Use of 3-beta-hydroxybutyrate in the treatment of canine diabetic ketoacidosis

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INTRODUCTION

Diabetic ketoacidosis (DKA) is a severe life-threatening complication of diabetes mellitus. To date, in veterinary medicine, urinary acetoacetate (AcAc) is the most commonly used parameter for monitoring dogs with DKA. Urine dipstick test provides a semiquantitative measure of urinary AcAc but does not register the presence of urinary 3-beta-hydroxybutyrate (3-HB), the predominant ketone body. In human medicine several studies have demonstrated that 3-HB is oxidized back to AcAc during the resolution of DKA. As a result, ketonuria may remain positive once ketosis has been reverted and it may give the misleading impression that ketosis is not improving. Another study in human diabetic patients demonstrated that the use of 3-HB as end-point for the intravenous insulin therapy is simple and earlier compared to the use of AcAc (our current end-point) (Noyes et al., 2007).
The aim of this study was to evaluate a new end-point for intravenous insulin therapy in the treatment of DKA in dogs.

MATERIAL AND METHODS

Dogs with DKA presented at the Veterinary Teaching Hospital of University of Bologna between June 2011 and April 2016 were prospectively enrolled in the study. The inclusion criteria for DKA were the following: blood glucose ≥ 250 mg/dL, ketonemia (3-HB ≥ 3.0 mmol/L) and/or ketonuria (urinary AcAc ≥ 1+), metabolic acidosis (pH < 7.3 or bicarbonate < 15 mEq/L) and at least two clinical signs consistent with DKA. All patients were treated with fluid therapy, a continuous rate infusion (CRI) of low dose of regular insulin (Macintire, 1993) and miscellaneous treatments for concurrent disorders. Each patient was monitored closely (tab 1). Dogs were divided into two groups, **3-HB group** and **AcAc group**, and two different end-points for intravenous insulin therapy were used. In the 3-HB group the CRI of insulin was stopped when pH > 7.3 and two 3-HB measurements (evaluated in one hour apart) were < 1 mmol/L; while in the AcAc group CRI of insulin was stopped when pH > 7.3 and absence of ketonuria has been recorded. Statistical analysis was performed using non parametric tests. A p value < 0.05 was considered significant.

RESULTS

Twenty dogs met the inclusion criteria; ten were included in the 3-HB group and ten in the AcAc group. The two groups resulted homogeneous regarding breed, sex, age, body weight, glucose concentration, 3-HB concentration, urinary AcAc, pH, bicarbonate concentration, anion gap and presence or absence of concomitant disorders at the time of diagnosis. The median time of CRI of insulin in the 3-HB group was 44 h, in the AcAc group was 36 h (fig.1). The median hospitalization time in the 3-HB group was 144 h while in the AcAc group was 156 h (fig.2). The differences were not significantly different.

First 24 h
-Capillary blood glucose: every h -Capillary 3HB: every 4 h -Blood gas analysis and urinary AcAc: every 8 h
Next 24 h until the end-point
-Capillary blood glucose: every 2 h -Capillary 3HB: every 4 h -Urinary AcAc: every 6 h -Blood gas analysis: every 12 h
After the endpoint
-Capillary blood glucose: 2-3-4 h after the end-point -Capillary 3HB: 4-12 h after the endpoint -Urinary AcAc: 6-12 h after the endpoint -Blood gas analysis: 24 h after the endpoint

