Journal of Animal and Veterinary Advances 9 (2): 287-291, 2010
ISSN: 1680-5593

Investigation of the Effect of Different Treatment Regimens on Blood Acid-Base Balance in Cows with Ketosis

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Abstract: In this study, the effect of different treatment procedures on blood acid-base balance was examined in cattle with ketosis. The animals were divided into four groups, three of them were study groups and one was control group. Each group consisted of 7 cattle counting up a total of 28 dairy cattle. The blood samples were analyzed for blood gases estimations after and before the applications. During the study, intravenously (iv) 750 mL 30% dextrose solution was given to all study groups. Following the dextrose solution, Subcutanous (sc) insulin was given twice in 48 h intervals to the first study group. Intramuscular (im) dexamethasone and prednisolone were given to the second and third study groups, respectively. No drug was applied to the control group. As a result, blood pH levels was significantly increased in group I compared to the other groups ($p<0.05$) and blood pH levels of group I were higher after treatment than before treatment ($p<0.01$). Blood chlor levels of group II were significantly increased ($p<0.05$) after treatment compared to the before treatment. This study showed that ketosis changes the blood acid-base balance in cattle and insulin-dextrose combination was more affective for amelioration of these disturbances related with ketosis compared to other treatment methods.

Key words: Acide-base balance, cow, ketosis, treatment, blood sample, blood chlor

INTRODUCTION

Calving is the most important period in dairy cows, because nutritional requirements increase rapidly with lactation. Ketosis or acetonaemia, which is seen mainly in times of high milk production, is one of the most important and metabolic disease of lactating cows. While, the occurrence of primary ketosis in high-producing cows, that is manifested either in clinical or subclinical form, is associated with primary energy deficiency; secondary ketosis can occur when a primary disease or any problem related inappetite in cows (Nowakowski and Filar, 2005; Radostits *et al*., 2000).

Clinical form of ketosis is rare, while in a range of cases it preceeds in its subclinical form, resulting in considerable economical loss, inappetence and decrease of milk production, infertility, therapy costs. The economical losses in the subclinical ketosis is that the condition may remain undetected, then not dealt with and yet have adverse effects on productivity, which parallel those elicited by clinical ketosis (Duffield, 2000; Oetzel, 2004; Rajala-Schultz *et al*., 1999). While, incidence level of clinic ketosis is 2-15%, in the subclinic ketosis it is 7.6-31.2%. Some researchers reported that there is a decrease of 3.0-5.3 kg day^{-1} of milk production in the subclinical ketosis, compared to healthy animals. There also can be an average reduction in production upto 25% or 353.4 kg per lactation during clinical ketosis (Duffield, 2000; Nowakowski and Filar, 2005; Radostits *et al*., 2000; Rajala-Schultz *et al*., 1999).

Course of clinical and subclinical ketosis related to moreover damage of liver, hypoglycemia, hyperketonemia and elevated serum concentrations of isopropyl alcohol have all been suggested as the cause of nervous signs (Foster, 1988; Kaneko, 1997; Lenyo, 2006). Clinical signs of lactation ketosis include diminished appetite, a dorp in milk production, rapid loss of body weight, hard dry feces, abnormal gait, hyperesthesia or lethargy, depraved chewing and licking, acetone-odor breathing and acetone-odor skin (Radostits *et al*., 2000).

When treating cows for negative energy balance, it is essential to meet the need for glucose so that the ketogenic process in the liver are reversed. A quick-acting glucose supplement is required immediately. Treatments for ketosis include dextrose, glucocorticoids, insulin, glycerin, sodium propionate and propylene glycol, but effect of these are different (Nowakowski and Filar, 2005; Radostits *et al*., 2000). For example, Shpigel *et al*. (1996),

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reported that glucose and dexamethasone, Schwalm and Schultz (1976) found insulin and glucose combination more effective at the treatment. Sakai *et al.* (1993), found that supplemental insulin enhanced the therapeutic effect of glucose infusion in the treatment of ketosis. Slow release insulin has also been used for therapy of ketosis and has resulted in increased Dry Mater Intake (DMI) and milk yield (Moore and Ishler, 1997).

