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ReviewArticle

Ketosis Of Cows, its Types, Causes, Methods and Treatment of Injuries

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Abstract

During the first 6 to 8 weeks of lactation, ketosis is the most prevalent metabolic illness in high-performance dairy cows. The main signs of this condition are an abundance of so-called ketone bodies in a cow's bodily fluids. Acetoacetic acid, acetone, and hydroxybutyric acid (HBA) make up ketone bodies. The majority (about 70%) of the total volume of ketone bodies in the blood is made up of HBA. Loss of appetite, a preference for grass over concentrated feed, and an acetone odor in their mouth and urine are all clinical signs of ketosis in cows. Together with those symptoms, there is a decrease in production, a rise in concomitant disease (mastitis, metritis, and displaced abomasum), and subpar ovarian function. An rise in milk's fat content while a decrease in protein content is one of the hallmarks of ketosis. There is currently agreement that the cutoff value for SCK should be at least 1.2 mmol/L of HBA in blood plasma. Ketosis prevention is based on carefully regulating food doses during the first two months of lactation with the right energy-protein ratio in order to maintain perinatal cows in good health, or with roughly 3.5 points in the five-point body condition scoring. Oral administration of glucose precursor products is advised, especially for at-risk herds. On average, 7–14% of all the cows in a herd go into ketosis. According to the source, statistics on the prevalence of SCK generally vary greatly. Also, the issue is most frequently seen in animals with a high capacity for milk production who are malnourished. The goals of this review are to provide the current situation on the prevalence of ketosis, the potential for diagnosis, the effects on dairy cows, and to offer some suggestions for the treatment and prevention of ketosis.

Keywords: Dairy cattle; Ketone bodies; Ketosis; Metabolic disorders

Introduction

When energy requirements (such as increased milk production) exceed energy intake and produce a negative energy balance, a metabolic condition known as ketosis develops. This is typically because the metabolism of carbohydrates and volatile fatty acids is impeded. The need for glucose and amino acids is constant in pregnant and nursing animals, and ketosis develops when the increased rate of fat metabolism—which happens in response to the higher energy demands—becomes excessive. In the liver, the free fatty acids produced by lipid metabolism are esterified into fatty acyl CoA. Large amounts of the keto acid's acetoacetic acid and -hydroxybutyric acid are generated when the liver overoxidizes fatty acids in response to increasing energy needs. These acids diffuse into the bloodstream. The subsequent spontaneous decarboxylation of acetoacetic acid yields acetone. The term "ketone bodies" (sometimes known as "acetone bodies") refers to these three compounds: acetoacetate, hydroxybutyrate, and acetone [33].

Ketone bodies are typically seen in blood of mammals in concentrations of less than 1 mg/100 ml. In ruminants, the concentration is a tiny bit higher than this. Less than 1 mg of ketone bodies are excreted daily by an average person [30]. According to the presence or absence of clinical ketosis indicators in cattle, the

terms clinical and sub-clinical ketosis refer to two distinct features of ketosis in dairy cattle. As previously stated, the threshold for the definition of ketosis is a serum BHBA concentration between 1,200 and 1,400 mol/L. If the aforementioned increase in BHBA occurs along with clinical symptoms, it is referred to as clinical ketosis, and subclinical ketosis is defined as elevated circulating ketone body concentrations without accompanying clinical symptoms [23]. Although the wasting and nervous clinical manifestations of bovine ketosis are the two extremes of a range of syndromes in which wasting and nervous indications can be present to varied degrees of prominence. The wasting variant, which is the more prevalent of the two, manifests as a steady but mild decline in appetite and milk production over a period of 2-4 days. The pattern of appetite loss in herds that feed the different feed components individually is frequently atypical in that the cow initially refuses to consume grain, then ensilage, yet may still eat hay. Depraved appetite is another possibility. With the nervous form, symptoms typically appear bizarrely and abruptly. Walking in circles, crossing one's legs, pushing one's head against a wall or leaning against it, appearing to be blind, aimless movements and wandering, vigorous licking of the skin and inanimate objects, a depraved appetite, and chewing motions with salivation are some of the distinctive signs of the syndrome, which is more suggestive of delirium than of frenzy. Ketosis, hypoglycemia, and ketonuria are symptoms of the illness [28]. Blood sugar levels drop from the typical range of about 50 mg/dL to 20–40 mg/dL. Blood glucose levels above 40 mg/dL and frequently above normal are typically present in ketosis related to various illnesses [28].

