases and in severe cases decreases drastically
7. Mild cases may appear as if, the “cow is not doing well”
8. There will be woody appearance (loss of cutaneous elasticity due to loss of subcutaneous fat)
9. There will be sweet odour of ketone bodies in breath and milk (Leblanc, 2010).

2.1.3.2. Nervous form:

In some cases there may be nervous symptoms also, referred to as “nervous form of ketosis”.
The symptoms include:

1. Walking in circles
2. Crossing of legs
3. Head pushing and
4. Aimless movements (Leblanc, 2010).

2.1.4. Biochemical changes

The disease usually occurs before 6 to 8 weeks post partum. The incidence peaks when the cows approach peak lactation. The characteristic features of the disease are:

1. Decrease in blood glucose, from the normal 50 to 60 mg per 100 ml to as low as 25 mg per 100 ml (Leblanc, 2010; Chapinal *et al*., 2011; McArt *et al*. 2013a & b).

2. Increased ketone bodies in blood, milk and urine is observed before the onset of clinical signs (from the normal 10 mg/ ml to as high as 50 mg/ 100 ml in blood) as reported by Duffield (2009), Leblanc (2010), Chapinal *et al*. (2011) and McArt *et al*. (2013a & b).

3. Increase in free fatty acids and triacyl glycerols in plasma (Chapinal *et al*., 2011; Huzzey *et al*., 2011; McArt *et al*. 2013a & b).

4. Decrease in liver glycogen (Chapinal *et al*., 2011 and Larsen and Kristensen, 2012).

5. Increase in liver lipid content which can lead to fatty liver and subsequent liver damage (Chapinal *et al*., 2011; Koltes and Spurloc 20111).

6. Decrease in the concentration of plasma gluconeogenic amino acids and increase in the concentration of ketogenic amino acids (Preynat *et al*., 2009; Chapinal *et al*., 2011; Larson *et al*., 2012; Amrutkar *et al*., 2016).

2.1.4.1. Ketone bodies: Chapinal *et al*., (2011) observed that the ketone bodies are:

1. Acetone – major ketone body in milk, urine & breath
2. Acetoacetate
3. β-hydroxy butyrate - major ketone body in blood (McArt *et al*., 2013a).

The ketone bodies in urine are diagnosed by a simple laboratory test called 'Rotheras' test' (Leblanc, 2010).

2.1.5. Treatment

The treatment has been described in detail by Block (2010), which is as follows:

1. Intravenous injection of glucose

This is oriented towards increasing the amount of glucose available to the cow. Once glucose is available, fat will be mobilised for energy and not for production of ketone bodies (Huzzey *et al*., 2011; Janovic *et al*., 2011; Koltes and Spurloc, 2011).

2. Intramuscular injection of glucocorticoids or ACTH (Huzzey *et al*., 2011).

3. Oral administration of gluconeogenic precursors like sodium propionate or propylene glycol (McArt *et al*., 2012). While sodium propionate is not much palatable, propylene glycol is highly palatable and is largely preferred nowadays.

4. Administration of methionine, a glucogenic amino acid has also been found to be beneficial, even though the benefits are minimal (Preynat *et al*., 2009; Amrutkar *et al*., 2016).

5. Administration of nicotinic acid, an antilipolytic agent @ 12 g per day, has also been found to be beneficial (Garge *et al*., 2012; Bertoni *et al*., 2013).

2.1.6. Prevention

Bakshi et al., (2017) has described the following 'nine point' preventive recommendations for ketosis:

1. Phase feeding strategy: Adoption of the phase feeding strategy is an effective control measure for ketosis. There are three main stages in the lactation cycle of the dairy cow, viz., early lactation (14-100 days), mid lactation (100 to 200 days) and late lactation (200-305 days). The animal should be fed with nutritious feed in such a way as to meet its requirement of the recommended amounts of DM, protein, energy, minerals and vitamins; with the nutritive requirements being the highest in quality and quantity in early lactation followed by mid and late lactation, in descending order.

