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Scientific Report

Diabetic ketoacidosis in a buck: a case report

Jayalakshmi, K.*; Selvaraj, P.; Veeraselvam, M.; Yogeshpriya, S. and Venkatesan, M.

Department of Veterinary Medicine, Veterinary College and Research Institute, Orathanadu, Thanjavur-614 625, Tamil Nadu Veterinary and Animal Sciences University (TANUVAS), Chennai-51, Tamil Nadu, India

*__Correspondence:__ *K. Jayalakshmi, Department of Veterinary Medicine, Veterinary College and Research Institute, Orathanadu, Thanjavur-614 625, Tamil Nadu Veterinary and Animal Sciences University (TANUVAS), Chennai-51, Tamil Nadu, India. E-mail: jayalkshm22@gmail.com*

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Abstract

Background: Diabetic ketoacidosis (DKA) is a disorder of carbohydrate metabolism that causes frequent urination, emaciation, extreme tiredness and dehydration. There is little or no information available on DKA in male goat (buck). The present study was carried out to report a rare case of DKA in a buck. **Case description:** A 1.5 year old buck was presented with anorexia and cough. On physical examination of buck showed fever, dullness, poor body condition and pale conjunctival mucous membrane. **Findings/treatment and outcome:** The peripheral blood smear revealed the mixed infection of *Theileria* sp. and *Anaplasma* sp. The blood picture showed anaemia and leukocytosis. The animal was treated with buparvaquone (2.5 mg/kg**)** and long acting oxytetracycline (20 mg/kg). Post treatment evaluation was done 7 days after initial treatment. Animal showed mild improvement in feed intake, the body temperature becomes normal, but showed tachycardia with weak pulse. Subsequently, animal showed severe emaciation with frequent urination. Urinalysis revealed glycosuria, ketonuria and acidic urine (pH = 6.0). Serum biochemistry revealed hyperglycemia, hypoinsulinemia, increased level of fructosamine and triglycerides and confirmed spontaneous DKA. It was treated with biphasic isophane insulin (1.0 IU/kg) twice a day, regularly. The blood glucose level becomes normal after insulin therapy. Animal resumed adequate feed intake, improvement in haemoglobulin (Hb), packed cell volume (PCV), total erythrocyte count (TEC), and weight gain was observed. **Conclusion:** This case study gains significance, due to its successful recovery after insulin treatment, but it requires lifelong insulin therapy to manage insulin dependent diabetes mellitus (IDDM) in this goat.

Key words: Diabetes mellitus, Diabetic ketoacidosis, Goat, Insulin

Introduction

Diabetic ketoacidosis (DKA) is a syndrome characterized by hyperglycemia, glycosuria, ketonuria, and acidosis as a result of a relative or absolute insulin deficiency and an excess of insulin counter-regulatory hormones (ICRH) (Magee *et al*., 2001; Pandey *et al*., 2013). This hormonal imbalance promotes glycolysis, glycogenolysis and inhibits peripheral utilization of glucose by muscle results in hyperglycemia. In normal physiological circumstances, insulin limits the lipolysis. During lipolysis, free fatty acids are released into the circulation and converted into triglycerides and ketones in the liver. Some of the ketones are used as energy source and the rest of them buffered in the blood and excreted through urinary and respiratory systems. In DKA, the inhibitory function of insulin on lipolysis ceased and surplus quantity of ketones is produced in the circulation, the buffering capacity of ketones is exceeded and systemic acidemia develops (Causmaecker *et al*., 2009). The animal with DKA showed symptoms of frequent urination, increased thirst, emaciation, extreme tiredness, glycosuria, ketonuria, dehydration and increased susceptibility to secondary infection (Braun *et al*., 2008; Sahinduran *et al*., 2016).

Diabetes mellitus has been most commonly reported in small animals but rarely reported in other species such as cattle, horses, goats and sheep (Lutz *et al*., 1994; Braun *et al*., 2008). While reports on diabetes mellitus in small ruminants are very rare, studies on experimental induction of diabetes mellitus in goats with alloxan and streptozocin are available (Haghdoost *et al*., 2007). Not many research reports were available on public domain on the possible cause of spontaneous diabetes in goats. Few reports described the causes in cattle, horse and other animals, but not in goats (Stogdale, 1986; Clark, 2003). The present article describes the occurrence of a DKA in a non descriptive buck, which also had a concurrent mixed blood protozoan infection.

