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Siram Suvarnavibhaja

Poramin Yuennan

Ratanaporn Tangwangwiwat

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Original Article

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Siram Suvarnavibhaja[1,*] Poramin Yuennan[1] Ratanaporn Tangwangwiwat[1] Aomusa Kuaha[1]

Sirintorn Yibchokeanan[2]

Abstract

The objective of this study was to compare blood glucose concentrations obtained from two portable blood glucose meters (PBGM), Sure-step™ and Accucheck™, with reference method, glucose oxidase test. Blood samples were collected from dogs consulting in Small Animal Hospital, Chulalongkorn University. A hundred and thirty four blood samples were collected in the study. Blood glucose concentrations were measured by using Sure-step™, Accucheck™ and glucose oxidase method respectively in all samples. The intra-class correlation was determined to evaluate the correlation between each PBGM and glucose oxidase test. The range of the blood glucose concentrations was 31.47 to 347.49 mg/dl. Overall intra-class correlation showed significant (p<0.05) in comparison of two PBGMs with the standard method (r=0.847 and 0.839 for Sure-step™ and Accucheck™ respectively). Range of 15% deviation from reference method-value was accepted to access PBGMs clinically. The greater percentage of sample in particular range was observed in Sure-step™ (42.86%) rather than Accucheck™ (22.56%). In conclusion, although commercially available PBGM provided blood glucose concentration reasonably close to those obtained with reference method, Sure-step™ seemed to be more accurate than Accucheck™. However the utilization of these devices in terms of clinical decision could lead to erroneous in some cases.

Keywords: dog, glucose concentration, portable blood glucose meter

[1]*Department of Veterinary Medicine, Faculty of Veterinary Science, Chulalongkorn University, Bangkok 10330, Thailand*
[2]*Department of Veterinary Pharmacology, Faculty of Veterinary Science, Chulalongkorn University, Bangkok 10330, Thailand*
Correspondence: *siram.s@chula.ac.th*

Introduction

Glucose concentration is an important parameter for diagnosis and therapeutic monitoring. An accuracy of measuring method is vital as it results in medical decision by physicians and veterinarians. Hyper- and hypoglycemia can be harmful and needs to be addressed prior to instant resuscitation. Currently, automated machines are commonly used by many standard laboratories. Such machines commonly measure by using glucose oxidase and hexokinase method as a gold standard. Although it provides the highest accuracy, it takes somewhat long period of time for processing making a delay in decision for resuscitation. The Portable Blood Glucose Meters (PBGMs) have been invented to yield fast result and use very small amount of blood. The PBGM therefore are widely used worldwide (Cohn et al., 2000).

In Thailand, many PBGMs were produced and commercially available from various manufacturers. Basically, two glucose measuring techniques were commonly utilized based on the principle of electrochemical system and reflectance photometry which are Accucheck™ Advantage II model (Roche Diagnostics, Germany), and Sure-step™ Onetouch (LifeScan, Inc. Milpitas, CA, USA) respectively. Such products have been used for veterinary patients in Small Animal Hospital, Chulalongkorn University for several years. However, the comparative evaluation of accuracy never been made especially using dog blood. Many limitations of the PBGMs to measure blood glucose concentration exist, for example, overestimated level of glucose concentration during anemia and underestimated glucose level upon erythrocytosis (Wess et al., 2000; Stein et al., 2002). Certain oxidizing agents, for instance, ascorbic acid, could overestimate glucose concentrations measured by Accucheck™, and underestimate by Sure-step (Tang et al., 2000). For these reasons, the veterinary practitioners still use PBGMs with suspicion in accuracy and reliability as no any study comparing between this two PBGM models.

Regarding to differences in method of measurement between two PBGMs, Sure-step™ Onetouch is believed to yield more accurate result than Accucheck™ Advantage II does because using of glucose oxidase reaction like the standard protocol. However, Sure-step™ Onetouch take a little longer in processing comparing to Accucheck™ Advantage II. Moreover, Sure-step™ Onetouch purposes a safety for the user as it does not cause "springboard effect" as other products do because a test-strip is made up of paper instead of plastic, hence, lesser chances for a blood sample to contaminate to an examiner.

