Effect of hematocrit on accuracy of two point-of-care glucometers for use in dogs

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Objective—To determine the effect of Hct on blood glucose readings of dogs obtained by use of 2 point-of-care (POC) blood glucometers and a laboratory analyzer.

Animals—184 dogs, including 139 Greyhounds.

Procedures—Venous blood samples collected from 184 dogs with a range of Hcts (measured in EDTA-anticoagulated blood) were immediately analyzed with a handheld glucometer specifically developed for veterinary use and a glucometer developed for use in humans. The remainder of each blood sample was placed in fluoride oxalate tubes, and plasma glucose concentration was measured with a laboratory analyzer. Agreement between results for the POC glucometers and laboratory analyzer and effect of Hct on glucometer accuracy was assessed via regression analysis.

Results—Significant differences were detected between results of the glucometers and the reference laboratory analyzer. The Hct affected the correlation between results for the glucometers and the laboratory analyzer. Deviations of the glucometers from the reference interval varied with Hct. The glucometer for veterinary use more closely correlated with the glucose concentration when Hct was within or above its reference interval. The glucometer for use in humans more closely approximated laboratory reference glucose concentrations in anemic dogs.

Conclusions and Clinical Relevance—Hct had a relevant impact on the correlation between whole blood and plasma glucose concentrations in dogs. Significant variations between results obtained with the 2 glucometers could be critical when interpreting blood glucose measurements or selecting a POC glucometer for an intensive care setting and precise glycemic control in critically ill dogs. (*Am J Vet Res* 2011;72:1204–1208)

In humans, it has been found that Hct affects the performance of blood glucometers.[1–6] An increase in Hct results in a decrease in measured glucose concentration,[5,6] and glucometers become progressively more inaccurate as Hct increases.[3] A decrease in Hct also may result in an increase in measured glucose concentrations for some glucometers.[1]

Handheld POC glucometers are widely used in veterinary hospitals for measurement and monitoring of blood glucose concentrations. Greyhounds have a naturally high Hct,[7] and given the reported inaccuracy of POC glucometers in humans, it is possible that glucometer results may be misinterpreted by veterinarians during examination of racing Greyhounds. Similarly, abnormal results for measurement of blood glucose concentrations in critically ill dogs[8] and anemic dogs may be misinterpreted. The accuracy of glucometer measurements is paramount to the management of diabetic and hypoglycemic patients that also may have abnormal Hcts. It is important to evaluate POC glucometers in the species in which they are used because glucometers may provide results that differ from those for a laboratory standard or from those of other POC glucometers, and results may differ at extremes of blood glucose concentration or Hct.

The purpose of the study reported here was to compare measurements of canine blood glucose concentrations obtained by use of 2 POC glucometers against a reference method and to assess the impact of Hct on glucose concentration. A portable glucometer developed for use in humans and a handheld glucometer specifically developed for veterinary use were evaluated.

Abbreviation

POC Point-of-care

Materials and Methods

Animals—A total of 184 dogs were included in the study. Of these, 139 were Greyhounds from racing

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kennels in Western Australia (n = 78) and from racing kennels in Ireland (61). Racing Greyhounds were selected because they have a naturally high Hct,[7] and it was suspected that this high Hct would result in aberrant measurement of blood glucose concentrations obtained by use of portable POC glucometers. In addition, 16 anemic dogs and 29 ill dogs that had an Hct within the reference interval that were hospitalized in the veterinary hospitals at Murdoch University or the University College Dublin were also used to examine glucometer measurements for dogs with a wide range of Hct. The study was performed in accordance with the requirements of the Australian Code of Ethics for the Care and Use of Animals for Scientific Purposes, the Murdoch University Animal Ethics Committee, and the University College Dublin Animal Ethics Committee.

Sample collection—A blood sample (approx 4 mL) was obtained via jugular venipuncture from each healthy dog; a smaller volume was obtained from ill dogs. The blood sample was used to obtain measurements with each glucometer immediately after sample collection. Part of each blood sample was placed into tubes that contained EDTA[a] for Hct determination; the remainder of each sample was placed into sodium fluoride oxalate–containing tubes[b] for laboratory measurement of blood glucose concentrations within 24 hours after collection.

Measurement of blood glucose concentrations—A POC glucometer developed for use in humans[c] and a POC glucometer developed for veterinary use[d] and validated for use in domestic animals were evaluated. Both systems used factory-set conversion factors to derive plasma-equivalent glucose values. The glucometer for use in humans used glucose oxidase and the amperometric electrochemical method to measure the electrical current generated by the glucose reaction at a specific time point. The glucometer for veterinary use used glucose dehydrogenase and the coulometric electrochemical method to measure the glucose concentration in whole blood. All instrument calibration and testing were performed in accordance with manufacturer instructions. Both glucometers had a minimum detection limit of 1.1 mmol/L; therefore, any value below the limit of detection was recorded as 1.0 mmol/L for the purpose of analysis. An automated hexokinase chemistry system[e] on blood samples in fluoride oxalate was used as the comparative or reference method for measuring plasma glucose concentrations in Ireland and Australia.