2. Avoid excessive fattening before calving (Janovic *et al*., 2011; Koltes and Spurloc, 2011; Knegsel *et al*., 2014).

3. Increase the concentrate intake moderately in the late dry period, but as rapidly as possible after calving and then maintain the intake (Block, 2010).

4. Feed at least 1/3rd of the DM as good quality roughage (Leblanc, 2010).

5. Avoid abrupt dietary changes, especially to poor quality feeds (Leblanc, 2010).

6. Avoid feeding of silage high in butyric acid (Block, 2010).

7. Maximise intake by providing better cow comfort, exercise and absence of stress (Huzzey *et al*., 2011).

8. Monitor urine and milk ketones weekly for early detection (Leblanc, 2010; Chapinal *et al*., 2011; McArt *et al*., 2013a & b)

9. Select cows with vigorous appetites (Block, 2010; Janovic *et al*., 2011)

2.2. Milk fever

It is an afebrile, hypocalcaemic disease of cattle usually associated with parturition and initiation of lactation (Littlediek *et al*., 1980). It is a disease of milk production, seen only in lactating cows and not seen in beef cows (Mulligan and Doherty, 2008).

2.2.1. Synonyms: DeGaris and Lean (2009) observed that the synonyms of the disease are:

1. Parturient paresis
2. Hypocalcaemia or parturient hypocalcaemia
3. Parturient apoplexy
4. Eclampsia (mainly in bitches)
5. Paresis peurperalis

2.2.2. Incidence: Kronqvist *et al.* (2011) has detailed the effect of variables such as breed, age etc. on disease incidence as;

1. Incidence is highest in Jersey breed
2. Uncommon before the 3rd parturition
3. Incidence is highest at 5th or 6th parturition
4. Incidence is highest in the most productive years of the cow
5. Most cows have some degree of hypocalcaemia associated with parturition
6. Only in cows with severe hypocalcaemia, overt clinical signs appear

2.2.3. Pathogenesis:

Period in which calcium homeostasis is challenged most severely and is most subject to failure is at the time the udder initially fills with milk and lactation begins (DeGaris and Lean, 2009). Lactational demands of calcium exceed that of gestation by two to five times, because there is 1.20 g of calcium (Ca) and 0.90 g phosphorus (P) in each kg of milk produced and the availability is 68 and 58 per cent for Ca and P, respectively (Kronqvist *et al*., 2011). Therefore, the best approach in feeding a dairy cow is to keep the Ca: P ratio between 1:1 and 2:1 (Reindart *et al*., 2011).

Near parturition, inflow of calcium from the diet is temporarily insufficient to provide the calcium that is secreted in milk (Littlediek *et al*., 1980). All cows develop a temporary decrease in outflow of calcium from the bone as part of the initial adjustment to lactation (Mulligan and Doherty, 2008). The mobilisation of calcium from the bone to the blood is under the influence of parathyroid hormone (PTH) secreted by the parathyroid gland and 1, 25 - dihydroxy-cholecalciferol (vitamin D_3), secreted by the kidney (DeGaris and Lean, 2009). The huge demand for calcium produced by the onset of milk production can cause blood calcium levels to drop sharply, precipitating milk fever, either before or at calving (Kronqvist *et al*., 2011). Even though cows can mobilise skeletal calcium, the process is slow and made worse by the demands of high yielding stock (Lean *et al*., 2014).

Calcium is essential for the conduction of nerve impulses and hence hypocalcaemia leads to paresis and paralysis. In short, we can say that milk fever is primarily a result of disturbance in the function of the peripheral nervous system (DeGaris and Lean, 2009).

2.2.4. Clinical signs

There are three stages for the disease, based upon the characteristic clinical manifestations (DeGaris and Lean, 2009), viz:

Stage 1: This stage, the onset of parturient paresis, is often missed and is characterised by apprehension, anorexia, ataxia and limb stiffness.