This comparative study, therefore, was designed to assess the blood glucose concentrations obtained from two in-house PBGMs, Accucheck™ Advantage II and Sure-step™ Onetouch by comparing to the standard method, glucose oxidase test.

Materials and Methods

Animals: A hundred and thirty four canine blood samples were collected from client-owned dogs at Small Animal Hospital, Chulalongkorn University. The dog's owners were informed and signed consent forms for permission. The research protocol was approved by Chulalongkorn University Animal Care and Use Committee (approved no. 1031032). Inclusion criteria included blood samples freshly collected from dogs regardless of age, breed, and gender. The owners were asked to ensure that their dogs did not receive ascorbic acid, acetaminophen and dopamine interfering PBGM-measuring method (Tang et al., 2000). One and a half milliliter (ml) of blood sample of all dogs meeting the inclusion criteria were taken for subsequent analysis.

Treatment Protocols and Assessments: The whole blood samples were collected from laterally recumbent dogs with minimal restraint. A 3 ml disposable plastic syringe with 1 inch 21-23 G needle was used for blood drawing under sterile condition. Venipuncture was conducted from either cephalic or lateral saphenous vein depending on veterinarian's preference. The volume of 1.5 ml was acquired and measured for blood glucose level briefly after collection by Accucheck™ Advantage II and Sure-step™ Onetouch. The instruction by each manufacturer was followed strictly. Each tool was calibrated with control solution regularly as the company's recommendation. The remaining approximately 1.4 ml blood sample was kept in lithium heparinized eppendorf and then centrifuged at 3,000 rpm for 15 min. Plasma was isolated and stored in -20 ^{o}C freezer until analyzed by glucose oxidase test as standard method. The duration between taking blood and storage was less than 30 min.

Glucose oxidase test: Laboratory evaluation of plasma glucose using glucose oxidase test is composed of three main processes. Firstly, peroxidase-glucose oxidase (PGO) enzyme solution was established by mixing a capsule of PGO enzyme in 100 ml distill water and o-dianisidine solution was prepared by dissolving 50mg o-dianisidine dihydrochloride in 20 ml of distilled water. PGO enzyme reaction solution was then prepared by mixing 100 ml PGO enzyme solution with 1.6 ml o-dianisidine solution as it was indispensable for measuring of glucose in liquid specimen such as serum and plasma. Secondly, glucose standard from stock solution was prepared to establish a standard curve used to assess glucose concentration in plasma samples. Ultimately, ten microliter of sample was added in 1 ml of PGO enzyme reaction solution and

Table 1 Ranges of blood glucose concentration from three methods of measurement.

Measuring method	Minimum (mg/dl)	Maximum (mg/dl)
Glucose oxidase test	31.5	347.5
Accucheck™ Advantage II	31.0	342.0
Sure-step™ Onetouch	38.0	348.0

incubated in 37 °C water-bath for 30 min. The solution was then taken to read for optical density (OD) at wave-length of 425-475 nm spectophotometer. Glucose concentrations were obtained from comparing to the standard curve.

PBGMs: Accucheck™ Advantage II (Roche Diagnostics, Germany) and Sure-step™ Onetouch (LifeScan, Inc. Milpitas, CA, USA) were used in the study. They measure glucose concentration by using different analytic methods. Accucheck™ Advantage II detects electrical currents after blood sample reacting chemically with the strip while the Sure-step™ Onetouch measures the color chromogens produced by glucose oxidase catalytic reaction from blood sample through reflectance photometry.

Statistical analyses: The accuracy of each PBGM was evaluated by comparison of glucose concentration obtained from PBGMs to the level from standard method. The values of PBGMs reported as "low" and "high" were excluded because it was unable to compare to the standard method's values. To determine the accuracy of PBGMs, linear regression models and clinical oriented approach were used in this study. Linear regression model of the values acquired from reference method and PBGMs was constructed and intra-class correlation coefficient: r was calculated. T-test for correlation coefficient was determined and *p value* <0.05 was considered as statistically significant. Clinical oriented approach was determined by calculation of mean differences between the values of PBGMs and reference method, which were shown as mean (95% confidence interval). IBM™ SPSS™ Statistics software version 21 was used for statistical analyses in this study.