If the amount of carbohydrate in the diet of cows is insufficient to meet the glucose needs, glucose is produced by liver from body fat reserves. When large amounts of body fat are utilized, fat is sometimes mobilized faster than the liver can properly do. Rapid release of free fatty acids cause the accumulation of the major ketone bodies (acetoacetate, β-Hydroxybutyrate (BHB) and acetone) and can lead to ketosis (Bigner *et al.*, 1996; Oetzel, 2004). When acetoacetate and β-hydroxy-butyrate is produced in excessive amounts, the alkali salts is synthesized and alkali reserve diminishes because of is execive excretion from the body. This causes more decreases in the blood pH and also seen collapse of acid-base balance (Lenyo, 2006).

The primary objective of this field study is to examine the effect of different treatments on the blood acid-base balance in cows with ketosis.

MATERIALS AND METHODS

The materials of this study were obtained from the farms in Burdur province and dairy cows presented to the University of Mehmet Akif Ersoy, Faculty of Veterinary Medicine, Department of Internal Medicine for diagnosis and treatment of ketosis. Twentyone ketotic cattle were equally divided into three treatment groups; group I received 750 mL of 30% dextrose intravenously plus 200 U insulin twice at 48 h interval, group II was given 750 mL of 30% dextrose intravenously and 0.04 mg kg^{-1} of dexamethasone intramuscularly and group III received 750 mL of 30% dextrose intravenously and 0.2 mg kg^{-1} of prednisolone intramuscularly. The application was in progress with daily injection in successive 2 days. No drug was applied to the control group.

For determination of the ketotic cows, rothera test was used in urine samples. Blood samples were collected from the diseased cows before and after treatment. Blood samples were taken from juguler vein into 1 mL tubes treated with sodium heparin kept on ice and analyzed within 3 h of collection. Blood pH, pO_2, pCO_2, BE, tCO_2, HCO_3, Na^+, Cl^-, Hb and Hct were simultaneously measured with the OPTI CCA blood gas analyzer.

All animals were clinically examined and rothera test was repeated in urine samples after treatment. The data was evaluated using ANOVA and Duncan test for the inter group analyses and t-test was employed for the within group analyses. SPSS statistical and computer package program was used for these analyses (Jerrold, 1996).

RESULTS AND DISCUSSION

In this study, the mean blood pH levels significantly increased in the group I when compared to the other groups ($p<0.05$) after the treatment. Mean blood chlor levels of the group II were significantly low ($p<0.01$) before treatment compared to the other groups, but after treatment no significant differences were determined between groups (Table 1).

Mean blood chlor levels of the group II were significantly higher ($p<0.05$) in after treatment measurement. But average blood pH levels of group I were higher ($p<0.01$) in after treatment than before treatment (Table 2).

Ketosis is a disorder that is associated with elevated concentrations of circulating ketone bodies, hypoglycemia, fatty infiltration and degeneration in the liver (Duffield, 2000; Lenyo, 2006). In recent years, there has been a decline in incidence of ketosis because of improved feeding and management. On the other hand, due to genetic improvements increasing in milk production lead to continued susceptibility of future cow. Since, the lactation ketosis is difficult to eliminate, the incidence of ketosis should be reduced with proper management (Moore and Ishler, 1997; Oetzel, 2004).

The cows in this study, exhibited clinical signs of weight loss, diminished appetite and milk production and acetone-odor breathing, which conforms with already reported signs (Kaneko, 1997; Moore and Ishler, 1997). Clinical symptoms disappeared and the urine Rothera test become negative after the treatment.

Ketosis is a metabolic disease, which occurs due to carbohydrate and lipid metabolism disorders and frequently cause acid-base balance disturbance in cows. In the cows excessive amounts of body fat are mobilized and only partially oxidized, resulting in the formation of ketone bodies. If these ketoacids build up in the blood, pH reduce and this result leads to the progress of metabolic acidosis (Bigner *et al.*, 1996; Lenyo, 2006). Markusfeld (1987), who studied a large number of cows, recorded 30.4% ketosis and acidosis in an average of 29.1% of cows. Sakai *et al.* (1993), claimed that urine pH was acidic in the ketotic cows, suggesting metabolic acidosis in ketotic cows.