Case description

A 1.5 year old non descriptive male goat (buck) was presented for a ten day history of anorexia, coughing and low body condition during the month of June 2017. The animal was regularly fed with neem leaves and other grasses. Owner kept the animal as a pet in his home. The buck had not been dewormed, vaccinated, nor received any medication on presentation.

On clinical examination, the animal showed dullness

and depression, pale conjunctival mucous membrane and low body condition. Tracheal and thoracic auscultation and superficial lymph nodes examination did not show any abnormality. The rectal temperature was 41°C, respiratory rate, heart rate and pulse rates were 22/min, 89/min and 76/min, respectively. There was a suspension of rumen motility. The peripheral blood smear for the screening of intra-erythrocytic parasites, whole blood and a serum sample for haematobiochemical analysis and faecal sample for screening of helminthic egg and oocyst were collected and analyzed. The peripheral blood smear was stained with Giemsa stain for 30 min after methanol fixation for 1 min and examined microscopically (Khaki *et al*., 2015). Approximately 20,000 red blood cells (RBCs) in 100 fields per slide were screened. Morphologically *Anaplasma* sp. was observed as solid dots on the periphery of RBCs and *Theileria* sp. appeared as rod-shaped in the RBCs.

The animal was treated with buparvaquone (Zubion, Intas Pharmaceuticals Ltd., India) (2.5 mg/kg) and long acting oxytetracycline (20 mg/kg) (Pfizer Inc., Newyork), melaxicum (Melonex, Intas Pharmaceuticals Ltd., Ahmedabad, India) (0.5 mg/kg) and B-vitamins (3.0 ml) (Belamyl, Sarabhai Zydus Animal Health Ltd., Ahmedabad, Gujarat) intramuscularly. The owner reported mild improvement on the next day. The long acting oxytetracycline (20 mg/kg) was repeated after 48 h.

Post treatment evaluation was done seven days after initial treatment for blood parasitic infections. The animal showed mild improvement in feed intake. Subsequently, the animal showed severe emaciation, frequent urination with reduced feed intake and unable to stand and walk without assistance (Fig. 1), hence, further clinical assessment was warranted. Again peripheral blood smear, whole blood, serum and urine samples were collected for laboratory analysis on 8th day. Thoracic radiography and abdominal ultrasonography were done. On clinical suspicion for diabetes, additional serum biochemistry assessments for glucose, insulin, triglycerides, fructosomine and cholesterol were carried out apart from routine parameters on 8th, 9th and 10th day post initial treatment. Urinalysis was carried out by using URISCAN strip and biochemical test such as Benedict's test and sodium nitroprusside test (Rothra's test) was performed in urine sample to detect glucose and ketone bodies on days 8, 9, 10, and 14 post initial treatment.

Results

The initial peripheral blood smear was found to be positive for *Theileria* sp. and *Anaplasma* sp. (Fig. 2). The haematological analysis showed decreased levels of haemoglobulin (Hb), packed cell volume (PCV), total erythrocyte count (TEC), mean corpuscular haemoglobulin concentration (MCHC), and increased level of white blood cell (WBC) count (Table 1). The serum biochemistry revealed a slightly elevated level of glucose (122 mg/dl), but other parameters were normal (Table 1). The case was reviewed 7 days after initial treatment for blood parasitic infections and was found to have resumed feed intake; the feed intake was at reduced levels, the rectal temperature was 39.2°C, heart rate and pulse rates were 98/min and 89/min, respectively, but the strength of pulse was weak. On further laboratory analysis, the peripheral blood smear was negative for haemoprotozoa. The blood picture showed severe anaemia (decreased level of Hb, PCV, TEC, and MCHC) and persistent leukocytosis (WBC count 55×10^3) on 8th, 9th, and 10th day post initial treatment (Table 2). The serum biochemistry revealed hyperglycemia of 238, 312, and 411 mg/dl and elevated level of triglycerides of 40, 57, and 65 mg/dl on the 8th, 9th and 10th day post initial treatment, respectively, decreased level of insulin 0.29 and 0.2 mIU/L and increased level of fructosamine 350 and 406 µmol/L on 9th and 10th day, respectively (Table 3). The urinalysis showed glycosuria, ketonuria and acidic urine (pH = 6.0) and was negative for haemoglobulin and pus cells on day 8, 9 and 10 post initial treatment (Table 4). On thoracic radiography, there was no remarkable lesion in lungs. The liver, spleen and kidney were found to be normal in the ultrasonographic assessment.