The most significant metabolic change brought on by ketosis is the increase of ketone bodies, particularly BHBA, as was previously indicated [31,26]. Although the pathophysiology of bovine ketosis is not fully understood, it has been discovered to be linked to two phenomena: a high glucose requirement and strong adipose mobilization. Early lactation has both of these symptoms. Adipose tissue is mobilized during this period of negative energy balance, and milk production raises the need for glucose. In other cases, such as in type 1 or diabetes mellitus, blood glucose is present but cannot be utilized by cells. High blood serum concentrations of nonesterified fatty acids are present in conjunction with adipose mobilization (NEFAs). Although gluconeogenesis is the preferred method for converting NEFA to glucose, during periods of high gluconeogenesis, a significant amount of serum NEFAs are diverted to the liver's manufacture of ketone bodies [13]. Hence, high serum concentrations of NEFAs and ketone bodies and low quantities of glucose are characteristics of the clinicopathologic state of ketosis [15].

Because of the sharp increase in lactose synthesis during early lactation, the need for glucose is considerably enhanced. As a result, more nonesterified fatty acids (NEFAs) are taken up by the mitochondria of liver cells, increasing fat mobilization in adipose tissue. Increased NEFA levels cause hepatocytes to produce more lipogenesis and ketogenesis. High ketone body concentrations slow down the citric acid cycle, gluconeogenesis, and the rates of fatty acid -oxidation in hepatocytes. There have been conflicting reports on the metabolic changes that occur in the liver during ketosis, with some research suggesting that gluconeogenesis is unaffected by ketogenic conditions [2,19,34]. The most popular theory contends that because oxaloacetate is not readily accessible in mitochondria, acetyl-CoA is directed toward incomplete oxidation (Ketogenesis) [18]. This notion has been challenged, though, because it has been shown that starved animals have decreased gluconeogenic flow and that the activity of phosphoenolpyruvate carboxykinase in the mitochondria and cytosol is unaffected by ketogenic conditions [19].

Krebs' theory, which claims that maintaining a low level of oxaloacetate is what causes ketogenesis, is likely accurate, but its justification is flawed: the mitochondrial NADH/NAD+ ratio is considerably larger than it is in the cytoplasm, which results in the low concentration of oxaloacetate. The decreased rate of gluconeogenesis during ketotic periods with inappetance should be explained by the minimal rate of intramitochondrial phosphoenolpyruvate generation as a result [35]. Many studies on the causes of ketosis have produced conflicting results [11,14,19]. In a nutshell, when physiologic mechanisms for the adaption to negative energy balance fail, ketosis and/or fatty liver ensue. Ketosis may result from inadequate feedback control of the release of nonesterified fatty acids from adipose tissue, which is another plausible cause of ketosis and fatty liver. Hepatic gluconeogenesis may not provide enough glucose for lactation and body demands, which is one potential cause of ketosis. These two metabolic abnormalities can cause different types of ketosis, which may call for various therapeutic and preventative measures [14].

Lower milk production, decreased fertility, increased risk of additional periparturient disorders such displaced abomasum, lameness, mastitis, metritis, and retained placenta, as well as a higher culling rate are some of the unfavorable effects of ketosis [7,27]. The stage of the lactation cycle that occurs between late pregnancy and early lactation, often known as the periparturient interval, is undoubtedly the most fascinating. The last three weeks before parturition to three weeks following parturition have traditionally been considered to represent the length of the transition period [4,11]. This is the phase when the majority of serious infectious illnesses and metabolic abnormalities occur. The periparturient period is when cows are most affected by ketosis, retained fetal membranes, milk fever, merits, and misplaced abomasums. Immune suppression throughout the periparturient period during this time makes people more susceptible to infectious illnesses [4,21]. Acetonemia, also known as ketosis, is a condition in which the blood's concentration of ketone bodies—acetone, acetoacetate, and -hydroxybutyrate—increases to the point where they finally start

to diffuse into urine and/or milk. Ketosis is a lactation condition that typically affects dairy cows and is characterized by high milk production and an unfavorable energy balance [20]. According to many research, ketosis can be quite expensive because it happens during the lactation's most productive phase [26,31].