Hct—The Hct of each blood sample was measured by use of one hematology system[f] in Australia and another hematology system[g] in Ireland. External quality-control testing on these instruments revealed that measurement of Hct was accurate, compared with the PCV, within < 1 SD.

Statistical analysis—Results were expressed as a change from the glucose concentration as measured by use of the reference method for each glucometer (ie, glucose concentration as measured by use of the reference method – glucose concentration as measured by use of a glucometer). Results were also compared between the 2 glucometers. Significance of the effect of Hct was assessed by use of a repeated-measures ANOVA and paired *t* tests, and linear regression analysis for results of each glucometer versus results for the reference plasma glucose method was performed by use of commercially available software.[h]

Results

Hematocrit values between 9% and 67% were obtained. There was a significant effect of Hct on glucose concentration for both POC glucometers, compared with the laboratory plasma hexokinase method. Repeated-measures ANOVA and a Levene test of equality of error variances revealed that Hct had a significant ($P < 0.001$) effect on the differences in measurement variances of both glucometers. The mean ± SD difference between results for the glucometer for veterinary use and plasma glucose concentrations for the entire cohort was 0.814 ± 1.39 mmol/L (range, 0.070 to 0.927 mmol/L). The corresponding mean for results of the glucometer for use in humans and plasma glucose concentrations for the entire cohort was –1.405 ± 0.575 mmol/L (range, –1.489 to –1.322 mmol/L).

Results of linear regression analysis were summarized (**Table 1**). When the effect of Hct was considered during examination of the differences between results obtained with each glucometer and the reference method, slopes of the regression equations were different. A slope of –6.256 was obtained for the glucometer for use in humans, which differed significantly ($P < 0.001$) from the slope of –3.142 obtained for the glucometer for veterinary use (**Figures 1 and 2**). At higher Hcts (> 55%), results obtained with the glucometer for use in humans were less than those of the laboratory reference method, whereas results obtained with the glucometer for veterinary use more accurately predicted those of the laboratory reference method. There was a significant effect of increasing Hct on results obtained

Table 1—Results of linear regression analysis for the relationship between glucose concentrations measured by use of 2 POC glucometers and the plasma glucose concentration measured by use of a reference method in venous blood samples obtained from dogs with various Hcts.

Variable	Glucometer for veterinary use*	Glucometer for use in humans*	Both glucometers combined*
Slope	–6.256 (–7.230 to –5.282)	–3.142 (–4.042 to –2.241)	–3.277 (–4.374 to –2.180)
x-intercept (%)	0.63 (0.60 to 0.65)	0.01 (–0.13 to 0.15)	1.26 (1.00 to 1.51)
y-intercept (mmol/L)	3.93 (3.44 to 4.43)	–0.4512 (–0.3053 to –0.5971)	3.840 (3.290 to 4.389)
R^2	0.4576	0.2052	0.1592
SE of estimate (mmol/L)	0.5636	0.5099	0.6216

*Values were significantly ($P < 0.001$) affected by Hct. Values in parentheses represent 95% confidence intervals.

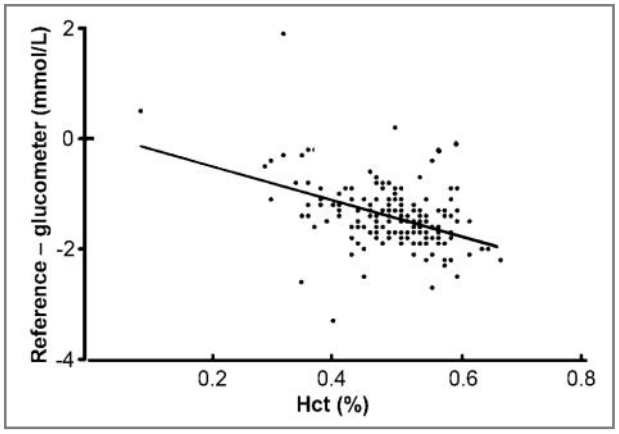

Figure 1—Results of linear regression analysis of the difference between blood glucose concentrations measured with a reference method and with a glucometer developed for use in humans in venous blood samples obtained from dogs with various Hcts. Each symbol represents results for 1 dog. Slope of the regression line is –6.256. The line of perfect agreement would have a y-intercept of 0.