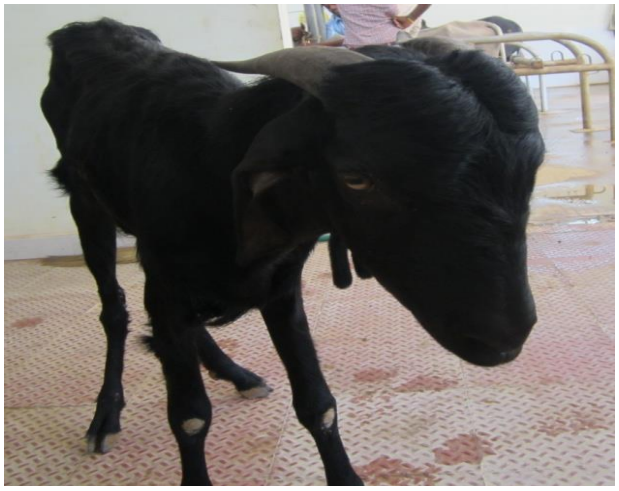

Fig. 1: Goat affected with diabetes mellitus before insulin treatment

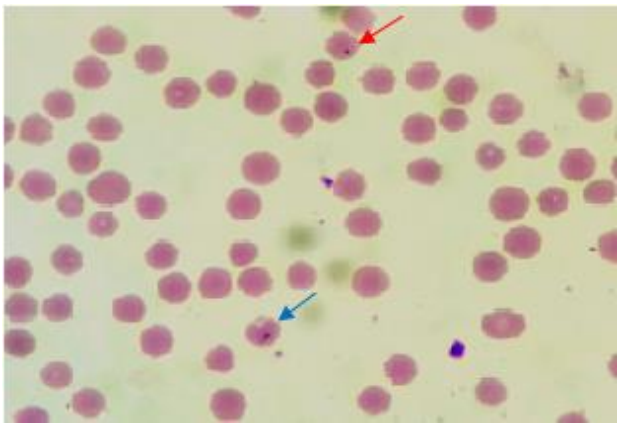

Fig. 2: *Theileria* sp. (red arrow) and *Anaplasma* sp. (blue arrow) in Giemsa stained peripheral blood smear (×100)

The treatment was started when blood glucose level was 411 mg/dl with an injection of biphasic isophane insulin (30/70%) (Human Mixtard, Novo Nodisk India Private Ltd., Bangalore, India) at 0.3 IU/kg body weight (BW) (Bonagura and Twedt, 2014). The blood glucose level was monitored at 3 h intervals and the dose of insulin was increased at the rate of 0.1-0.2 IU/kg BW based on the rate of reduction of glucose level. The dose was finally standardized to 1.0 IU/kg BW over a period of 48 h. The blood glucose level got reduced to 73 from 411 mg/dl after 48 h of insulin treatment (Fig. 3). Meanwhile, the excretion of glucose through urine was also quantified after insulin treatment. Initially, urine glucose was >2.0% (>2000 mg/dl) and it reduced to 0.5% and became negative after 36 and 48 h, respectively. Thereafter the goat was regularly treated with biphasic insulin (1.0 IU/kg) twice a day subcutaneously. Feed intake increased after insulin treatment. Haematology, serum biochemistry and urinalysis were reviewed two days after insulin dose optimization. The improvement was observed in blood picture; leukocyte count and blood glucose were normal (Tables 2, 3 and 4). The case was clinically reviewed at weekly intervals. Measurement of blood glucose and urinalysis were done at weekly interval for four weeks. Mild fluctuations of glucose levels without glycosuria and ketonuria were noticed (Table 5). Post insulin treatment evaluation was done after one month (Tables 2, 3, and 4). The blood picture revealed an improvement and weight gain was observed as it increased from 25 to 32 kg along with the mild elevation of blood glucose 89 mg/dl.

