The Journal of Veterinary Medical Science

NOTE

Internal Medicine

Evaluation of newly developed veterinary portable blood glucose meter with hematocrit correction in dogs and cats

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J. Vet. Med. Sci.
79(10): 1690–1693, 2017
doi: 10.1292/jvms.17-0184

Received: 5 April 2017
Accepted: 3 August 2017
Published online in J-STAGE: 18 August 2017

ABSTRACT. This study evaluated the accuracy of a newly developed veterinary portable blood glucose meter (PBGM) with hematocrit correction in dogs and cats. Sixty-one dogs and 31 cats were used for the current study. Blood samples were obtained from each dog and cat one to six times. Acceptable results were obtained in error grid analysis between PBGM and reference method values (glucose oxidation methods) in both dogs and cats. Bland–Altman plot analysis revealed a mean difference between the PBGM value and reference method value of −1.975 mg/d*l* (bias) in dogs and 1.339 mg/d*l* (bias) in cats. Hematocrit values did not affect the results of the veterinary PBGM. Therefore, this veterinary PBGM is clinically useful in dogs and cats.

KEY WORDS: blood sampling, canine, feline, plasma

Portable blood glucose meters (PBGMs) are used in the diagnosis and management of diabetes mellitus in veterinary practice. Various PBGMs for human medicine are commercially available from several companies. However, canine and feline blood glucose concentrations obtained with human PBGMs are commonly lower than those obtained with gold standard methods (the hexokinase or glucose oxidase reaction) [1, 12]. Therefore, PBGMs specifically for veterinary medicine are required for accurate measurement and diagnosis. The BS-7110 (Arkray, Kyoto, Japan) is a newly developed PBGM for veterinary medicine. The BS-7110 provides rapid and highly accurate test results for canine and feline blood samples. The required sample volume is approximately 0.3 μl. The measuring time is 5 sec, and the measuring range is 10 to 600 mg/d*l*. Furthermore, this device has automatic hematocrit correction. High hematocrit values interfere with glucose measurement when using PBGMs [1, 5]. This issue is related to the internal calibration of PBGMs based on the standardized 45% hematocrit value. In human medicine, PBGMs with hematocrit correction are commercially available [4]. However, to the authors' knowledge, there is no PBGM with hematocrit correction available in veterinary medicine. The purpose of this study was to compare blood glucose concentrations obtained with the BS-7110 with those obtained with glucose oxidase methods in dogs and cats. Furthermore, we investigated whether hematocrit affected the results of blood glucose concentration testing with the BS-7110.

In total, 61 dogs and 31 cats were used for this study. Out of 61 dogs, 51 dogs (21 Beagles, 7 Miniature dachshund, 5 Toy poodle, 2 Golden retriever, 2 Jack Russell terrier, 2 Pomeranian, 2 Miniature schnauzer, 1 Boston terrier, 1 Chihuahua, 1 English cocker spaniel, 1 Papillon, 1 Pembroke Welsh corgi, 1 Mix, 1 Labrador retriever, 1 Shih tzu, 1 West Highland white terrier, 1 Yorkshire terrier; 1–15 years old; 6 intact male, 1 intact female, 23 castrated male and 21 spayed female) were absence of diabetes mellitus and 10 dogs (3 Miniature dachshund, 2 Border collie, 2 Toy poodle, 1 Maltese, 1 Miniature schnauzer, 1 Shih tzu; 7–16 years old; 2 intact male, 4 intact female, 3 castrated male, 1 spayed female) were presence of diabetes mellitus. Out of 31 cats, 14 cats (13 Mix, 1 Chinchilla Persian; 3–17 years old; 8 castrated male and 6 spayed female) were absence of diabetes mellitus and 17 cats (12 Mix, 2 Russian blue, 1 American curl, 1 Devon rex, 1 Tonkinese; 5–20 years old; 14 castrated male, 3 spayed female) were presence of diabetes mellitus. Blood samples were obtained from each dog and cat between one and six times during the study period. The interval between repeated blood sampling in the same dog or cat was over 1 week. Dogs and cats were either housed at the Nippon Veterinary and Life Science University or were patients at the Nippon Veterinary and Life Science University Veterinary Medical Teaching Hospital. This study was approved by the Nippon Veterinary and Life Science University Animal Research Committee (28S-61).