Several prevalence rates have been observed, with some researchers reporting that it ranges from 11.1 to 21%, and the prevalence rate of ketosis is highly tied to nutrition and farm management [31,26] Yet, stubborn researchers found that up to 33% of cows in some herds in the United Kingdom tested positive for milk or urine ketones, lost weight, and had lower milk production [16]. According to Emery et al., [8] 20 to 30% of subclinical cases of ketosis progressed to clinical ketosis in some high-producing herds, which contained roughly 50% of the cows. Ketosis during lactation seldom results in death [20]. It has been determined that exotic pure/crossbred animals exhibit a higher prevalence of ketosis than native pure/nondescript animals. Breeds of cattle are discovered to be highly correlated with prevalence. The development of hypoglycemia, which can pose a challenge to the successful operation of dairy farming and ultimately ruin the life of dairy farmers, is a common occurrence in animals with high genetic potential, as these animals are unable to withstand the pressures caused by the high nutritional demands generated by the production of milk [31]. It has been determined that dairy cattle's fatty liver condition and ketosis are closely related [32].

Since the late 1990s, ketosis has become one of the most significant metabolic disturbances of dairy cows in North America, surpassing incidence rates of ruminal acidosis and milk fever [25]. In fact, after a few weeks of calving, over 40% of dairy cows in North America exhibit various degrees of ketosis, with incidences varied greatly between farms and rising as high as 80% in certain dairy herds [6].

Blood testing: The simplest method for early detection of ketosis in cattle is periodic blood testing of the herd for BHBA concentration, but plasma BHBA analysis is neither cost-effective nor practical for routine analysis, and cow side monitoring instead uses the amount of acetoacetate or BHBA in milk and urine. Blood and milk BHBA and blood and milk acetoacetate correlation coefficients are 0.66 and 0.62, respectively, and the concentrations of BHBA and acetoacetate in urine and milk are lower than those in blood [9,28]. The advantages of cowside tests are their low cost, quick turnaround time, and flexibility in usage. The fact that the concentration of ketone bodies in these fluids will vary not only on the blood ketone level but also on the volume of voided urine or the milk supply, is a minor cause of inaccuracy. With subclinical ketosis, milk is less variable, easier to collect, and may provide fewer false negatives. Traditional methods for measuring milk and urine ketone levels involve reacting acetone and acetoacetate with sodium nitroprusside. Based on the strength of the reaction, the results can be semi-quantitatively interpreted. There are a number of commercially available test powders and test strips that are frequently accompanied by a color chart that permits grading depending on the reaction's color intensity into categories like negative, trace, small, moderate, and big [28]. According to conventional knowledge, urine tests are insufficiently specific (report too many false positives) and milk powder tests are insufficiently sensitive for detecting subclinical ketosis [1]. Milk and/or urine screening: According to several studies, the sensitivity and specificity of the nitroprusside powder test with milk are 28–90% and 96–100%, respectively [10]. More recently, there has been a milk strip test that grades the amount of BHBA in milk based on its content in lmol/L. Its stated sensitivity and specificity in various investigations are 73-96% and 69-96%, respectively [3]. These discrepancies are caused in part by the use of different cut points for urine BHBA and different plasma BHBA reference values (1200 and 1400 mol/L) for the classification of subclinical ketosis. Both the BHBA strip test and the nitroprusside test will have elevated readings if the somatic cell count is greater than 1 million cells/mL [28]. When used in conjunction with serum BHBA concentrations above 1400 flmollL16, nitroprusside tablets have reported sensitivity and specificity of 100% and 59%, respectively, while nitroprusside strip tests have reported sensitivity and specificity of 78% and 96% with a urine cut point corresponding to "small" on the color chart or 49% and 99% with a urine cut point corresponding to "moderate" on the color chart [28,1]. At a urine cut point of 100 mol/L BHBA, BHBA test strips are reported to have a sensitivity and specificity of 73% and 96%, respectively, and 27% and 99% at a urine cut point of 200 mol/L BHBA, respectively [1].

The proper nutrition of the cows, control of body condition, and the use of specific feed additives during the dry and nursing periods are all essential components of preventing clinical ketosis. While creating the ideal diet for dairy cattle, it's vital to consider factors including dry matter intake, fiber digestibility, particle size distribution, energy density, fat incorporation in early lactation rations, protein content, feeding strategies, and rumen size [28]. It has been determined that using sodium propionate on a daily basis (0.25 lb for each cow) after calving can help dairy cattle farms avoid ketosis. In addition to having greater blood sugar levels and less ketone bodies in their blood, treated cows with sodium propionate also produce more milk [29]. It has been discovered that administering oral propylene glycol effectively increases milk output in dairy cattle and effectively prevents ketosis in dairy cattle farms. Throughout the first 30 days of lactation, treated cows receiving 300ml of oral propylene glycol daily produced 0.23kg more milk every milking, for a difference of 0.69kg/cow per day. Moreover, cows treated with propylene glycol had a 1.50 times higher chance of resolving their subclinical ketosis and a 0.54 times lower chance of developing clinical ketosis. These outcomes demonstrate the beneficial effects of oral propylene glycol treatment in young cows with sub-clinical ketosis by assisting in the resolution of their sub-clinical ketosis and avoiding clinical ketosis.