Blood pH levels in all study groups were higher after treatment than before treatment, which confirms the idea

Table 1: The mean values of some blood gases in ketotic cows pre and postreatment and their statistical evaluations

	Parameters (X±SX)								
Groups	pH	pCO_2 (mmHg)	pO_2 (mmHg)	BE (mmol L^{-1})	tCO_2 (mmHg)	HCO_3 (mmol L^{-1})	Na^+ (mmol L^{-1})	K^+ (mmol L^{-1})	Cl^- (mmol L^{-1})
Pretreatment (n = 7)									
Control group	7.46±0.01	40.42±1.84	31.42±0.94	4.15±0.55	29.52±0.72	28.31±0.68	143.43±0.81	3.67±0.05	105.57±0.94^b
Group I	7.44±0.01	40.00±1.95	38.85±2.87	3.90±0.79	28.42±1.58	27.18±1.51	143.57±0.78	3.54±0.23	104.71±1.04^b
Group II	7.43±0.02	38.75±3.06	37.75±2.83	3.82±1.27	26.25±2.62	25.07±2.53	140.50±3.30	3.77±0.22	97.25±2.52^a
Group III	7.43±0.03	37.60±3.35	38.00± 2.75	3.24± 1.28	25.58± 2.13	24.40± 2.05	144.20± 1.46	3.46±0.25	103.20±0.66^b
p-value	0.575^{NS}	0.843^{NS}	0.105^{NS}	0.913^{NS}	0.330^{NS}	0.307^{NS}	0.420^{NS}	0.744^{NS}	0.002**
Postreatment (n = 7)									
Control group	7.46±0.01^b	40.42±1.84	31.42±0.94	4.15±0.55	29.52±0.72	28.31±0.68	143.43±0.81	3.67±0.05	105.57±0.94
Group I	7.49±0.01^a	40.71±1.26	37.71±1.30	6.55±1.55	31.67±1.64	30.42±1.60	144.86±0.63	3.28±0.10	104.00±0.89
Group II	7.45±0.00^b	40.66±1.47	35.50±1.38	3.46±0.92	28.95±1.06	27.70±1.01	144.00±1.06	3.70±0.08	105.33±1.22
Group III	7.44±0.01^b	39.60±2.89	42.20±3.24	3.44±1.59	28.08±2.22	26.86±2.14	143.00±1.38	3.44±0.06	105.00±1.34
p-value	0.012*	0.765^{NS}	0.726^{NS}	0.162^{NS}	0.180^{NS}	0.167^{NS}	0.227^{NS}	0.338^{NS}	0.613^{NS}

^{NS}: Not Significant; *: p<0.05; **: p<0.01; a,b: The differences between the groups of the same line marked with different letters are significant

Table 2: The blood gases concentrations of cows receiving three different treatment regimens and their statistical evaluations

	Parameters (X±SX)								
Groups	pH	pCO_2 (mmHg)	pO_2 (mmHg)	BE (mmol L^{-1})	tCO_2 (mmHg)	HCO_3 (mmol L^{-1})	Na^+ (mmol L^{-1})	K^+ (mmol L^{-1})	Cl^- (mmol L^{-1})
Group I (n = 7)									
Pretreatment	7.44±0.01	40.00±1.95	38.85±2.87	3.90±0.79	28.42±1.58	27.18±1.51	143.57±0.78	3.54±0.23	104.71±1.04
Postreatment	7.49±0.01	40.71±1.26	37.71±1.30	6.55±1.55	31.67±1.64	30.42±1.60	144.86±0.63	3.28±0.10	104.00±0.89
p-value	0.004 **	0.765^{NS}	0.726^{NS}	0.162^{NS}	0.180^{NS}	0.167^{NS}	0.227^{NS}	0.338^{NS}	0.613^{NS}
Group II (n = 7)									
Pretreatment	7.43±0.02	38.75±3.06	37.75±2.83	3.82±1.27	26.25±2.62	25.07±2.53	140.50±3.30	3.77±0.22	97.25±2.52
Postreatment	7.45±0.00	40.66±1.47	35.50±1.38	3.46±0.92	28.95±1.06	27.70±1.01	144.00±1.06	3.70±0.08	105.33±1.22
p-value	0. 459^{NS}	0. 601^{NS}	0.512^{NS}	0.827^{NS}	0.394^{NS}	0.391^{NS}	0.376^{NS}	0.775^{NS}	0.040 *
Group III (n = 7)									
Pretreatment	7.43±0.03	37.60±3.35	38.00± 2.75	3.24± 1.28	25.58± 2.13	24.40± 2.05	144.20± 1.46	3.46±0.25	103.20±0.66
Postreatment	7.44±0.01	39.60±2.89	42.20±3.24	3.44±1.59	28.08±2.22	26.86±2.14	143.00±1.38	3.44±0.06	105.00±1.34
p-value	0. 658^{NS}	0. 664^{NS}	0.354^{NS}	0.925^{NS}	0.441^{NS}	0.432^{NS}	0.567^{NS}	0.942^{NS}	0.276^{NS}