Table 1: Pre-treatment haematobiochemical parameters

Hematology		Serum biochemistry	
Haemoglobulin (g/dl)	4.8	Total protein (g/dl)	6.0
PCV (%)	17	Albumin (g/dl)	2.5
RBC (10^6/µL)	7.9	Globulin (g/dl)	3.5
WBC (10^3/µL)	40	Glucose (mg/dl)	122
MCV (fl)	21.5	BUN (mg/dl)	24
MCH (pg)	6.0	Creatinine (mg/dl)	0.8
MCHC (g/dl)	28.2	AST (U/L)	398

PCV: Packed cell volume, RBC: Red blood cell, WBC: White blood cell, MCV: Mean corpuscular volume, MCH: Mean corpuscular haemoglobulin, MCHC: Mean corpuscular haemoglobulin concentration, BUN: Blood urea nitrogen, and AST: Aspartate aminotransferase

Table 2: Haematological parameters before and after insulin treatment

Parameters	Before insulin treatment			Two days after insulin dose optimization (14th day PIT)	One month after insulin treatment
	Day 8 PIT	Day 9 PIT	Day 10 PIT		
Haemoglobulin (g/dl)	3.4	3.2	3.1	4.7	9.0
PCV (%)	11.8	11.5	11.2	14.0	28
RBC (10^6/µL)	6.9	6.5	6.1	8.5	15.8
WBC (10^3/µL)	55	62	69	13.8	12.9
MCV (fl)	17.0	17.6	18.3	16.4	17.7
MCH (pg)	4.9	4.9	5.08	5.5	5.6
MCHC (g/dl)	28.8	28.6	27.6	33.5	32

PCV: Packed cell volume, RBC: Red blood cell, WBC: White blood cell, MCV: Mean corpuscular volume, MCH: Mean corpuscular haemoglobulin, MCHC: Mean corpuscular haemoglobulin concentration, and PIT: Post initial treatment

Table 3: Serum biochemistry before and after insulin treatment

Parameters	Before insulin treatment			Two days after insulin dose optimization (14th day PIT)	One month after insulin treatment
	Day 8 PIT	Day 9 PIT	Day 10 PIT		
Total protein (g/dl)	5.6	5.6	5.4	5.9	6.8
Albumin (g/dl)	2.3	2.2	2.2	2.6	3.1
Globulin (g/dl)	3.3	3.4	3.2	3.3	3.7
Glucose (mg/dl)	238	312	411	77	89
BUN (mg/dl)	30	32	29	22	31
Creatinine (mg/dl)	0.6	0.7	0.8	0.6	0.9
AST (U/L)	412	414	408	381	56
Cholesterol (mg/dl)	126	130	132	118	112
Triglycerides (mg/dl)	40	57	65	-	4.4
Fructosamine (µmol/L)	-	350	406	-	185
Insulin (mIU/L)	-	0.29	0.2	-	-

BUN: Blood urea nitrogen, AST: Aspartate aminotransferase, and PIT: Post initial treatment

Table 4: Urinalysis before and after insulin treatment

Parameters	Before insulin treatment			After insulin treatment		One month after insulin treatment
	Day 8 PIT	Day 9 PIT	Day 10 PIT	Day 12 PIT	Day 14 PIT	
Specific gravity	1.061	1.078	1.090	1.028	1.023	1.032
Urine pH	Acidic	Acidic	Acidic	Alkaline	Alkaline	Alkaline
Protein	-	-	-	-	-	-
Glucose	+	+	+	-	-	-
Ketone bodies	+	+	+	-	-	-
Bilirubin	-	-	-	-	-	-
Urobilinogen	-	-	-	-	-	-
Erythrocytes	-	-	-	-	-	-
Leukocytes	-	-	-	-	-	-

(+): Positive, (-): Negative, and PIT: Post initial treatment

Table 5: Measurement of blood glucose and urinalysis after insulin treatment

Parameters	First week	Second week	Third week	Fourth week
Blood glucose (mg/dl)	78	80	87	82
Urine glucose	-	-	-	-
Ketonuria	-	-	-	-
Specific gravity	1.022	1.021	1.023	1.023
Urine pH	Alkaline	Alkaline	Alkaline	Alkaline

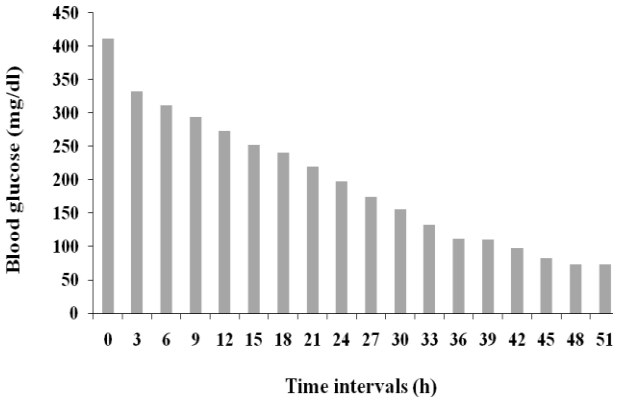

Fig. 3: Reduction of blood glucose level after insulin treatments

Discussion

Diabetes is a metabolic and common endocrine disorder in humans and many animals (Haghdoost *et al*., 2007). It has been most commonly reported in small animals, but rarely reported in other species such as cattle, horses, goats and sheep (Clark, 2003; Braun *et al*., 2008; Sahinduran *et al*., 2016).