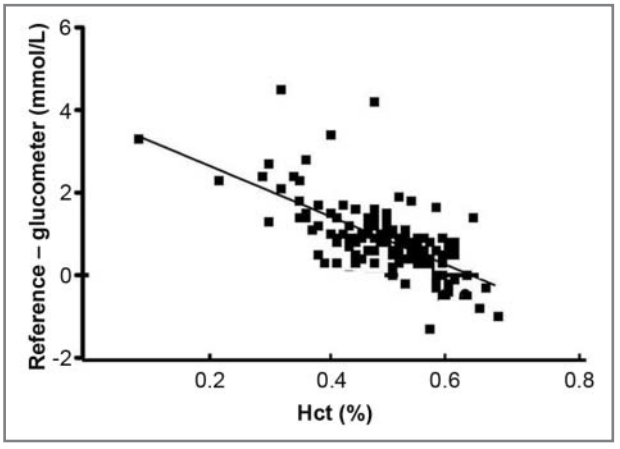

Figure 2—Results of linear regression analysis of the difference between blood glucose concentrations measured with a reference method and with a glucometer developed for veterinary use in venous blood samples obtained from dogs with various Hcts. Slope of the regression line is –3.142. *See* Figure 1 for remainder of key.

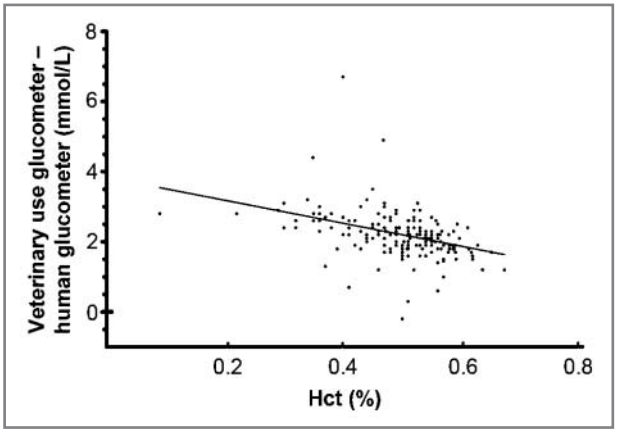

Figure 3—Results of linear regression analysis of the difference between blood glucose concentrations measured with a glucometer for veterinary use and with a glucometer for use in humans in venous blood samples obtained from dogs with various Hcts. Slope of the regression line is –3.277. *See* Figure 1 for remainder of key.

with the glucometer for use in humans. With increasing Hct, there was an increasing difference between blood glucose concentration measured with the glucometer for use in humans and that measured with the reference method; when the Hct was > 50%, most results for the glucometer for use in humans differed by > 1.5 mmol/L (20%) from those of the reference method.

The mean difference of blood glucose concentration in samples with an Hct < 38% increased significantly when the glucometer for veterinary use was used, whereas results of the glucometer for use in humans more closely approximated the blood glucose concentration measured by use of the reference method. At an Hct of 30%, differences in glucose concentrations for the glucometer for veterinary use were 1.3 to 2.7 mmol/L (approx 20% of the range of measurements obtained by use of the laboratory reference method), which increased to a difference of 2.4 to 3.3 mmol/L at an Hct of 20% and 9%, respectively. Over the Hct range of 9% to 67%, results obtained with the glucometer for veterinary use typically were higher than, and those of the glucometer for use in humans typically were lower than, the blood glucose concentration measured by use of the laboratory reference method. Within an Hct range of 38% to 57%, results obtained with the glucometer for veterinary use more closely approximated those of the laboratory reference method.

Variation between the 2 glucometers was –0.2 to 4.9 mmol/L, with regard to Hct. A slope of – 3.277 was obtained when blood glucose concentrations for the 2 glucometers were compared with respect to Hct (Table 1). The difference between the blood glucose concentration measured over a range of Hct values with the glucometer for veterinary use and with the glucometer for use in humans was plotted (**Figure 3**).

Discussion

The ability of POC blood glucometers to reliably provide results equivalent to laboratory-derived plasma concentrations is important and can impact clinical decisions. Adjusting treatments is important in critical care settings, particularly in dogs with sepsis, liver failure, and diabetes mellitus, wherein precise glycemic control is paramount. These dogs can often also have substantial changes in Hct.

In humans, increases in Hct have been reported[1,4,6,9] to result in decreases in measured glucose concentrations, and decreases in Hct reportedly result in increases in measured glucose concentrations for some glucometers. Glucometers developed for use in humans are widely used in veterinary hospitals.

Results obtained with both glucometers used in the study reported here revealed variation with changes in Hct, compared with results obtained by use of a laboratory reference method. The glucometer for veterinary use was more inaccurate in samples with a lower Hct, but the glucometer for use in humans had more variation in samples with a higher Hct. The glucometer for use in humans is likely to be less accurate in Greyhounds and more accurate in anemic dogs, whereas the glucometer for veterinary use is more likely to be ac-

curate when used in Greyhounds but less accurate in anemic dogs.