Results

Clinical cases and initial evaluations: The entire 134 samples were classified as low (< 60 mg/dl), middle (60 – 180 mg/dl) and high (>180 mg/dl) ranges of measurement (MacManus et al., 1988), which were 7, 122 and 5 samples respectively. Ranges of glucose concentration obtained from glucose oxidase test, Accucheck™ Advantage II and Sure-step™ Onetouch were shown in Table 1.

Agreement between each PBGM and reference method: The glucose concentrations of 134 blood samples measured by reference method and either Accucheck™ Advantage II (Fig 1) or Sure-step™ Onetouch (Fig 2) were plotted as linear regression model. The result showed statistically significant correlation (p<0.05) between both PBGMs and the standard method. Correlation coefficient (r) of Accucheck™ Advantage II was 0.839 and Sure-step™ Onetouch was 0.848.

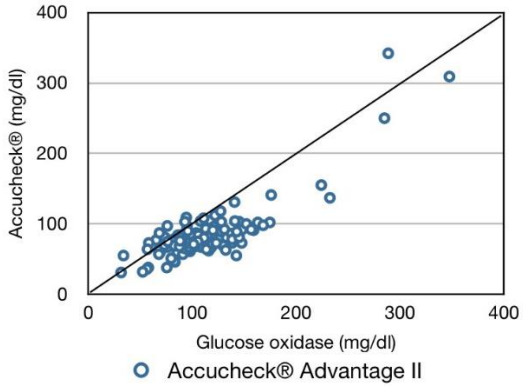

Figure 1 Scatter plot of glucose concentration obtained from Accucheck™ Advantage II samples (y-axis) versus reference method (x-axis).

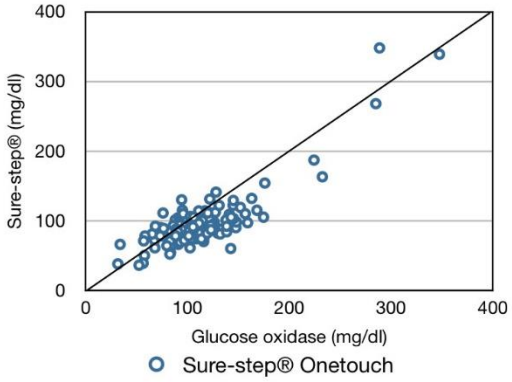

Figure 2 Scatter plot of glucose concentration obtained from Sure-step™ Onetouch samples (y-axis) versus reference method (x-axis).

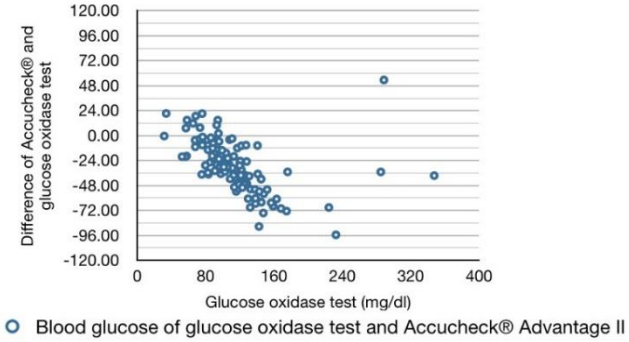

Figure 3 Bland Altman difference plot shows different values of Accucheck™ Advantage II and reference method over the reference values.

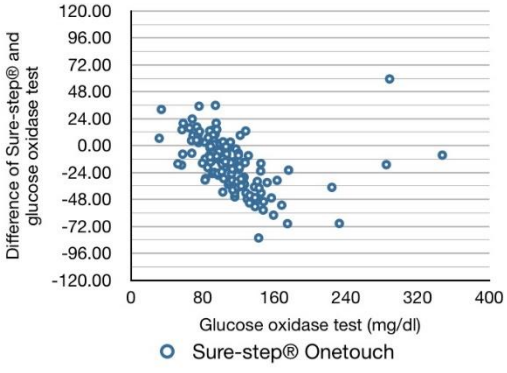

Figure 4 Bland Altman difference plot shows different values of Sure-step™ Onetouch and reference method over the reference values.

Table 2 Ranges of difference (%) of value obtaining from each PBGM compare to the reference method and percentage of samples was within 15% differences from reference method.