Our clinical and laboratory findings are concomitant with the report of Braun *et al*. (2008). However, insulin level observed in this case (0.29 and 0.2 µU/L on subsequent days) was lower than those observed in the case report of Braun *et al*. (2008), who reported an insulin level of 6 µU/L in a female goat. Healthy control goats were found to have an insulin level of 17-24 µU/L in his study. These indicate the worst severity of insulin dependent diabetes mellitus in the male goat in this study. Braun *et al*. (2008) attributed the possible causes of anaemia were parasitism, hyperglycemia and hypoinsulinemia in their study. The hypoinsulinemia may be due to degeneration of β-cells of pancreas fail to produce insulin. Stogdale (1986) described secondary diabetes mellitus in cattle due to viral infections (foot and mouth disease, bovine viral diarrhoea) and metabolic disorders such as fatty liver, fat cow syndrome and chronic insulinitis (Kitchen and Roussel, 1990; Nazifi *et al*., 2004). Currently, insulin dependent diabetes mellitus (IDDM) in human is thought to be the result of autoimmune reaction to β-cells triggered by various viral infections in genetically predisposed individuals (Handwerger *et al*., 1980). The development of autoimmune reaction in IDDM is due to expression of new antigenic site on surface of β-cells or breakdown of normal immunological tolerance induced by viral infection (Cudworth and Festenstein, 1978). In this study, no attempt was made to investigate genetic and viral infections. Taniyama *et al*. (1993) reported that selective loss of β-cells and lymphocytic islet adenitis due to autoimmune reaction induced by some viral infections in cattle.

Persistent leukocytosis in this study is concordant with the report of Xu *et al*. (2013), who observed that inflammation in DKA state is associated with elevated total WBC and neutrophil counts and that it may play a role in the development of profound pathophysiology. The stress due to hyperglycemia and ketonemia may be responsible for leukocytosis in this study. Treatment with insulin had a favourable effect on goat's blood glucose control and WBC count became normal. In this study elevated level of serum fructosamine is a good indicator of hyperglycemia in the diabetic goat. The serum frucosamine level in the present study was 350 and 406 µmol/L on subsequent days, which was lower than those observed in the case report of Braun *et al*. (2008), who reported a level of 552 µmol/L (normal 170-250 µmol/L). Serum fructosamine concentrations were reported to increase when glycemic control in diabetic

dogs worsens and decreases when glycemic control is improved. The serum fructosomine concentration is not affected by acute increase in blood glucose due to either stress or excitement (Nelson, 2015). The elevated level of triglycerides in this study is in accordance with the report of Jones *et al*. (2014), who reported that the impaired activity of lipoprotein lipase in insulin dependent diabetes mellitus is responsible for the increased levels of triglycerides. The lipoprotein lipase activity is limited by insulin. During insulin deficiencies the control of lipoprotein lipase activities are broken down and this leads to increased synthesis of endogenous free fatty acids in the liver. However, the ultrasound assessment of liver is normal. This is in accordance with the report of Levinthal and Tavill (1999), who reported that Type 1 diabetes is not associated with liver fat accumulation if blood glucose level is well controlled. Hepatic fat accumulation is a well-recognized complication of Type II diabetes in humans with a reported frequency of 40-70% regardless of blood glucose control.

In the present study, the treatment of diabetic goat with biphasic isophane insulin was carried out based on the current protocols used in small animals (Bonagura and Twedt, 2014). The treatment enabled the goat to improve and led to a good quality life without any polyuria, glycosuria and ketonuria. It also gains BW; however, it requires lifelong administration of insulin to manage this insulin dependent diabetes mellitus in this male goat. The client was advised for lifetime care.

In this study the possible cause of DKA was unknown and there is a lack of documentation on possible causes in a goat in the published reports also. Incidentally, there was a mixed infection with *Anaplasma* sp. and *Theileria* sp. in this goat and its possible influence on the occurrence of diabetes is also uncertain. This case study gains significance due to its successful recovery after insulin treatment and the good quality of life being experienced by the goat now.

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