Results obtained with the 2 glucometers differed significantly. Generally, there was a difference of 2 to 3 mmol/L between results for the glucometers. Hospitals often acquire multiple glucometers over time, and use of multiple glucometers of various brands and assay methods for a single patient can introduce considerable variability and confound interpretation of results. For example, during interpretation of blood glucose concentration curves in diabetic patients, the glucose concentration in a single blood sample may act as a confounder and potentially misrepresent a nadir.

Analysis of results of the present study suggested that when blood glucose concentrations are interpreted, a single measurement method should be selected and, to be representative of true variations in blood glucose concentrations, results from different glucometers should not be interpreted at different times. Although measurements obtained with the glucometers used in this study had up to 20% variation from the reference method, this often correlated to only 2 mmol/L, which may have little effect on interpretation of a blood glucose concentration curve when monitoring a diabetic dog but may be more consequential in the precise glycemic control of a septic dog or a dog receiving constant rate infusions of insulin for management of diabetic ketoacidosis.

Correlation of results for glucometers with those of the reference hexokinase method in dogs with anemia could have been better refined by inclusion of a greater number of anemic dogs. Of the 184 dogs assessed, only 17 were considered anemic (Hct < 37%), with most only mildly anemic (Hct, 30% to 37%). Given the number of Greyhounds included in the study, there was a bias for assessing dogs that had a higher Hct.

The effect of interfering substrates or medications was not investigated in the present study because the objective was to simulate clinical situations. Various contributing factors for this phenomenon have been reported in the medical literature.[1,10] Analytic interference may have contributed to some variation in glucometer measurements, but the impact of Hct on glucose concentration was consistent over a range of Hcts.

Multiple operators of the POC glucometers were involved in the present study, which may have introduced error and made the difference between glucose values derived with the POC glucometers and the laboratory-derived values more pronounced. However, this scenario most accurately reflects common practice situations and was selected in this study to mimic the manner in which testing with a POC glucometer typically is performed.

Altitude, temperature, and humidity also cause variability in measurements of blood glucose concentrations by use of POC glucometers.[11,12] Glucometers were used in Ireland and Australia in variable climatic conditions, and variability in results of blood glucose concentrations obtained with the POC glucometers were consistent for both locations. The effect of climate was considered unlikely to cause the variances in glucose measurements detected between the glucometers and the reference method.

Accuracy of the glucometers in the present study may also have been affected by the use of whole venous blood because POC glucometers for humans often use capillary or arterial blood. Glucose concentrations in venous samples may underestimate those in arterial samples by 15%, and capillary samples also have lower blood glucose concentrations than do arterial samples.[13] It is theorized that with a high Hct, timed diffusion of glucose from blood onto the test strip is delayed as a result of the number of RBCs, which leads to spuriously low glucose values. This may account for some of the difference observed in results obtained with the glucometer developed for use in humans. It has also been theorized that size of RBCs may impact POC glucometers and lead to spuriously low results.[14] Dogs and humans have RBCs of similar size (7 µm and 6 to 8 µm, respectively),[15,16] and it is considered unlikely that RBC size caused the observed differences between measurements for the glucometers and the reference method.

The glucometer for veterinary use and the glucometer for use in humans that were used in the present study have different technologies for measurement of blood glucose concentrations, and both glucometers were affected by Hct. It may be the calibration of the test strips by manufacturers, rather than the measurement technology, that impacts the correlation of glucose measurement with laboratory hexokinase methods. It has been proposed that filters used in glucometer strips to separate RBCs from plasma may cause inaccuracy in POC glucometers[14] and may have contributed to differences between results for the glucometers and the reference hexokinase method.

Results for the glucometer validated for veterinary use appeared to correlate closely with results for the laboratory reference method across a wide range of blood glucose concentrations. In addition, results for that glucometer were minimally affected by an Hct within or higher than the reference interval.

Additional laboratory-based experiments to assess a greater range of glucose concentrations and Hcts may allow development of a correction algorithm for Hct for each POC blood glucometer. This may enable more precise glycemic management for dogs with anemia or a naturally high Hct.

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b. Glucose FH/1.3, catalogue No. 41.1394.005, Sarstedt Haematology, Newton, NC.
c. Ascensia Elite XL, Bayer, Elkhart, Ind.
d. AlphaTrak, Abbott Laboratories, Abbott Park, Ill.
e. Rx Daytona autoanalyzer, Randox Laboratories, Crumlin, Northern Ireland.
f. Advia 120, Siemens Diagnostics, Deerfield, Ill.
g. Advia 2120, Siemens Medical Solutions Diagnostics GmbH [Dx], Erfurt, Germany.
h. GraphPad Prism, version 5.01, GraphPad Software, San Diego, Calif.

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