	Ranges of difference (%)	Absolute number of samples within 15% of references	Percentage of samples within 15% of references
Accucheck™ Advantage II	-61.4 - 27.8	30	22.56
Sure-step™ Onetouch	-57.8 – 46.67	57	42.86

Clinical-oriented approach study: The differences between the values obtained from reference method and either by Accucheck™ Advantage II (Fig 3) or Sure-step™ Onetouch (Fig 4) of 134 blood samples were scattered plot as the Bland Altman difference plot. Mean differences of Accucheck™ and reference method were -27.9 (-31.91, -23.95) mg/dl. Mean differences of Sure-step™ and reference method were -16.16 (-19.97, -12.35) mg/dl. No significant differences were detected between two mean differences statistically (p>0.05).

Ranges of difference of either Accucheck™ Advantage II samples or Sure-step™ Onetouch samples and reference method were shown in percentage (Table 2). Absolute number and percentage of samples which was within 15% differences from the reference method were also shown.

Discussion

The aim of this study was to clinically evaluate the accuracy of PBGMs that commonly used in small animal hospital in Thailand. The principle of methods was broadly categorized into electrochemical system (Accucheck™ Advantage II) and reflectance photometry (Sure-step™ Onetouch). That is a reason why we considered comparing these particular models to the gold-standard method, glucose oxidase test. This study was designed to collect the blood samples to measure blood glucose levels from client owned dogs visiting the hospital for either health check-up or illness consultation whereas several former studies measured glucose level from artificially glucose-added blood samples (Cohn et al., 2000). The reason is to simulate the clinical situation instead of laboratory setting. Because of unpredictable glucose level obtaining from the real patients, the glucose levels were not evenly distributed in this study (hypo-, hyper-, and euglycemia)

The correlation between either Accucheck™ Advantage II or Sure-step™ Onetouch and the standard method was statistically significant. Both PBGMs showed correlation coefficient over 0.8 and in term of Bland Altman difference plot, no significant differences were detected between two mean differences statistically (p>0.05). The particular finding means both PBGMs yielded acceptable and comparable glucose values. Interestingly, the minus values of mean differences indicate that both PBGMs underestimate glucose concentrations by mean.

The PBGM obtaining blood glucose concentrations which are within 15% differences from the reference value are clinically acceptable (Cohn et al., 2000). The number of samples within 15% differences was 2 times higher in Sure-step™ Onetouch over Accucheck™ Advantage II, which however lower than the previous study of Nganwai et al. (2008). It is probably due to they prepared various plasma glucose concentration by adding known amount of glucose to pool plasma sample while we collected every single sample from every single patient.

Comparing to the standard method, the glucose concentration measured by using PBGMs may vary due to four types of erroneous factors, technician or technical method, sample or sampling method, environment and machine (Cohn et al., 2000). Technical factors include pertinent calibration schedule, proper operating following machine instruction and appropriate amount of sample.

Sample or sampling method is dramatically essential. This study was conducted by using the samples from client-owned animals, therefore the variable in vivo factors from animal to animal are unavoidable. This makes veterinarians have to be aware of. These factors range from healthy to clinically ill animals, various sampling techniques, for example, site of venipuncture and sampling volume, patient's body temperature, degree of hemolysis, various amounts of biochemical substance containing in plasma sample, different types of medication, etc. (Tang et al., 2000; Wess et al., 2000). Environmental factors consist of ambient temperature, moisture, atmospheric pressure, etc. which influence the analytic method. Finally, the machine factors include measuring strip lot. Relevance of the PBGM relies on many sorts of determinants such as regular maintenance schedule, etc.

In terms of preservatives, this study did not use NaF as a glycolysis stopping anticoagulant. The reasons are to simulate the clinical processes as in veterinary clinics, in addition, up to thirty minutes of entire processes from the venipuncture to sample freezing is acceptable and judged as similar as NaF using for preservation of glucose in plasma samples (McMillin, 1990).

In conclusion, blood glucose concentrations obtaining from both PBGMs in current study are clinically acceptable. Sure-step™ Onetouch seemed to be superior over Accucheck™ Advantage II in term of Bland Altman difference plot, however blood glucose concentration measuring by both PBGMs mainly considered underestimated.

