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Accuracy of blood beta-hydroxybutyrate and plasma acetoacetate for diagnosis of canine diabetic ketoacidosis

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Accuracy of blood beta-hydroxybutyrate and plasma acetoacetate for diagnosis of canine diabetic ketoacidosis

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Abstract

Diabetic ketoacidosis (DKA) is a life-threatening complication in diabetic dogs. It is caused by an increase in production and accumulation of ketone bodies in the blood, which results in metabolic acidosis. The objective of this study was to compare the diagnostic accuracy between the measurement of blood beta-hydroxybutyrate (β -OHB) concentration using a point-of-care sensor and plasma acetoacetate (AcAc) level using a urine strip test for the diagnosis of canine DKA. A total of 60 dogs were enrolled into each group: DKA (n=16), diabetic ketosis (DK) (n=5), and control (n=39). The following parameters including blood β -OHB, plasma AcAc, blood glucose, urinary AcAc, urinary glucose, and blood gas analysis were evaluated and compared among the groups. Both DKA and DK groups had higher concentrations of blood β -OHB and blood glucose than the control group ($P < 0.001$), but no statistical difference was found between the DKA and DK groups. Likewise, plasma and urinary AcAc were detected only in the DKA and DK dogs, but there were no significant differences between the groups. The sensitivity and specificity of the β -OHB POC sensor had a wide variation at various cut-off values. However, the cut-off value of blood β -OHB concentration at 2.1 mmol/L revealed 100% sensitivity. The sensitivity and specificity of plasma AcAc varied extensively at cut-off values ranging from 0 to 3+. Therefore, the presence or absence of plasma AcAc could not be used to diagnose dogs with DKA. Instead, blood β -OHB at the concentration of ≥ 2.1 mmol/L should be used for the screening of DKA.

Keywords: acetoacetate, beta-hydroxybutyrate, diabetic ketoacidosis, dog, point-of-care

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Introduction

Diabetic ketoacidosis (DKA) is a life-threatening condition for diabetic dogs, which requires an immediate diagnosis and urgent course of treatment. Diabetic ketoacidosis usually develops when the insulin is insufficient and there are increases in secretion of glucagon, cortisol, epinephrine and growth hormone, stimulating the production of ketone bodies, including acetoacetate (AcAc), beta-hydroxybutyrate (β -OHB), and acetone from the liver (Feldman and Nelson, 2004). Excessive accumulation of AcAc and β -OHB eventually results in metabolic acidosis. Diagnosis of DKA in dogs commonly relies on the detection of hyperglycemia, glucosuria, ketonuria, and metabolic acidosis (Kerl, 2001). In clinical setting, ketonuria is usually detected using a urine test strip based on the analysis with the nitroprusside reaction. However, the urine test strip only detects AcAc, which may produce false negative or false positive results in veterinary patients (Di Tommaso et al., 2009). Furthermore, dogs with DKA are often dehydrated, therefore, obtaining a urine sample from these animals may be difficult. A previous study has shown that the detection of plasma AcAc with a urine test strip in diabetic dogs and cats provides similar accuracy to the detection of urinary AcAc (Brady et al., 2003). Hence, the presence of plasma AcAc detected by the urine test strip is also suggested for the diagnosis of DKA in a suspicious dog when a urine sample is not currently available.

In human medicine, the measurement of β -OHB, which is the predominant ketone body in the blood circulation, is preferred over urine ketone testing for diagnosing and monitoring in patients with DKA (Goldstein et al., 2004). A point-of-care (POC) sensor for measurement of β -OHB is commercially available and has been validated for clinical setting in human patients (Khan et al., 2004). In veterinary medicine, the utility of β -OHB measurement for dogs has been performed. For example, serum β -OHB concentration measured by the enzymatic method was shown to be different between diabetic dogs with or without ketosis (Duarte et al., 2002). There was a positive correlation of β -OHB concentration which was determined by the enzymatic method and a POC sensor in dogs with DKA (Hoenig et al., 2008; Henderson and Schlesinger, 2010). A β -OHB POC sensor had higher diagnostic accuracy than the measurement of urinary AcAc with the urine test strip for dogs with DKA (Di Tommaso et al., 2009). Due to the limited data, further studies are needed for validation of the β -OHB measurement in dogs with DKA. Studies comparing the detection of β -OHB and the measurement of plasma AcAc for the diagnosis of canine DKA are currently unavailable. Therefore, the objective of this study was to compare the diagnostic accuracy between the measurement of β -OHB concentration in the blood using a POC sensor and plasma AcAc level using a urine strip test for the diagnosis of DKA in dogs.