^{NS}: Not Significant, *: p<0.05, **: p<0.01

of Kupczynski and Chudoba-Drozdowka (2001). Mean blood pH levels of group I were significantly increased, which exhibits insulin and dextrose combination was more effective in the treatment of ketosis, this result in the current study corresponded to those of other previous studies (Sakai *et al*., 1993; Schwalm and Schultz, 1976).

In normal cows, infused glucose stimulates insulin secretion to enhance tissue uptake of the infused glucose (Sakai *et al*., 1993). Insulin secretion of ketotic cows can be depressed (Bigner *et al*., 1996; Schwalm and Schultz, 1976; Bigner *et al*., 1996), claims that insulin secretion is impaired during metabolic acidosis, which may reduce tissue uptake of glucose and resulting in greater glucose loss through urine. Metabolic acidosis in humans with ketoacidotic diabetics is most often associated with tissue resistance to insulin rather than with the inability to secrete insulin (Bigner *et al*., 1996). Insulin causes an increase of glucose uptake in peripheral tissues via GLUT-4, lipogenesis, glycogen and protein synthesis and suppresses lipolysis and hepatic gluconeogenesis (Kaske *et al*., 2001; Sakai *et al*., 1993). In addition, there were reduced liver triglyceride and Non-Esterified Fatty Acids (NEFAs) levels (Moore and Ishler, 1997). Some researchers have found that the addition of more insulin to the system does not help to suppress fatty acid mobilization, increase adipose tissue uptake, or stimulate hepatic glycolysis (Sakai *et al*., 1993).

Mean levels of pCO_2 and HCO_3^- in this study was confirmed by Kupczynski Chudoba-Drozdowska (2001). In the study, Kupczynsk and Chudoba-Drozdowska (2001) it was claimed that an increase in serum sodium (Na^+) content of cows with subclinical ketosis. On the contrary, Lenyo (2006), who reported the concentration of Na^+ in blood of the ill cows reduces while potassium (K^+) increases, which display the activation of compensatory body functions, aimed at utilization of hydrogen ions. Seifi *et al*. (2007), suggest that serum Na^+ and K^+ concentrations were not influenced by treatment. Similarly, Hamada *et al*. (1982), clamied that serum Na^+, K^+ and NEFA concentrations were not influenced by insulin treatment. In corresponding study, concentrations of Na^+ were not statistically influenced by treatment. Mean K^+

values of all groups in the study were lower than the results of other studies and the findings correlates with the results of Kupczynski and Chudoba-Drozdowska (2001). This decrease might be result of metabolic acidosis, because of K^+ infiltration into extracellular fluid.

Mordak and Nicpon (2006) stated that low level of blood Chlor (Cl^-) is observed in cows which are seen clinically healthy after parturition. This situation was suggested to result from appetite, atony in the stomach, decrease of Cl^- absorption in the ileum and metabolic acidosis (Kaneko, 1997).

In the study, mean blood Cl^- concentration observed in group II was close to the minimum values of the physiological range of healthy cows, however, the mean values obtained in this group after treatment was higher than before treatment. Similar results have been found in another study carried out previously by Kupczynski and Chudoba-Drozdowska (2001). Besides, the cause of this increase is believed to be due to glucocorticoids, which stimulates appetite and the rate of gluconeogenesis, obstruction of relapses and repress of the milk yield (Kaneko, 1997; Shpigel *et al*., 1996). On the other hand, Seifi *et al*. (2007) reported that serum Cl^- concentrations were not influenced by treatment.

CONCLUSION

As a result, it has been observed that the pH and Cl^- levels are close minimum optimal values in cows with ketosis. In the corresponding study, insulin and dextrose combination gave better results than other treatments, this combination also helped to return normal values of the acid-base balance in ketotic cows.

ACKNOWLEDGEMENT

Supported by Akdeniz University Scientific Research Project Unit, project number is 2003.01.0108.008.

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