Journal of Veterinary Science and Public Health

J. Vet. Sc. Public Health, v. 8, n. 2, p. 081-025, 2021

COMPARISON AMONG GLYCEMIC VALUES OBTAINED BY PORTABLE GLUCOMETERS AND REFERENCE LABORATORY METHOD IN WISTAR RATS (*RATTUS NOVERGICUS*)
HEADINGS: GLUCOMETERS IN RATS

Ardilles Juan Carlos Alves dos Santos[1*], Eva Luana Almeida da Silva[2], Jeine Emanuele Santos da Silva[2]

1. Laboratório de Anatomia - Departamento de Nutrição - Universidade Federal do Piauí - UFPI. Picos, Piauí.
2. Laboratório de Biofísica Teórico - Experimental e Computacional – Departamento de Morfologia e Fisiologia Animal - Universidade Federal Rural de Pernambuco - UFRPE. Recife, Pernambuco.

*Autor para correspondência: ardillesjuan@hotmail.com
DOI: 10.4025/revcivet.v8i2.56508

ABSTRACT
Glucose is the main source of energy used by the cells, and it is in constant flow through the body. One of the ways to measure blood glucose is through a portable glucometer. This device was initially developed to measure blood glucose in humans, but is currently being used to measure blood glucose in animals. The devices were used in this study to test its reliability in rat blood samples. To perform the tests, 0.5 ml of blood was collected for measurement on portable glucometers and 2 ml for the reference laboratory test. Although the average glycemic values of male Wistar rats (submitted to an eight-hour fast) obtained by two portable devices do not differ significantly from that obtained by the reference laboratory test, the use of those should be done carefully.
Keywords: Glucometer, blood glucose, glycemia in animals, insulin, diabetes

INTRODUCTION

Glucose is used by the body cells as the principal energy source in animals and humans, so it is necessary to maintain its blood concentration at normal levels (Bush, 2004). Blood glucose has a constant flux, being transported from the hepatic reservoir to different parts of the body. Under normal conditions, there is a balance between their production and use (Luppi et al., 2007).

In mammals, changes in blood glucose concentration occur after food intake. Initially, there is an increase due to pronounced glucose absorption, leading to inhibition of hepatic glycogenesis and concomitant release of pancreatic insulin (Kaneko, 2008). Usually, the glycemic peak is reached between 30 to 60 minutes, with a consequent reduction in glucose to baseline levels, which may reach lower values during periods of fasting. However, this hypoglycemia is transient and results from the inertia of the regulatory mechanisms, because generally the higher the glycemia, the greater the subsequent hypoglycemia, and the blood glucose levels later return to baseline values (Polakof, Mommsen, Soengas, 2011).

Situations that lead to a persistent decrease or increase in blood glucose can cause serious complications to animal health (Faria, 2007). Hypoglycemia has been reported in ruminants as a metabolic disorder associated with postnatal mortality, ketosis, toxemia of pregnancy, lipid mobilization syndrome, among others (González, 2000).

The persistence of fasting hyperglycemia is the most important diagnostic criterion for diabetes mellitus in humans according to the American Diabetes Association - ADA (2010) and has been reported in several mammals (equines, cattle, sheep, and pigs), being more frequently found in dogs and cats (Polakof, Mommsen, Soengas, 2011).

Individuals are considered normoglycemic when submitted to fasting for eight hours and show glycemic values below 100 mg/dl and/or below 140 mg/dl after administration of 75g of glucose dissolved in the water. Individuals with prediabetes are those with glycemic values equal to or greater than 100 mg/dl in fasting, and equal to or greater than 140 mg/dl and less than 200 mg/dl after administration of 75 g of glucose dissolved in water. On the other hand, individuals with glycemic values greater than 126 mg/dl in fasting and values greater than 200 mg/dl after glucose administration are considered diabetic (BRAZILIAN DIABETES SOCIETY, 2019).