Table 1: Monitoring protocol used for diabetic ketoacidosis

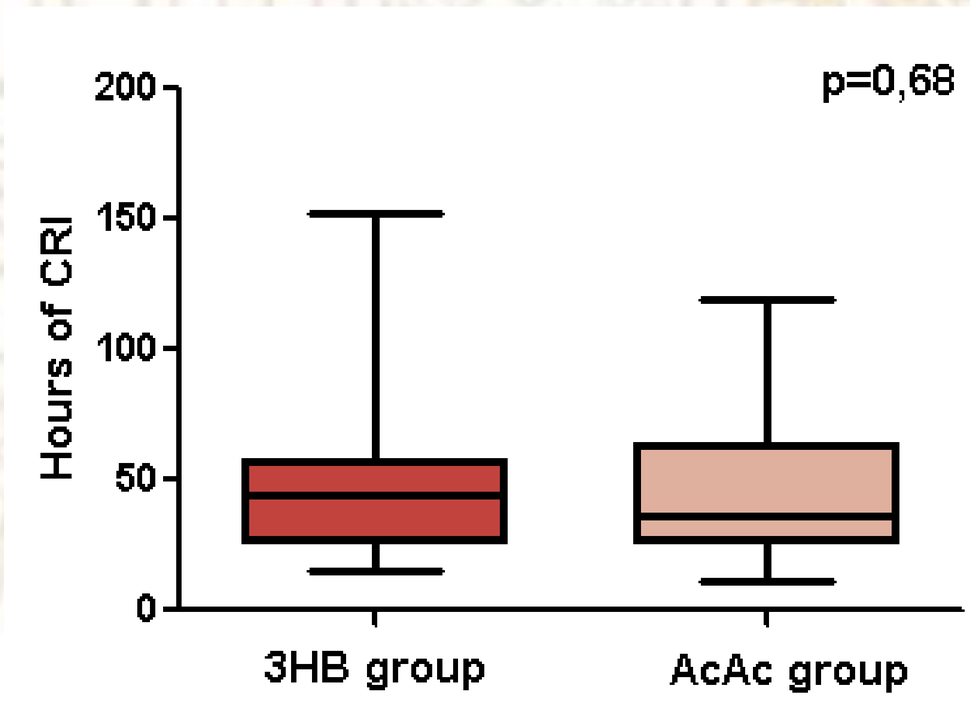

Fig 1: Box plots comparing the median time of constant rate infusion (CRI) of insulin between 3-HB group and AcAc group. The horizontal lines of the box represent the 25 th, 50 th (median) and the 75 th percentiles. Outlying horizontal lines of the box represent minimum and maximum values.

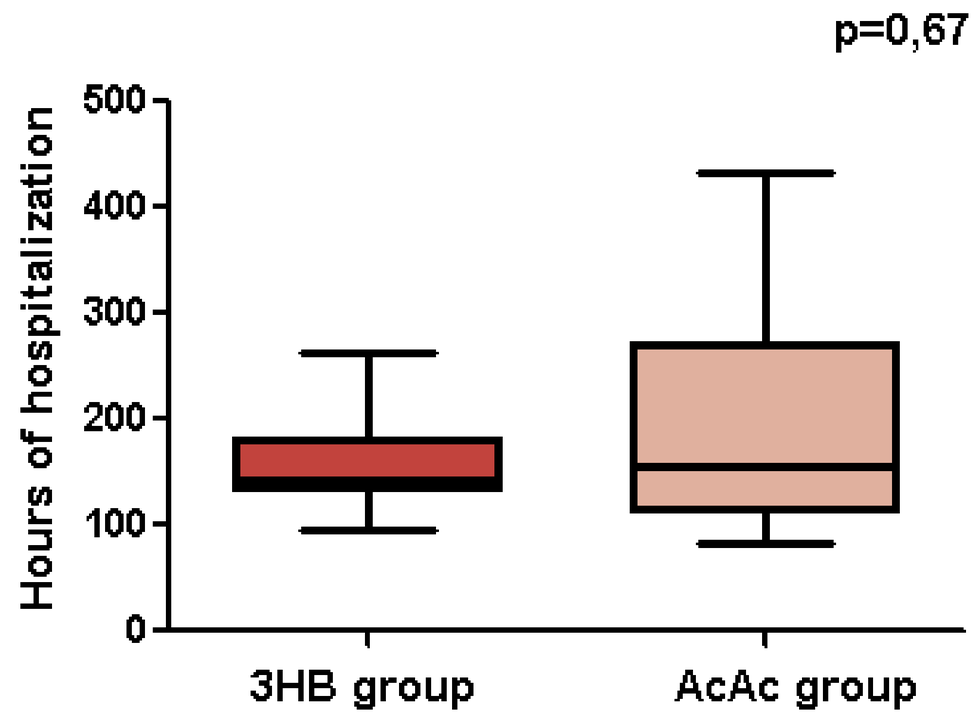

Fig 2: Box plots comparing the median time of hospitalization between 3-HB group and AcAc group. The horizontal lines of the box represent the 25 th, 50 th (median) and the 75 th percentiles. Outlying horizontal lines of the box represent minimum and maximum values.

CONCLUSIONS

The results show that the use of 3-HB in monitoring dogs with DKA does not reduce the hours of CRI of insulin if compared with urinary AcAc. However, the measure of 3-HB is a quick and easy procedure for samples collection and therefore the authors recommend the use of 3-HB in monitoring dogs with DKA.