Materials and Methods

This study was approved by the Chulalongkorn University Laboratory Animal Care and Use Committee (Protocol No. 1431095). Written

consent was obtained from dogs' owners prior to sample collection.

Dogs: Samples were collected from dogs presented at the Small Animal Teaching Hospital of Chulalongkorn University from December 2014 through November 2015. A total of 60 dogs were enrolled and classified into 3 groups: 16 dogs in the DKA group, 5 in the DK group (diabetic ketosis without metabolic acidosis) and 39 in the control group. Signalment and clinical data of all dogs were recorded.

Inclusion criteria of dogs in the DKA group were as follows: 1) hyperglycemia (blood glucose level > 250 mg/dL), 2) glucosuria (urinary glucose $\geq 1+$), 3) ketonuria (urinary AcAc $\geq 1+$) and 4) the presence of metabolic acidosis (venous blood pH < 7.35 and bicarbonate < 15 mmol/L). The DK group consisted of dogs that met the first 3 criteria with the absence of metabolic acidosis. The control group consisted of dogs that were clinically healthy dogs presented at the hospital for purposes of vaccination, neutering, or health check. These dogs had a blood glucose level less than 250 mg/dL without glucosuria, ketonuria and metabolic acidosis.

Sample Collection and Analysis: Blood samples were collected from all 60 dogs that were fasted for a minimum period of 12 hours, and the administration of insulin was not performed for all dogs in the DKA group and the DK group. A blood sample of 1 mL was collected from the cephalic or saphenous vein into a 1-mL syringe coated with heparin. A few drops of blood were applied directly to a glucometer (Accu-check Active, Roche, Busel) and β -OHB POC sensor (FreeStyle Optium H β ketone test strips, Abbott Diabetes Care, Witney) for the measurement of glucose and β -OHB, respectively. A venous blood gas analysis was performed on the heparinized blood using an automated analyzer (Rapidlab 348, Siemens, Erlangen) in order to determine blood pH, bicarbonate (HCO_3^-), and partial pressure of carbon dioxide (PvCO_2). The rest of the heparinized blood was centrifuged at 1,500 g for 3 minutes, and plasma was used for the detection of plasma AcAc using a urine test strip (Combur 9 Test, Roche, Mannheim). A urine sample of 0.5 mL was also collected from individual dogs via voiding or urinary catheterization, and was tested for the level of urinary glucose and urinary AcAc using a urine test strip (Combur 9 Test, Roche, Mannheim).

Statistical Analysis: The maximum level of blood glucose concentration determined by the POC sensor is 600 mg/dL. The blood glucose level was recorded as 600 mg/dL when the glucose POC sensor reading was "HI". The range of blood β -OHB concentration detected by the POC sensor is between 0.0-8.0 mmol/L. The β -OHB concentration was recorded as 8 mmol/L when the β -OHB POC sensor reading was "HI". The urinary glucose level was recorded as a scale ranging from 0 to 4+ as follows: 0 (0 mg/dL), 1+ (50 mg/dL), 2+ (100 mg/dL), 3+(300 mg/dL) and 4+ (1,000 mg/dL). The plasma and urinary AcAc levels were recorded as a scale ranging from 0 to 4+ as follows: 0 (0 mmol/L), 1+ (1 mmol/L), 2+ (5 mmol/L) and 3+ (15 mmol/L).

All of the following parameters including

blood glucose level, blood β -OHB concentration, plasma AcAc level, urinary AcAc level, urinary glucose level, venous blood pH, venous HCO_3^- , and PvCO_2 were compared among all groups of dogs using one-way analysis of variance (ANOVA) or Kruskal-Wallis test, and multiple comparison was performed with the least significant difference (LSD). Diagnostic accuracy from the measurement of blood β -OHB concentration and plasma AcAc level in the DKA and DK groups was calculated based on the sensitivity (the proportion of positives in the DKA group) and specificity (the proportion of negatives in the DK group) at various cut-off values. Statistical significance was considered at a *P*-value of < 0.05 .