Stage 2: This stage is marked by progressive muscular weakness, sternal recumbency and depression. The head is usually turned to the flank and an S-shaped curvature of the neck may be present. Other signs include dilated pupils, decreased pupillary light reflexes, reduced anal reflex, decreased defecation and urination, no rumen motility, protrusion of the tongue and frequent straining.

Stage 3: This stage occurs in about 20 per cent of cases and is characterised by lateral recumbency; severe depression or coma; subnormal temperature; a weak, irregular heart rate and slow, irregular, shallow respirations. The pupils are dilated and unresponsive to light. Bloating may occur. Changes in serum ions include hypocalcemia, hypophosphatemia, and hypomagnesemia. With prolonged anorexia, serum sodium and potassium levels may decrease.

2.2.5. Biochemical changes

Reindart *et al.* (2011) has described the biochemical changes in milk fever, as follows:

1. Both total calcium and ionised calcium will be low. Calcium level of blood plasma of affected animals declines from the normal 9 to 12 mg per dl to 3 to 7 mg per dl.
2. Decreased phosphorus
3. Decreased magnesium
4. Decreased insulin and as result, increased glucose

2.2.6. Treatment

De Garis and Lean (2009) have outlined the treatment for milk fever, as:

1. Intravenous calcium salts (Ca, 1 g per 45 kg of body weight) are usually effective. Intra venous infusion of calcium borogluconate solution is usually practiced. Calcium borogluconate is commonly used; a 25 per cent solution contains 10.40 g of calcium per 500 ml.
2. Intra muscular injection of phosphorus
3. Intra muscular injection of Vitamin D_3 or its analogues
4. Intra muscular injection of analgesics

2.2.7. Prevention

1. Feeding a diet which is low in calcium and high in phosphorus, at least five days before parturition. This will cause a slight hypocalcaemia, which in turn causes an increased secretion of PTH and 1, 25 - dihydroxy-cholecalciferol, which are essential for the mobilisation of calcium from the bone. Under the continued stimulation of these two hormones, bone tissue is prepared to meet much of the calcium demands of lactation (Lean *et al*., 2014).

2. Insufflation of the udder: This is a very old technique and is not at all practiced nowadays. Earlier, insufflation of air into the udder of the cow was successfully used to treat milk fever, whereby, insufflation increased the pressure in the udder, thus decreasing milk secretion and subsequently reducing the chances of milk fever (Littledike *et al*., 1980). However, this is not practiced nowadays as reduction in milk yield is not at all a desirable outcome in dairy farming, under any circumstance (Block, 2010).

3. Ensuring adequate Ca: P ratio: The best approach in feeding a dairy cow is to keep the Ca: P ratio between 1:1 and 2:1. Feeding of diets high in Ca during the pre-partem period can result in a high incidence of parturient paresis in dairy cattle. A 350 kg cow requires only about 30g of Ca per day to meet the maintenance and fetal Ca demands in late gestation. Low Ca diets (<20 g Ca/d) fed during the last two weeks before parturition is effective in preventing parturient paresis. Maintaining a Ca: P ratio of 1: 3.3, two weeks prior to parturition will prevent the occurrence of milk fever. However, it should be borne in mind that feeding of P above 80 g per day will increase the incidence of milk fever, because excess P will reduce the intestinal Ca absorption. If the ration is low in Ca, the resulting negative balance of Ca can stimulate the activity of parathyroid gland. Low Ca intake will make the cow in negative Ca balance and in a state of withdrawal of Ca from bone thus maintaining the normal blood Ca level of 9-12 mg per dl (DeGaris and Lean, 2009; Lean *et al*., 2014).

