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ETHIOPATHOGENETIC MECHANISMS INVOLVED IN KETOSIS OF DAIRY COWS

MECANISME ETIOPATOGENETICE IMPLICATE ÎN CETOZA VACILOR DE LAPTE

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ABSTRACT | REZUMAT

Ketosis of dairy cows is a disorder with complex aetiology, and the belated diagnosis of it, makes the cure difficult. The aim of the study was to understand the etiological factors and metabolic mechanisms with influence in causing ketosis, therefore helping us to prevent it. The study was conducted under normal farm conditions, where three risk factors, with a potential role in causing ketosis, were individualized: high milk production (group A), hypoenergetic fodder rations (group B) and low environmental temperatures (group C). These etiological factors initiate metabolic processes that have a different starting point, but end in ketosis. The cows from groups A and B had the blood sugar level closer to the lower limit of the benchmarks and the lipemia values were closer to the superior limit of the benchmark values. These values suggest a negative energetic balance. The average of beta-hydroxybutyrate was between benchmarks but, taken individually, led to diagnosing subclinical ketosis with levels over 14.4 mg/dl for three cows out of 10 in group A and two cows out of 10 in group B. The cows kept outside, under low temperatures (group C) revealed a normal energetic profile with lower levels of blood sugar than benchmark, but higher lipemia levels and beta-hydroxybutyrate are less than 14.4 mg/dl. Based on these results, we concluded that ketosis in dairy cows can be metabolically triggered by hypoglycaemia (energy deficiency), as well as by hyperlipemia with hepatosteatosis, in which case the evolution of the disease is worse. Therefore, low environmental temperatures do not induce ketosis without other factors to generate an energetic shortage.

Keywords: cows, ketosis, ethiopathogenetic mechanisms, energetic profile

Cetoza vacilor de lapte este o tulburare cu etiologie complexă, iar diagnosticul tardiv al acesteia, face ca vindecarea să fie dificilă. Scopul studiului a fost de a înțelege factorii etiologici și mecanismele metabolice cu rol în etiopatogeneza cetozei, ajutându-ne astfel s-o prevenim. Cercetările au fost efectuate în condiții de fermă, unde au fost individualizați trei factori de risc cu rol potențial în producerea cetozelor: producția ridicată de lapte (grupul A), rațiile alimentare hipoenergetice (grupul B) și temperaturile scăzute ale mediului (grupul C). Acești factori etiologici au un punct de plecare diferit, dar inițiază procese metabolice care duc la cetoză. Vacile din grupurile A și B au avut valorile glicemiei apropiate de limita inferioară a valorilor de referință, iar valorile lipemiei s-au apropiat de limita superioară a valorilor de referință. Aceste valori sugerează un bilanț energetic negativ. Valoarea medie a beta-hidroxibutiratului din sânge se situează în limita valorilor medii de referință, dar luată în mod individual, a condus la diagnosticarea cetozei subclinice cu niveluri de peste 14,4 mg/dl pentru trei vaci din 10 în grupul A și două de vaci din 10 în grupul B. Vacile ținute în aer liber, cu temperaturi scăzute (grupul C) a relevat un profil energetic normal, cu niveluri ale glicemiei apropiate de valorile minime fiziologice, în timp ce lipemia tinde spre limita superioară, la fel și beta-hidroxibutiratul, dar cu valori mai mici de 14,4 mg/dl. Pe baza acestor rezultate s-a concluzionat că cetoza la vacile pentru lapte poate fi declanșată metabolic de hipoglicemie (deficiență energetică), precum și de hiperlipemie cu hepatosteatoză, caz în care evoluția bolii este mai gravă. Temperaturile scăzute ale mediului nu induc cetoza în lipsa altor factori etiologici care să genereze hipoglicemie.

Cuvinte cheie: vaci, cetoza, mecanisme etiopatogenetice, profil energetic

Nowadays, dairy cows have an unstable homeostasis equilibrium that can be unbalanced by factors such as nutrition, milk production level or stalling condition (4), and various conditions may be associated with them (1, 3, 21). Ketosis is a disorder described for over 100 years. However, the complex aetiology and belated diagnosis makes it difficult to cure. In addition, ketosis usually causes subclinical symptoms, so it is a noticeable problem in dairy farms (7, 17). For example, during the first part of lactation, the quantity of solids ingested (SI) by a cow is an average of 3-3.5kg SI/100kg body weight (bw). This means that a cow weighing 600 kg and ingesting 18-21 kg solids ensures the need for maintenance and milk production.