Results

Overall, the median age of the 60 dogs was 8 years (range: 1-15 years). There was no difference in the age among the dogs of all groups. Twenty-one (35.0%) dogs were intact males, 6 (10.0%) were neutered males, 17 (28.3%) were intact female, and 16 (26.7%) were

neutered female. The breeds of dogs included in the study were Poodle (30.0%), Shih-tzu (16.7%), mixed breed (18.3%), Pug (8.3%), Chihuahua (6.7%), Pomeranian (5.0%), Golden Retriever (3.3%) and each of the following breeds including Maltese, Doberman Pinscher, Miniature Pinscher, Boxer, Bichon Frise, Terrier, and Dachshund (11.7%). The majority of the dog breeds included in the DKA group was Poodle (75.0%).

In this study, all dogs in the DKA group ($n=16$) had never been diagnosed with DM or were being treated with insulin. The range of blood glucose level of these dogs was from 335 to 600 mg/dL (mean \pm S.D.: 509.1 ± 90.1 mg/dL). The dogs had blood β -OHB concentration ranging from 2.1 to 8.0 mmol/L (mean \pm S.D.: 5.1 ± 1.9 mmol/L). The plasma AcAc (range: +1 to +3) was detected in 15 of the 16 DKA dogs. The urinary AcAc (range: +1 to +3) and urinary glucose (range: +2 to +4) were detected in all 16 dogs. These dogs also had metabolic acidosis (Table 1).

Table 1 Comparison of clinical parameters in DKA, DK and control groups.

Parameter	DKA (n=16)	DK (n=5)	Control (n=39)	<i>P</i> -value
Blood glucose (mg/dL)*	509.1 \pm 90.1 ^a	462.0 \pm 152.7 ^a	75.6 \pm 14.7 ^b	<0.001
Blood β -OHB (mmol/L)*	5.1 \pm 1.9 ^a	4.4 \pm 2.7 ^a	0.3 \pm 0.2 ^b	<0.001
Plasma AcAc (mmol/L)	5 (0-15) ^a	5 (1-15) ^a	0	0.985
Urinary AcAc (mmol/L)	5 (1-15) ^a	5 (1-15) ^a	0	0.435
Urinary glucose (mg/dL)	1000 (100-1000) ^a	300 (300-1000) ^a	0	0.611
Venous blood pH*	7.1 \pm 0.1 ^a	7.4 \pm 0.1 ^b	7.4 \pm 0.1 ^b	<0.001
HCO_3^- (mmol/L)*	8.9 \pm 2.1 ^a	20.9 \pm 3.2 ^b	21.7 \pm 4.3 ^b	<0.001
PvCO_2 (mmHg)*	28.3 \pm 6.5 ^a	33.3 \pm 2.1 ^a	33.9 \pm 11.9 ^a	0.050

* Data are presented as Mean \pm S.D., otherwise Median (range)

^{a, b} Different superscript letters in each parameter in the same row signify a statistical significance.

There were 5 dogs included in the DK group, and they had a range of blood glucose level between 287 and 600 mg/dL (mean \pm S.D.: 462.0 ± 152.7 mg/dL) and blood β -OHB concentration ranging from 1.5 to 7.9 mmol/L (mean \pm S.D.: 4.4 ± 2.7 mmol/L). Three of the DK dogs had unknown history of DM and had never been treated with insulin. The blood glucose level and blood β -OHB concentration were 570.0 ± 51.96 mg/dL and 6.2 ± 1.6 mmol/L, respectively. The other 2 dogs, on insulin therapy, had blood glucose level and blood β -OHB concentration at 300.0 ± 18.38 mg/dL and 1.7 ± 0.3 mmol/L, respectively. The plasma AcAc (range: +1 to +3), urinary AcAc (range: +1 to +3), and urinary glucose (range: +3 to +4) were detected in all dogs with DK. No dogs in the DK group had metabolic acidosis, and the venous blood pH, HCO_3^- , and PvCO_2 were within the normal range (Table 1).

All dogs in the control group ($n=39$) had blood glucose level and blood β -OHB concentration ranging from 54 to 141 mg/dL (mean \pm S.D.: 75.6 ± 14.7 mg/dL) and 0.1 and 1.1 mmol/L (mean \pm S.D.: 0.3 ± 0.2 mmol/L), respectively. The plasma AcAc, urinary AcAc, and urinary glucose were not detected in these dogs. They had venous blood pH, HCO_3^- , and PvCO_2 within the normal range (Table 1).