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บทคัดย่อ

ความน่าเชื่อถือของเครื่องตรวจน้ำตาลในเลือดชนิดพกพาสำหรับการใช้งานในโรงพยาบาลสัตว์เล็ก

ศิราม สุวรรณวิภัช[1] ปรมินทร์ ยืนนาน[1] รัตนพร ตั้งวังวิวัฒน์[1] ออมอุสาห์ กัวหา[1] ศิรินทร หยิบโชคอนันต์[2]

การศึกษาครั้งนี้มีวัตถุประสงค์ในการประเมินประสิทธิภาพด้านความถูกต้องของเครื่องตรวจระดับน้ำตาลในเลือดชนิดพกพายี่ห้อ Surestep™ และ Accucheck™ สำหรับการใช้ในสุนัขโดยเปรียบเทียบกับวิธีมาตรฐานกลูโคสออกซิเดส ตัวอย่างเลือดสุนัขทั้งหมด 134 ตัวอย่าง จะถูกตรวจระดับน้ำตาลด้วยเครื่องตรวจระดับน้ำตาลชนิดพกพาทั้งสองชนิดและถูกตรวจด้วยวิธีมาตรฐานตามลำดับ พิสัยของระดับน้ำตาลจากตัวอย่างเลือดที่วัดได้อยู่ระหว่าง 31.47 ถึง 347.49 มิลลิกรัมต่อเดซิลิตร จากผลการวิเคราะห์ค่าสัมประสิทธิ์สหสัมพันธ์ภายในชั้นพบว่า ค่าระดับน้ำตาลที่ได้จากเครื่องตรวจระดับน้ำตาลในเลือดชนิดพกพาทั้ง 2 ยี่ห้อมีความสัมพันธ์กับค่าที่ตรวจได้จากวิธีมาตรฐานอย่างมีนัยสำคัญทางสถิติ ($p< 0.05$) เมื่อพิจารณาจากค่าสัมประสิทธิสหสัมพันธ์พบว่าเครื่องตรวจระดับน้ำตาลในเลือดชนิดพกพายี่ห้อ Surestep™ มีความสัมพันธ์กับวิธีมาตรฐานมากกว่าเครื่องตรวจระดับน้ำตาลในเลือดชนิดพกพายี่ห้อ Accucheck™ เพียงเล็กน้อย ($r = 0.847$ และ $r = 0.839$) เมื่อพิจารณาช่วงความคลาดเคลื่อนที่อยู่ในขอบเขต 15 % ของค่ามาตรฐานซึ่งเป็นค่าที่ยอมรับได้ทางคลินิกพบว่าเครื่องตรวจระดับน้ำตาลในเลือดชนิดพกพายี่ห้อ Surestep™ ให้จำนวนตัวอย่างตกอยู่ในช่วงนี้เท่ากับ 42.86 % มากกว่าจากเครื่องตรวจระดับน้ำตาลในเลือดชนิดพกพายี่ห้อ Accucheck™ ซึ่งให้จำนวนตัวอย่างเท่ากับ 22.56 % จากการศึกษาครั้งนี้สรุปได้ว่าเครื่องตรวจระดับน้ำตาลในเลือดชนิดพกพาทั้งสองยี่ห้อเมื่อนำมาใช้กับเลือดสุนัขมีความถูกต้องในภาพรวมเพราะให้ผลการตรวจที่มีความสัมพันธ์กับวิธีมาตรฐาน โดยเครื่องตรวจระดับน้ำตาลในเลือดชนิดพกพายี่ห้อ Surestep™ ดูจะมีความคลาดเคลื่อนน้อยกว่า Accucheck™ อย่างไรก็ตามผลการตรวจจากทั้งเครื่องทั้งสองยี่ห้อก็มีโอกาสส่งผลให้เกิดความคลาดเคลื่อนในการตัดสินใจทางคลินิกได้

คำสำคัญ: สุนัข ระดับน้ำตาล เครื่องตรวจระดับน้ำตาลในเลือดชนิดพกพา

[1]ภาควิชาอายุรศาสตร์ คณะสัตวแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ปทุมวัน กรุงเทพฯ 10330

[2]ภาควิชาเภสัชวิทยา คณะสัตวแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ปทุมวัน กรุงเทพฯ 10330

***ผู้รับผิดชอบบทความ E-mail:** siram.s@chula.ac.th*