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Maintenance requirements are 60g crude protein (CP), 6g calcium (Ca), 4.5g phosphorus (P), 6.0g salt and 25g carotene, all for 100 kg bw. The nutritional units (NU) necessary for maintenance are calculated using the equation: NU=(LW/200+1.5)x1.18. The production requirements for 1 litre of milk with 4% fat are: 0.45 NU, 60 g CP, 4 g Ca, 2g P, 2g salt and 25g carotene. The food requirements calculated for a cow with an average bodyweight of 600kg, during the first part of lactation and a production of 20 litres of milk per day with 4% fat, are: 14.3 NU, 1560g CP, 116g Ca, 67g P, 76g salt and 650g carotene (8). If these characteristics are not up to standard, there will be nutritional and metabolic disorders, most frequently the lipid-glucose balance known as ketosis. When high milk production and, sometimes, improper maintenance conditions are added, the energy deficit in dairy cows is accentuated.

The aim of the study is to evaluate if the ketosis in dairy cows can be metabolically triggered and if environmental conditions can be involved in ketosis.

MATERIALS AND METHODS

The study focused on 4 groups of dairy cows from the Holstein Frisian breed, with similar physiological condition during, their first month of lactation, aged between 3 and 7 years: group O (control) was made of cows with an average milk production of 20 litres per day, kept in prolonged stalling and fed with energetic equilibrated rations; group A was made of cows with an average milk production of more than 30 litres per day, kept and fed identically with the cows from group O; group B included cows with average milk production like group O and fed with hypoenergetic rations – further tests concluded that the rations covered only 12.4 NU (nutritional units) out of 14.3 daily requirements, energetic concentration (EC) was 0.8 (EC=12.4NU/15.5kgSI=0.8). In addition, the rations were mainly composed out of corn silage which fermented and produced a high amount of butyric acid (values over 50-100 g/day can cause subclinical ketosis); group C included cows kept in nature during fall, under average temperatures of 10°C, even lower overnight, as well as average milk production and feeding similar to the cows from group O (Table 1).

Subsequently, for 10 cows out of every group the beta-hydroxybutyrate (BHB) was determined, as well as some parameters involved in the energetic profile and which are usually modified in ketosis'diagnostics (glucose, total lipids and alkaline reserve) (1, 9, 14) using the Biochemistry Analyzer Cormay Accent 200 (PZ Cormay, Lomianki, Poland) and specific kits.

To observe the succession of metabolic phenomena in cows diagnosed with ketosis (BHB higher than 14.4 mg/dl), biochemical parameters were studied every 7 days, during 50 days after the first day of clinical symptoms (4, 12, 18).

RESULTS AND DISCUSSIONS

The cows from the control group (O) obtained the following average results: glucose 58.54.2 mg/dl, total lipids 33221 mg/dl, beta-hydroxybutyrate 5.71.8 mg/dl and alkaline reserve 250.5 mEq/L (milliequivalent/litre) (Table 2). All these values for the energetic profile were between the benchmarks (10, 19).

Cows from group A showed a level of glucose (50. 13.1 mg/dl) closer to the lowest limit of the average level and total lipids closer to the highest limit of the average level (477.928.1 mg/dl). The values of the BHB were 8.41.4 mg/dl (between the benchmarks), three cases of the group had the BHB levels over 14.4 mg/dl (subclinical ketosis) (5, 18).

The alkaline reserve (AR) had an average of 23.50.5 mEq/L (between benchmark), but like the BHB, three cases had the AR levels near the lower limit of the benchmark, which indicates the increased concentration of ketone bodies to bind bicarbonate.

The average values of the biochemical parameters of the cows in group B, showed an energetic deficiency similar to the cows in group A: GLU=47.5±2.1 mg/dl at the lower limit of the benchmarks, TL=469.9±25.1 mg/dl. These values emphasize a metabolic and energetic deficiency due to poor feeding and the fodder lacking soluble glucose, making the gluconeogenesis ineffective. This will cause the use of lipids from the body's natural deposits [16, 22]. This process is confirmed by the low values of blood sugar and high values of lipemia. The average value of BHB was a normal one, 10.3±1.1 mg/dl. Individually, two cows showed BHB levels over 14.4 mg/dl, confirming subclinical ketosis and not metabolic acidosis (AR=22.4±0.5 mEq/L) (4).

The cows in group C had average blood sugar levels of 54.7±2.3 mg/dl and average total lipids levels of 440.2±16.3 mg/dl, indicating a balanced energetic metabolism. These numbers show that low temperatures by themselves cannot induce ketosis, without other factors to induce energetic deficiency, hypoglycemia, hyperlipemia and hyperketonemia (3, 20).

Confirmation comes from the average values of BHB=6.9±0.7 mg/dl and alkaline reserve of 23.8±0.3 mEq/L (between benchmarks).