In the present study, the dogs in the DKA and DK groups had significant increases in blood β -OHB

concentration and blood glucose level than those of the control group ($P < 0.001$). However, there were no significant differences in the blood β -OHB concentration and blood glucose between the DKA and DK groups (Table 1). The plasma AcAc, urinary AcAc, and urinary glucose were detected in only the dogs of the DKA and DK groups, but there were no significant differences in the median values of these parameters between the groups (Table 1).

The sensitivity and the specificity of the β -OHB POC sensor and the urine test strip measuring plasma AcAc for the diagnosis of DKA were evaluated. The β -OHB POC sensor had the sensitivity between 100.0%-6.3% and the specificity between 40.0%-100.0% at the cut-off values from 2.1 to 8.0 mmol/L (Table 2). The sensitivity of the measurement of plasma AcAc at the cut-off values ranging from 0 to 3+ were between 100%-12.5% and the specificity were between 0%-80% at the same cut-off values (Table 3).

Table 2 Diagnostic accuracy for determination of blood β -OHB with a POC sensor for diagnosis of diabetic ketoacidosis in dogs.

Blood β -OHB concentration		
Cut-off (mmol/L)	Sensitivity (%)	Specificity (%)
≥ 2.0	100.0	40.0
≥ 2.1	100.0	40.0
≥ 2.2	93.8	40.0
≥ 2.3	93.8	40.0
≥ 2.4	87.5	40.0
≥ 2.5	87.5	40.0
≥ 3.0	81.3	40.0
≥ 3.2	81.3	40.0
≥ 3.5	75.0	40.0
≥ 3.8	75.0	40.0
≥ 4.0	75.0	40.0
≥ 4.5	62.5	40.0
≥ 5.0	50.0	60.0
≥ 5.5	43.8	60.0
≥ 6.0	43.8	60.0
≥ 6.5	25.0	80.0
≥ 7.0	25.0	80.0
≥ 7.5	6.3	80.0
≥ 8.0	6.3	100.0

Table 3 Diagnostic accuracy for determination of plasma AcAc with a urine test strip for diagnosis of diabetic ketoacidosis in dogs.

Plasma AcAc level		
Cut-off (Scale 0-3)	Sensitivity (%)	Specificity (%)
≥ 0 (0)	100.0	0.0
$\geq 1+$ (1)	93.8	0.0
$\geq 2+$ (5)	62.5	40.0
$\geq 3+$ (15)	12.5	80.0

Discussion

Most dogs included in this study were middle-aged to old, which is comparable to the age of the dog populations in previous large studies (Duarte et al., 2002; Hume et al., 2006). There was no difference in the age distribution among the 3 groups in the present study. Although the dog breeds were different from reports of previous studies (Hume et al., 2006), this indicates that breed prevalence is dependent on popularity in various countries. Therefore, the levels of blood β -OHB and plasma AcAc should reflect the ketotic status, and is less likely to be affected either by age or breed of the dog.

In this study, the blood glucose level and blood β -OHB concentration were significantly higher in all DKA and DK dogs than those of the control dogs (Table 1). However, these parameters were not significantly different and overlapping values were found between the DKA and DK groups. A previous study showed that there were significant increases in blood glucose and β -OHB in DKA dogs compared with DK dogs (Di Tommaso et al., 2009). Difference in the results between the present and previous studies might be explained by the variation of diabetic and ketotic status among individual dogs at the time of blood sample evaluation. According to the result of this study, the DK dogs without history of DM had similar blood glucose level and β -OHB concentration to the DKA dogs. It was likely that these dogs would make a transition from DK to DKA if they were left untreated. Another explanation is that the DK dogs had concurrent vomiting and dehydration which might result in metabolic acidosis, and these dogs were misclassified into the DKA group (Duarte et al., 2002).

Therefore, it is suggested that initial measurement of blood β -OHB concentration in new patients with suspicion of DKA should be interpreted with caution and the optimal cut-off value can be useful for the discrimination of DKA from DK status.