Moreover, in cows with sub-clinical ketosis, oral propylene glycol increases milk production throughout the early lactation period [22]. Propylene glycol is known to possibly lessen the mobilization of fatty acids from adipose tissue, and by this mechanism, it may offer protection against ketosis and fatty liver syndrome. Choline that has been ruminally protected, acts as a preventative against the imbalanced energy levels that result from fatty liver and/or ketosis. Choline is known to likely increase the release of very low-density lipoproteins from the liver. Also, decreasing or doing away with the dry phase is a management method that lessens the severity of the negative energy balance after calving and triglyceride accumulation in the liver and may guard against metabolic illnesses linked to unbalanced energy levels, such as ketosis [12]. It was also reported that prevalence and incidence of subclinical ketosis were significantly reduced (50%) due to monensin-based treatment in dry cows and heifers. The duration of subclinical ketosis for cows that had been treated with monensin was also shorter than others. Monensin treatment significantly reduced the incidence of subclinical ketosis. In addition, monensin significantly reduced the prevalence of positive milk ketone bodies tests [5]. According to some researches, 500mL of a 50% solution of intravenous glucose causes transitory hyperglycemia, increased insulin and decreased glucagon secretion, and a drop in the plasma content of non-esterified fatty acids. Most cows see a noticeable improvement; however relapses frequently happen if treatments are not repeated. In an effort to prolong the response, other sugars, particularly fructose, either alone or in combination with glucose and fructose (invert sugar), and xylitol have been used; however, idiosyncrasies to some preparations, such as polypnea, muscle tremor, weakness, and collapse, can occur while the injection is being administered [28]. Propylene glycol can be given as a drench to avoid the need for frequent injections.

Higher volumes are also employed in addition to the typical doses of 225g twice day for two days, followed by 110g daily for two days to cattle. You can inject propylene glycol (200-700g daily) or propionic acid salts in the feed and get decent results [28]. It has been proven that glucocorticoids are effective in treating cattle ketosis in both laboratory and real-world situations. Within 24 hours of treatment, hyperglycemia appears to be caused by the body's distribution of glucose rather than by gluconeogenesis [24,28]. Insulin promotes hepatic gluconeogenesis, inhibits fatty acid metabolism, and makes it easier for cells to absorb glucose. It is not frequently used but may be useful in early onset cases of ketosis that are refractory to glucose or corticosteroid therapy. It is provided in conjunction with either glucose or a glucocorticoid. Protamine zinc insulin is given in doses of 200–300IU per animal, SC every 24–48 hours, as needed. Moreover, lactational ketosis and ketosis in late-pregnant cows who are overweight, stressed, or carrying twin fetuses have been treated with anabolic steroids. Trenbolone acetate is efficacious as a single injection at experimental doses of 60 and 120 mg, although extensive field experiments have not been documented and the medicine is generally prohibited for use in food animals [28]. Glucagon While very gluconeogenic, glycogenolytic, and glucagon concentrations are decreased in the blood of fat cows during calving and cows with ketonemia, ketogenic is also powerfully gluconeogenic. Due to its very short physiologic half-life and transient effects after a single injection, it may be useful in both prevention and therapy, but this would necessitate a prolonged delivery method [17,28].

Conclusion

Animals go into ketosis when their blood and tissue levels of ketone bodies (acetoacetate, beta-hydroxybutyrate, and acetone) rise. The negative energy balance is mostly linked to ketosis in ruminants. Animals in ketosis typically have low blood glucose levels, and the main factor contributing to ketosis is a reduction in the amount of carbohydrates consumed by the animal. This results in a reduction in blood glucose levels, which in turn triggers the metabolism of fat to produce ketone or acetone bodies. Propylene glycol is the preferred treatment for ketosis, and ketosis in ruminants can be avoided by increasing dry matter intake, offering an appropriate carbohydrate diet, supplementing with yeast, using phytogenic feed additives, and other methods. As ketosis is one of the most significant and prevalent metabolic diseases in dairy animals, the animals should receive the correct care and management in order to prevent financial loss in the dairy business.

Acknowledgment

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Conflict of Interest

None.

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