Random blood samples (1–2 m*l* for dogs and cats) were obtained from the cephalic or jugular vein and transferred to heparinized plastic tubes. Seventy-nine whole blood (WB) and plasma samples from 61 dogs and 59 samples from 31 cats were

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used to assess accuracy. First, glucose concentrations in the WB samples were measured by glucose-dehydrogenase methods with the BS-7110. The intra-assay coefficient of variation (CV) for the BS-7110 in dogs (n=10) and cats (n=10) were 3.2 and 3.0%, respectively. This device was operated and calibrated according to the manufacturer's instructions. Residual WB samples were dispensed into hematocrit capillary tubes, then centrifuged at 12,000 ×*g* for 5 min to measure hematocrit. The remaining WB samples were immediately centrifuged at 2,000 ×*g* for 10 min to obtain the plasma. The glucose concentration of each plasma sample was measured with the glucose oxidation method using a YSI (Yellow Springs Instrument) 2300 STAT PLUS Glucose Analyzer (YSI Japan Co., Ltd., Tokyo, Japan) to obtain the reference glucose values. The intra-assay CV for the YSI 2300 STAT PLUS Glucose Analyzer in dogs (n=10) and cats (n=10) were 0.7 and 0.5%, respectively.

Spearman's rank correlation coefficient was used to identify significant correlations between measurements. Spearman's correlation coefficient (r) was obtained with GraphPad Prism 6 (GraphPad Software, Inc., San Diego, CA). Values of correlation coefficients (r) were interpreted as follows: 0.90–1.00, very high correlation; 0.70–0.89, high correlation; 0.50–0.69, moderate correlation; 0.30–0.49, low correlation; and 0–0.29, little correlation [5, 11]. PBGM data were evaluated using clinically relevant error grid analysis [2, 3]. The error grid compares reference method glucose values (x-axis) versus PBGM values (y-axis) in five zones associated with the following five risk levels: zone A, clinically accurate; zone B, altered clinical action but no or minimal effect on clinical outcome; zone C, altered clinical action with a likely effect on clinical outcome; zone D, altered clinical action with considerable medical risk; and zone E, altered clinical action with dangerous consequences [11]. Error grid analysis was conducted with Excel 2007 SP3 (Microsoft Corporation, Redmond, WA, U.S.A.). Bland–Altman difference plots were constructed to compare PBGM results with reference method glucose values using GraphPad Prism 6. The combined inherent imprecision of the reference method and PBGM values was calculated as $CV_{Both\ Methods}=(CV^2_{Ref} + CV^2_{PBGM})^{0.5}$ [5, 10]. In addition, the acceptance limit was calculated using the following formula: Acceptance limit=0 ± ($1.96 \times CV_{Both\ Methods} \times Average_{Both\ Methods}$).

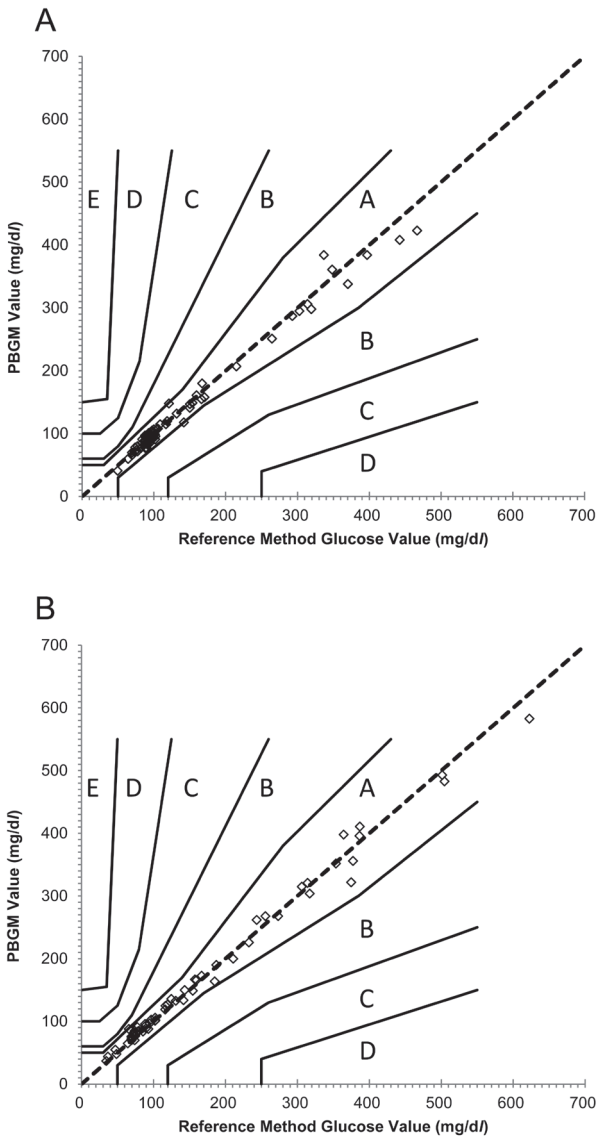

Fig. 1. Error grid analysis of blood glucose concentrations obtained with the portable blood glucose meter (PBGM) in (A) dogs (n=79 samples) and (B) cats (n=59 samples). Blood glucose concentrations measured with the PBGM are plotted against reference method glucose values.