Because the limit of detection of blood β -OHB concentration measured by the POC sensor ranges from 0.0 to 8.0 mmol/L, the diagnostic accuracy of the POC sensor for the determination of DKA was evaluated within this range. This study demonstrated 100% sensitivity at the cut-off value of 2.1 mmol/L, and the sensitivity dropped below 90% at the cut-off values more than 2.3 mmol/L. These results suggest that DKA dogs are most likely to have blood β -OHB concentration higher than or equal to 2.1 mmol/L. In contrast, the specificity of the β -OHB POC sensor was disappointed at most cut-off value. The POC sensor had 80% specificity at the cut-off values more than or equal to 6.5 mmol/L, which is close to the upper limit of the POC sensor. Therefore, the discrimination of DKA dogs from DK dogs could not be done correctly at any cut-off values. The major reason of dissatisfaction is due to the limited number of DK dogs that had broad variation of blood β -OHB concentration. Therefore, the specificity of the POC sensor is yet to be determined if there are more DK dogs in the study. Although, according to the results, the present study did not support the measurement of blood β -OHB concentration via a β -OHB POC sensor as a diagnostic tool for DKA, it should still be used for the screening of DKA in canine patients. Because dogs with DKA are at high risk of death, no or minimal false negative results should be warranted. In this case, selection of a cut-off value with which the test will have high sensitivity is a better choice. It is suggested to set

the cut-off value at 2.1 mmol/L, which provides 100% sensitivity and 40% specificity. At this cut-off value, DKA will definitely be ruled out when a dog has blood β -OHB concentration lower than 2.1 mmol/L. All dogs with possible DKA (blood β -OHB concentration \geq 2.1 mmol/L) will be detected, and other complementary tests should subsequently be used to confirm DKA. The β -OHB POC sensor could not be used as the only single test to differentiate between DKA and DK, therefore, an assessment of venous blood gas should be performed afterward to increase the likelihood of DKA in a suspicious dog.

Previous studies have attempted to determine the exact cut-off value of blood β -OHB concentration to differentiate between DKA and DK, but a definite cut-off value is still unknown. However, the optimal cut-off value suggested by previous studies is 3.8 mmol/L, which correlates with 72% sensitivity and 95% specificity in one study (Duarte et al., 2002) and 70% sensitivity and 92% specificity in another study (Bresciani et al., 2014). In addition, the cut-off values of 3.5 mmol/L and 2.8 mmol/L showed a positive likelihood ratio (+LR) and a negative likelihood ratio (-LR), respectively, which could predict or exclude DKA in dogs (Di Tommaso et al., 2009). Previous studies preferred the cut-off value with high specificity because the dogs were at higher risk of clinical disease of DKA and specific management should be initiated immediately.

The control dogs in the present study had a significantly lower blood β -OHB concentration compared with the dogs with DKA or DK. The absence of ketosis in these dogs was concurrently confirmed by the negative urinary AcAc and plasma AcAc. These results showed that a short period of fasting, approximately 12 hours, might have a minimal effect on the production of ketone bodies in the blood circulation, and fasting did not interfere with any ketone testing in this study. It was found that the normal range of blood β -OHB concentration determined in 39 control dogs (0.1-1.1 mmol/L) was higher than the reference range measured by an enzymatic method (0.02-0.15 mmol/L) determined in 50 healthy dogs (Duarte et al., 2002). Because the results from the β -OHB POC sensor and the enzymatic assay were not compared in the present study, it is possible that the POC sensor overestimated the β -OHB, as shown in a previous study (Henderson and Schlesinger, 2010). The overestimation of β -OHB might be helpful for close monitoring of ketosis in diabetic dogs.

A urine test strip is frequently used to measure AcAc in urine or plasma. In this study, ketonemia detected by a urine test strip within a range of 1+ to 3+ was found in 15/16 DKA dogs and all DK dogs. In addition, the diagnostic accuracy for DKA with the measurement of plasma AcAc was limited. The cut-off value of 0 (zero) showed 100% sensitivity and 0% specificity. Therefore, the presence of ketonemia from the urine test strip did not discriminate DKA from DK and, on the other hand, the absence of ketonemia did not exclude DKA based on the test result of plasma AcAc alone. Concurrent testing of either blood β -OHB or urine ketone, and blood gas analysis are warranted for the confirmation

of DKA in all dogs. It was not unexpected that the dogs with DKA might have very low AcAc concentration in the blood circulation, which did not reach a renal threshold and was excreted in the urine (Stojanovic and Ihle, 2011). The production of β -OHB over AcAc, as frequently found in human patients, may be involved, and an increase in β -OHB concentration in dogs with metabolic acidosis was expected (Miles and Gerich, 1983).

The limited number of dogs in the DK group is the major limitation of the present study. As discussed above, a cut-off value of blood β -OHB concentration for the discrimination of DK versus DKA could not be determined. However, the usage of β -OHB POC sensor also has other advantages, particularly in critical, suspicious dogs because it allows the measurement of blood β -OHB within 10 seconds, and only 1-2 μ L of blood sample is needed.