Table 1

The diet of the cows in group B

Chemical composition and NV*/kg fodder						Quantity	Nutritional requirements/600 kg cow 18-21	14.3	1560	116/67	76.0	650.0
SI**(%)	NU***	Protein (g)	Ca/P****(g)	Caroten (mg)	Fodder	(kg)	SI (kg)	NU	Protein (g)	Ca/P (g)	Salt (g)	Caroten (mg)
30	0.3	12	1.3/0.6	4	Corn silage	18	5.4	5.4	216	23.4/10.8	-	72
85	0.6	130	12.3/1.9	35	Alfalfa hay	4	3.4	2.4	520	49.2/7.6	-	140
85	0.6	60	12.3/1.9	35	Grass hay	4	3.4	2.4	240	49.2/7.6	-	140
85	0.4	22	6.2/2.3	-	Corn cobs	3	2.5	1.2	66	18.6/6.9	-	-
85	1.2	60	0.2/2.3	2	Corn	0.5	0.4	0.6	30	0.1/1.1	-	1
85	0.8	120	1.3/9.9	-	Wheat bran	0.5	0.4	0.4	60	0.6/4.9	-	-
					Salt						Lumps	-
					Total	30.0	15.5	12.4	1132	141.1/ 38.9	-	353

* NV=nutritional value; **SI=solids ingested; ***NU=nutritional units; Ca/P**** =calcium / phosphorus

Table 2

Energy profile from cows in groups A, B, C and O

Parameter / Measure		Beta hydroxybutyrate (BHB) mg/dl	Glucose (GLU) mg/dl	Total lipids (TL) mg/dl	Alkaline reserve (AR) mEq/l
Benchmarks (Merck Veterinary Manual, eighth ed.)		sub 14.4	62,0–12.0	300±150	24.5±2.5
Group O (average values)		5.7–1.8	58.5±4.2	332–21	25.0±0.5
	1	5.3	52.4	443	26.0
	2	14.8	39.8	586	22.0
	3	6.2	58.9	390	23.5
	4	5.6	64.3	375	23.5
	5	7.3	50.0	450	23.0
Group A	6	6.0	56.2	422	24.0
	7	11.6	42.6	524	22.5
	8	16.7	36.7	614	21.5
	9	15.0	38.8	573	22.0
	10	5.5	61.5	402	25.5
	St Sx*	8.4 1.4	50.1±3.1	477.9 28.1	23.0±0.5
	1	8.4	48.7	466	24.0
	2	11.9	44.6	454	22.5
	3	6.8	52.4	411	23.0
	4	7.1	56.2	388	24.5
	5	17.2	38.6	617	21.5
Group B	6	7.4	54.8	485	22.5
	7	16.1	36.5	598	21.5
	8	9.2	44.7	426	22.0
	9	8.6	53.2	390	23.5
	10	10.4	45.9	464	22.0
	St Sx*	10.3±1.1	47.5±2.1	469.9±25.1	22.4±0.5
	1	6.7	55.6	465	23.5
	2	5.9	62.3	356	24.5
	3	4.4	66.1	439	25.0
	4	6.2	52.4	461	24.5
	5	7.8	48.5	482	23.5
Group C	6	6.8	56.7	383	23.0
	7	10.8	42.6	504	22.0
	8	5.3	59.0	440	24.5
	9	11.0	44.1	494	22.5
	10	4.7	60.0	378	25.0
	St Sx*	6.9±0.7	54.7±2.3	440.2±16.3	23.8±0.3

* SSx=average and standard deviation of the average

Table 3

The dynamics of the energy profile of dairy cows with ketosis

Parameter / Measure		Beta-hydroxybutyrate (BHB) mg/dl	Glucose (GLU) mg/dl	Total lipids (TL) mg/dl	Alkaline reserve (AR) mEq/L
Healthy clinical cows (average)		5.7–1.8	58.5±4.2	332.0±21	25.0±0.5
Cows with ketosis	Day 1	15.9±1.2	38.1±1.7	597±22	21.7±0.2
	8	23.6±3.2	32.8±2.6	612±23	21.3±0.4
	15	27.3±3.9	26.7±2.2	514±23	21.0±0.3
	22	30.1±4.3	22.3±2.0	476±20	20.5±0.4
	29	32.2±4.8	25.4±2.1	405±18	19.0±0.3
	36	28.4±3.6	44.7±2.8	288±16	20.5±0.5
	43	11.3±2.2	48.6±3.1	254±12	22.0±0.4
	50	7.2±1.6	51.2±3.5	302±13	23.0±0.5

BHB has steadily risen until the fifth week, when it reached 32.24.8 mg/dl, then returned to physiological values after another 2 weeks (Table 3).