A positive correlation between PBGM values and reference method values was observed in both dogs (y=0.962, x=+4.304, r=0.991, n=79 samples) and cats (y=0.96, x=+8.244, r=0.996, n=59 samples). Error grid analyses of all canine and feline blood glucose measurements revealed distributions within zone A (Fig. 1A and 1B, respectively). According to the ISO 15197:2013 requirements for human use, a PBGM is considered accurate if 95% of measurements are within ± 15 mg/d*l* of the reference value when the glucose concentration is <100 mg/d*l*, and within ± 15% when the glucose concentration is ≥100 mg/d*l*. Over 95% of samples were within acceptable limits for both dogs (97%, 77 of 79 samples) and cats (98%, 58 of 59 samples).

Bland-Altman plot analysis revealed a mean difference between PBGM values and reference method glucose values of −1.975 ± 11.75 mg/d*l* (bias ± SD) in dogs (Fig. 2A) and 1.339 ± 13.43 mg/d*l* (bias ± SD) in cats (Fig. 2B). For dogs and cats, 62% (49/79 samples) and 68% (40/59 samples) of the samples were plotted within the calculated acceptability limits based on the combined inherent imprecision of the PBGM and reference method glucose values, respectively.

Low correlation was observed between hematocrit and PBGM values minus reference method glucose values in dogs (y=−0.1849, x=+6.617, r=−0.302, n=79 samples, *P*=0.007) (Fig. 3A). No significant correlation was observed between hematocrit and PBGM values minus reference method glucose values in cats (y=0.1866, x=−5.289, r=0.071, n=59 samples, *P*=0.597) (Fig. 3B).

PBGMs are used in veterinary medicine for rapid glucose monitoring. Recently, owners of diabetic dogs and cats have begun using PBGMs at home for better control of diabetes. We evaluated the newly developed BS-7110 PBGM in the current study. This device was developed for veterinary practice and has a hematocrit correction function. Glucose sensor chip with BS-7110 includes

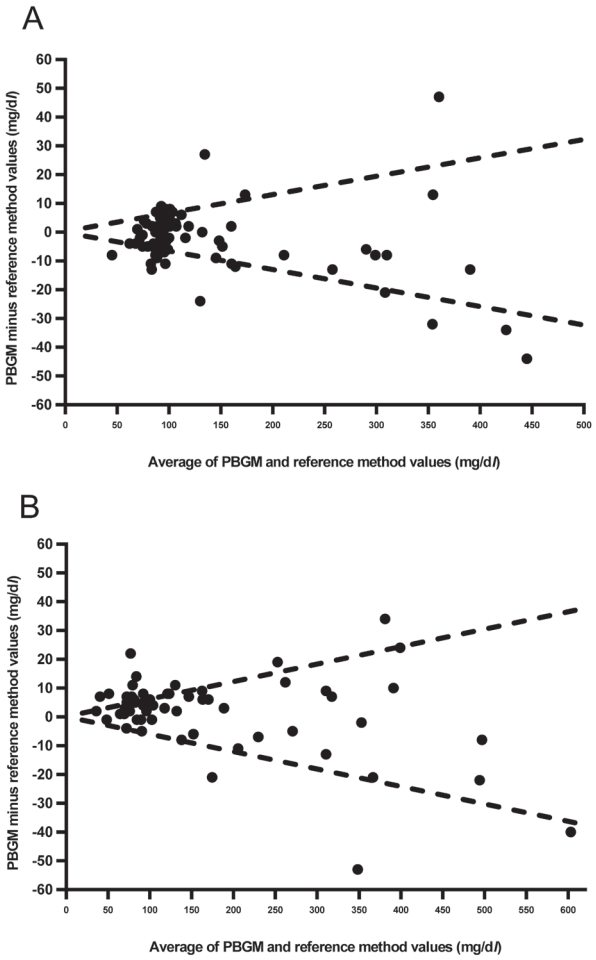

Fig. 2. Bland–Altman difference plots of blood glucose concentrations measured with the portable blood glucose meter (PBGM) and reference method glucose values in (A) dogs (n=79 samples) and (B) cats (n=59 samples). Dashed line represents 0 ± (1.96 × $CV_{Both\ Methods}$ × $Average_{Both\ Methods}$) and their intervals represent acceptable limits.