In conclusion, the detection of ketonemia using the β -OHB POC sensor is useful for the screening of DKA at the cut-off value of 2.1 mmol/L. DKA is unlikely in dogs with blood β -OHB concentration less than 2.1 mmol/L. However, the detection of ketonemia using a urine test strip regardless of plasma AcAc levels could result in overlapping findings between DKA and DK, and DKA might be probably overlooked when ketonemia is absent.

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บทคัดย่อ

ความแม่นยำของค่าเบตาไฮดรอกซีบิวทิเรตในเลือดและค่าอะซิโตะซิเตทในพลาสมา เพื่อการวินิจฉัยภาวะเลือดเป็นกรดจากคีโตนจากเบาหวานในสุนัข

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การเกิดภาวะเลือดเป็นกรดจากคีโตนจากเบาหวาน (DKA) ในสุนัขจัดเป็นภาวะแทรกซ้อนที่ร้ายแรงถึงชีวิต ซึ่งเป็นผลมาจากการสร้างและการสะสมของสารคีโตนในกระแสเลือดที่เพิ่มขึ้นจนส่งผลให้เกิดภาวะกรดจากการเผาผลาญ วัตถุประสงค์ของการศึกษานี้เพื่อเปรียบเทียบความแม่นยำระหว่างการวัดความเข้มข้นของเบตาไฮดรอกซีบิวทิเรตซึ่งวัดด้วยเครื่องตรวจวิเคราะห์ ณ จุดที่ดูแลสัตว์ป่วย และค่าอะซิโตะซิเตทในพลาสมาซึ่งตรวจด้วยแผ่นจุ่มตรวจปัสสาวะ เพื่อวินิจฉัยภาวะ DKA โดย แบ่งสุนัขจำนวน 60 ตัวออกเป็นกลุ่มที่มีภาวะ DKA (16 ตัว) กลุ่มที่เป็นโรคเบาหวานร่วมกับมีคีโตนแต่ไม่พบภาวะกรดจากการเผาผลาญ (DK) (5 ตัว) และกลุ่มควบคุม (39 ตัว) ทำการวัดและเปรียบเทียบพารามิเตอร์ระหว่างกลุ่ม ได้แก่ ระดับน้ำตาลในเลือด เบตาไฮดรอกซีบิวทิเรตในเลือด อะซิโตะซิเตทในพลาสมา การวิเคราะห์กรดต่างในเลือด ระดับน้ำตาลในปัสสาวะ และอะซิโตะซิเตทในปัสสาวะ การศึกษาพบว่า สุนัขกลุ่ม DKA และ DK มีความเข้มข้นของเบตาไฮดรอกซีบิวทิเรตในเลือดสูงกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ ($P < 0.0001$) แต่ไม่พบความแตกต่างระหว่างกลุ่มทั้งสอง ตรวจพบอะซิโตะซิเตทในพลาสมาและปัสสาวะเฉพาะในสุนัขกลุ่ม DKA และ DK แต่ไม่พบความแตกต่างระหว่างสองกลุ่มนี้เช่นกัน ค่าความไวและความจำเพาะของเบตาไฮดรอกซีบิวทิเรตในเลือดเปลี่ยนแปลงไปตามค่าที่อ่านผลเป็นบวก (cut-off value) แต่ค่า อย่างไรก็ตาม cut-off value ของเบตาไฮดรอกซีบิวทิเรตในเลือดสูงสุดที่ 2.1 mmol/L มีความไว 100% ในขณะที่ค่าความไวและความจำเพาะของอะซิโตะซิเตทในพลาสมาเปลี่ยนแปลงอย่างมากในช่วงระดับ 0 ถึง 3+ การตรวจพบหรือไม่พบอะซิโตะซิเตทในพลาสมาจึงไม่สามารถวินิจฉัย DKA ได้ อย่างแม่นยำ และผลการศึกษาในครั้งนี้แนะนำให้ใช้ค่าเบตาไฮดรอกซีบิวทิเรตในเลือดตั้งแต่ 2.1 mmol/L เพื่อคัดกรองสุนัขที่มีภาวะ DKA

คำสำคัญ: อะซิโตะซิเตท เบตาไฮดรอกซีบิวทิเรต ภาวะเลือดเป็นกรดจากคีโตนจากเบาหวาน สุนัข เครื่องตรวจวิเคราะห์

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