4. Dietary Cation Anion Difference (DCAD): A recent method of controlling parturient paresis in dairy cows when the Ca intake exceeds the requirement is to manipulate the anion cation balance of the diet. Diets high in cations especially sodium and potassium tend to induce milk fever compared with those high in anions, primarily chloride and sulfur (reduces the incidence of milk fever). Analysing the feed stuffs for sodium, potassium, chlorine and sulfur and determining the value of (Na + K) – (Cl + S) to produce a significantly negative total will effectively prevent parturient paresis (-ve DCAB concept). To prevent the occurrence of milk fever when high Ca diets are fed to dry cows, dietary cation anion balance must be reduced below -3 mEq per 100g of dietary DM. Decreasing DCAD to –ve values such as these, wherein the anions predominate, will stimulate the PTH and Vitamin D_3 to mobilise Ca (which is a cation) from the bone, thereby increasing the blood Ca level and reducing the chances of milk fever (DeGaris and Lean, 2009; Block 2010; Lean *et al*., 2014; Bakshi *et al.*, 2017).

2.3. Grass tetany

Grass tetany or hypomagnesaemia, as the name indicates, is due to low blood levels of magnesium (Allcroft and Burns, 1968). Magnesium (Mg) is essential for normal muscle and nerve function and a deficiency can occur if the animal does not get enough of Mg in the diet or if absorption is interfered with by other minerals (Littledike *et al*., 1980). Therefore, grass tetany is easily precipitated by a fall in dietary Mg (Blasi, 1998).

2.3.1. Synonyms: Blasi (1998) have enlisted the synonyms of the disease as:

1) Hypomagnesemia
2) Grass staggers

2.3.2. Etiology:

1. Lush immature grass: The risk is highest, early in the grazing season given the lushness and low Mg content of spring grass (Blasi, 1998; Powell *et al.*, 2013; Zelal, 2017).

2. Heavy milk yield in early lactation is another predisposing factor (Blasi, 1998).

3. Higher Nitrogen (N) and potash/ potassium (K) fertilised pastures: will be low in Mg as well as Ca. This is of great significance in India, where farmers apply plenty of farmyard manure/ cow dung, which is a rich source of N and/ or chemical fertilizers like muriate of potash (MOP), NPK mixture etc., which are rich in these two minerals, viz., K as well as N, for getting rich vegetative growth of fodder plants. This in turn leads to high content of N and/ or K in pasture grasses and corresponding high incidence of grass tetany in the cows which consume them, because excess of dietary N and/ or K, will interfere with the absorption of Mg (Grummer, 1995; Blasi, 1998; Powell *et al.*, 2013, Zelal, 2017).

4. Cows only have a limited body reserve of Mg and can only absorb a small proportion of Mg in their diet. Therefore, any nutrient imbalance in diet, such as excess of K, interferes with the absorption of Mg from rumen, which is the primary site of Mg absorption, in ruminants. High Ca and P in the diet can also cause Mg deficiency. It should also be noted that, on a low P diet Mg interferes with Ca absorption (Allsop and Pauli, 1975; Grummer, 1995; Blasi, 1998; Powell *et al.*, 2013, Zelal, 2017).

5. Binding of Mg and Ca by organic material in the digesta, decreases Mg absorption (Grummer, 1995).

6. High rumen NH_3 concentration; resulting from the addition of excess urea in the diet (maximum permissible level of urea in concentrate mixture for cattle is 1 % and $1/3^{rd}$ of the total N of the ration) or from consumption of pastures fertilized with excess of ammonium sulphate, decreases availability of Mg (Grummer, 1995; Blasi, 1998; Powell *et al.*, 2013, Zelal, 2017).

7. Kidneys have a role in conservation of Mg and the renal threshold of Mg is 1.80 mg per 100 ml of serum Mg. In hypomagnesaemia, the Mg excretion through urinary route is more (Kronqvist *et al*., 2011, Zelal, 2017).

8. Marked decrease in food intake causes decrease in Mg and Ca (Grummer, 1995; Blasi, 1998; Kronqvist *et al*., 2011, Zelal, 2017).