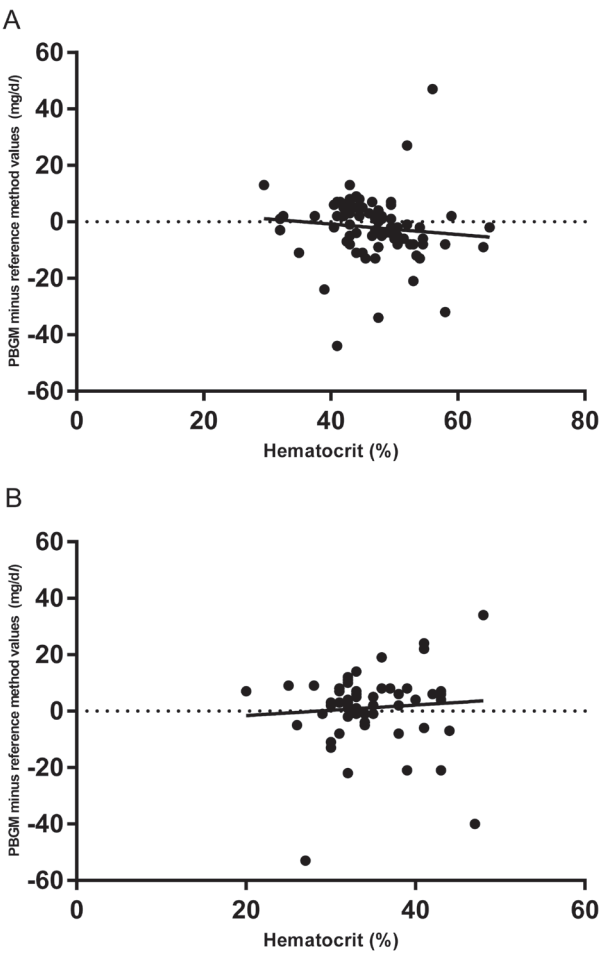

Fig. 3. Correlation between portable blood glucose meter (PBGM) minus reference method glucose values and hematocrit in (A) dogs and (B) cats. Dashed lines represent 0 mg/d*l* of difference between the two analytical methods. Solid line represents line with linear regression.

2 polar zone for measuring glucose and hematocrit. One polar zone measures glucose concentrations by glucose-dehydrogenase methods. The other polar zone measures hematocrit by detecting electric resistance. Detected electric resistance correlates with hematocrit. Finally, BS-7110 show blood glucose concentration with hematocrit correction by arithmetic processing. Additional information on this correction algorithm for arithmetic processing is available in the patent documents [6–8]. If the accuracy of the BS-7110 PBGM can be demonstrated, this device would be the first PBGM with hematocrit correction in veterinary medicine.

A high level of correlation between the PBGM value and reference method glucose value was observed in dogs and cats in the current study. Furthermore, 100% of the data points were within zone A of the error grid for both dogs and cats, indicating highly accurate PBGM performance. These percentages are higher than the results of similar previous studies that used human PBGMs (99.1% for dogs and 92.5% for cats plotted in zone A [5]; 38.4% for dogs and 76.8% for cats plotted in zone A [12]). Furthermore, according to the ISO 15197:2013 requirements, >95% of samples were within the calculated acceptable limits in dogs and cats in the current study [9]. These results indicate that the BS-7110 is accurate and reliable for measuring blood glucose concentrations in dogs and cats. A previous study found that nine human PBGM devices did not fulfill ISO 15197:2013 accuracy requirements when used in dogs, with all devices having <74% of total measurements within acceptable limits [1]. Our previous study using human PBGMs also had few samples within the calculated acceptable limits (11% of dogs, 39% of cats) [12]. With respect to the Bland–Altman plots, 62% of dogs and 68% of cats of the samples were plotted within the calculated acceptability limits. This performance is superior to that reported in similar previous studies (30 and 53% within the acceptability limits for dogs [11]; 7.5 and 52.5% for cats [5]. Both study used two types of PBGM [5, 11].). Our results demonstrate that the BS-7110 PBGM is clinically useful and is applicable in the veterinary clinical setting.

In our previous study, WB glucose concentrations measured with the PBGM without hematocrit correction were lower than plasma glucose concentrations measured with the reference method in samples with high hematocrit [12]. Specific PBGMs are

affected by hematocrit values; anemic dogs and cats have higher glucose concentration results with WB PBGM measurement than with plasma reference methods [1, 13, 15, 16]. The detailed mechanism of hematocrit interference in blood glucose measurement by PBGMs is unknown. However, the viscosity of the blood, blocking of the plasma glucose from reaching the reaction surface of the test strip, and changes in diffusion kinetics could be considered [14]. In canine samples there was low correlation between hematocrit values and PBGM minus reference method glucose values (r=−0.302). Furthermore, in feline samples, there was little correlation between hematocrit values and PBGM minus reference method glucose values (r=0.071). As such, hematocrit values did not affect the glucose concentration measured with the PBGM in either dogs or cats in the current study.

In conclusion, the BS-7110 glucose values were in agreement with the reference method values in dogs and cats. Furthermore, changes in hematocrit did not affect the WB glucose concentration as measured with the BS-7110. The current study demonstrated good performance of a new PBGM that automatically compensates for hematocrit and that can be used in veterinary practice.

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