BHB growth occurred simultaneously with low blood sugar (14). Glucose concentrations decreased progressively until the fourth test (22 days after the onset), when GLU=22.32.0 mg/dl, a value that is less than 2.6 times compared to clinically healthy cows, with a value of GLU=58.54.2 mg/dl. The lowering effect of the blood glucose was associated with the first 2 months of lactation, when the milk production should be maximized; instead, the cows with ketosis had significantly reduced milk productions, resulting in energy savings (13, 15). After this critical point, blood glucose level began to show physiological values (Fig. 1).

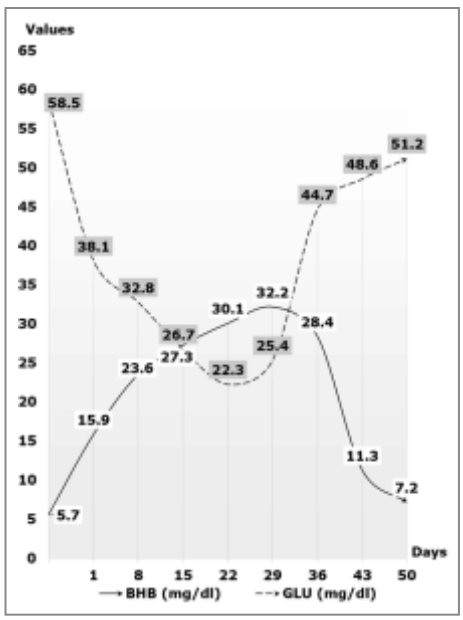

Fig. 1. The evolution of GLU and BHB in cows with ketosis. GLU=glycemia; BHB=Beta-hydroxybutyrate

Total lipids presented an opposite process to glucose; the highest average (61223 mg/dl) was in the second week of testing, after that, it started to recover gradually down to baseline levels after the 5th week of testing (after 29 days).

AR reached a minimum average of 19.00.3 mEq/L during the fifth week of testing, matching the maximum level of BHB, then gradually returned to physiological values with decreasing ketonemia (7, 11). This proves that ketonemia was associated with a condition of metabolic acidosis complicating the symptoms of the disease. Standard deviation of the averages (Sx) of blood biochemical parameters for the energetic profile is high, emphasizing that the group of cows was not homogeneous in terms of their development. In addition, biochemical parameters are interdependent, they could change first and then induce changes in others. In fact, the group of cows was chosen by serum concentration of BHB in the first test (BHB>14.4 mg/dl), which proves the existence of subclinical ketosis from the beginning, showing the progressive course of the disease.

The negative energetic level in the organism is due to a glucose deficiency, since dairy cows use a high quantity of blood sugar for the process of milk synthesis of the mammary gland (approximately 50 g of glucose for 1 litre of milk) (3). This energetic deficiency leads to using the lipid deposits, translating into the high total lipids (2, 6, 23). Therefore, high milk production levels associated with low energetic rations are involved in the aetiology of ketosis, confirmed by the values of the BHB, which is more than 14.4 mg/dl.

The evolution of glucose displayed an opposite pattern to the serum lipids. Thus, the pathogenesis of ketosis (increased BHB) can be initiated, by both hypoglycemia and hyperlipemia with liver steatosis. Lipemia was the first biochemical blood parameter from the energetic profile that changed significantly in cows with ketosis. Lipemia rose sharply, then returned to baseline after 29 days, implying a prolonged process of liver steatosis, even after the lipidic mobilization from the deposits. Therefore, steatosis is a consequence of ketosis and it is also a causing factor by reducing the functional capacity of the liver (gluconeogenesis is insufficient in ketosis).

Regarding the dynamics, the average lipemia value in cows with ketosis showed a sudden increase followed by a progressive decline, evolving in the opposite with the average value of glucose; this indicates that ketosis can be initiated by both hypoglycemia and hyperlipidemia. The energetic deficiency unadapted to physiological needs is a trigger for ketosis. Instead, low environmental temperatures cannot initiate ketosis without other etiological factors that cause energetic deficits. On the other hand, increased blood levels of BHB is the triggering factor of the ketosis. It occurred simultaneously with the decrease of AR and metabolic acidosis that complicates the evolution of the disease.

CONCLUSIONS

Ketosis in dairy cows can be metabolically triggered by hypoglycaemia (energy deficiency), as well as by hyperlipemia with hepatosteatosis, in which case the course of the disease is worse. Therefore, low environmental temperatures do not induce ketosis without other factors to generate an energetic shortage.

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