9. Cows above four years of age are more susceptible (Blasi, 1998; Kronqvist *et al*., 2011, Zelal, 2017).

2.3.3. Pathogenesis:

Changes in blood Ca concentration are of pivotal patho-physiologic importance in the development of grass tetany (Blasi, 1998). Deficiency of Mg may lead to a refractory condition of bones such that they cannot function as a source of Ca even when severe hypocalcaemia develops at the start of lactation (Kronqvist *et al*., 2011). PTH also is seen decreased in such cases.

If both dietary and bone sources of Ca and Mg are reduced in the face of a relatively high lactational demand for Ca and Mg, there is an acute disruption of Ca and Mg homeostasis (Blasi, 1998).

Decrease of Mg concentration in cerebro spinal fluid (CSF) are associated more closely with the development of clinical signs, than are blood Mg concentration (Littledike *et al*., 1980). Decrease of Mg concentration in CSF shall result due to inadequate maintenance of proper ionic concentration of Mg in the interstitial fluid of CSF. The net result is abnormal CNS function (Blasi, 1998). In short, grass tetany is primarily a result of altered CNS function, in contrast to milk fever which is primarily a result of disturbance in the function of the peripheral nervous system (Zelal, 2017).

2.3.4. Clinical signs:

Blasi (1998) have summarised three forms for the disease, based upon the characteristic clinical manifestations:

1. Tetanic syndrome type

This is the most common type. It manifests as a tetanic disorder with CNS signs. Nervousness, ataxia, disorientation, paddling, thrashing, convulsions, muscle twitching, recumbency with spasms and opisthotonus, ultimately resulting in coma and death, are the characteristic features of this syndrome. Death can ultimately occur but in some cases sudden death is the first and only sign.

2. Paretic type

Listlessness, stiff and staggering gait, paresis, recumbency, ultimately resulting in coma without spasms and death are the features of this form.

3. Subclinical type

Decreased appetite, decreased milk yield, slight nervousness and anaemia are seen in this form. If not treated promptly, this form can quickly progress to any of the other two forms.

2.3.5. Biochemical changes:

Tetany is usually preceded by a fall in serum magnesium to 0.50 mg per dl from the normal, 1.80 to 2.40 mg per dl (Kronqvist *et al*., 2011)..

2.3.6. Treatment:

1. Acute cases can treated by giving magnesium, calcium and phosphorus in dextrose solutions intra venous (Blasi, 1998). 'Mifex' (450ml) is the most popular trade preparation which contains Ca, Mg and P in the most ideal proportions to meet the normal requirement of the lactating cow. It contains organic P, calcium borogluconate, magnesium and dextrose (Zelal, 2017).

2.3.7. Prevention

1. Supplement with Mg during high risk periods and up to 30 days prior to calving (Block, 2010).

2. Avoid excessive application of nitrogenous, potassium and phosphatic fertilizers, in pasture. If possible, completely avoid nitrogen and potassium fertilizer applications in the spring of the year (Powell *et al.*, 2013).

3. Manage grazing so that animals are grazing forages greater than 6 inches in height. This technique is referred to as, 'holding off pasture until 6 inches tall', because Mg becomes more available in mature, when compared to younger plants (Blasi, 1998).

4. Minimise stress (Blasi, 1998).

3. Conclusion

We have seen in detail, the 'deadly trio' among metabolic diseases of lactating dairy cows, viz., ketosis, milk fever and grass tetany. The underlying basic causes of all these diseases, viz., hypoglycemia, hypocalcemia and hypomagnesemia are augmented by management practices directed toward improving and increasing production. They are therefore correctly considered as 'production diseases', affecting high yielding animals, in early lactation and hence economic losses caused by these diseases are huge. A thorough understanding of the etiology, pathogenesis, clinical signs, biochemical changes, treatment and control measures of each of these diseases, will go a long way in adopting appropriate prevention strategies, unique to each one of these, which will ultimately reduce and/ or prevent the occurrence of these diseases, thereby ensuring better economic returns to the farmers.

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Competing Interests

The authors declare that there are no competing interests.

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