Liver diseases lead to prolonged postprandial hyperglycemia due to secondary glycogenesis decrease (Lassen, 2006; Rebar, 2008). Stressful situations such as painful stimuli, temperature changes, and water deprivation can cause hyperglycemia, by the animal cortisol production increase (Hess, 2010). Pancreatic tumors also lead to increased glucose. This hyperglycemia can be caused by increased glucagon release, promoting the release of glucose from its physiological reserves, or decreased insulin release in addition to hormonal factors (Lassen, 2006; Gilon & Graves, 2011; Fukuta et al., 2012; Mared et al., 2012; Metzger & Rebar, 2012; Mattin et al., 2014).

In research, rodents like rats are commonly used in animal models of type I or type II diabetes mellitus induction because they have pathophysiology similar to occurs in humans, according to the study by Ribeiro et al. (2007). The glycemic values considered for humans have been a reference for rats experimentally induced to diabetes mellitus. Then, animals with blood glucose values equal to or greater than 126 mg/dl in fasting are considered diabetic (Moura et al., 2012).

Periodic glucose level assessments and glycemic curves can be performed with the aid of portable devices (photometric or amperometric sensor) and laboratory methods (Vandresen et al., 2009; Aleixo et al., 2010; Argollo, Faustino, Pedreira, 2010).

Portable glucometers have been used in Veterinary Medicine for being small, light, simple to handle, and require a small blood volume to perform the exam (Foster et al., 1999; Cohn et al., 2000; Wess & Reusch, 2000a; Wess & Reusch, 2000b; Stein & Grego, 2002). Therefore, it is essential to verify the effectiveness of this method when compared to a reference laboratory method, since this last is more complex and classically more accurate (Pica et al., 2003).

Glucometers are designed to monitor blood glucose levels in diabetic human patients. The results provided by this equipment have been used more frequently in guiding the clinical treatment to be administered to patients, so they must provide accurate information (Cohn et al., 2000). Although there are glucometers for veterinary clinics available on the market (Mori et al., 2017), those developed for use in humans are widely used by veterinarians to assist in monitoring and treating their patients (Brito-Casillas et al., 2014).

In addition to the use in the veterinary clinical routine, portable devices have been used in research, as an alternative to reduce the maintenance costs of equipment and supplies needed to perform biochemical tests. The speed in obtaining results is another factor considered when choosing this equipment in an experimental routine (Morley et al., 2018). However, due to the peculiarities of the different animal models used, it is necessary to assess the reliability of the results obtained in the measurements using these devices. Thus, the present study evaluated the efficiency of two portable glucometers concerning a reference method for measuring glycemia in Wistar rats (*Rattus novergicus*), commonly used as an animal model for diabetes.

MATERIALS E METHODS

Portable glucometers

The two portable devices used in this study have a function-based in a photometric biosensor, and have different characteristics despite belonging to the same company. While Accu-chek Performa® (Roche, São Paulo, SP, Br) analyzes only the glycemic index, Accutrend Plus® (Roche, São Paulo, SP, Br) analyzes the glycemic index, total cholesterol, triglycerides and lactate, depending on the test strip used. In addition, the first device mentioned uses 0.6 μL of blood and presents the analysis result in an average time of five seconds. On the other hand, Accutrend plus® requires a volume of capillary blood that varies from 30 to 50 μL and the result is obtained in 12 seconds. The glycemic value is shown on the equipment display in units of mg/dl, according to the manufacturer's information. Both glucometers were developed to monitor glycemic levels in humans using a capillary blood sample obtained by a puncture at the fingertip (Stein & Greco, 2002). Before being used, the devices were calibrated following the manufacturer's guidance.

Animals, blood collection and analysis

All animals in the experiments were used according to the protocols (license number 050/2014, CEUA-UFRPE) approved by the Local Ethics Committee on Animal Use (CEUA) of the Rural Federal University of Pernambuco (UFRPE). *Rattus norvergicus albinus*, variety Wistar, male, adults, clinically healthy, and with body weight between 300 – 330 g were used (n = 30). They are from the bioterium of the Department of Animal Morphology and Physiology (DMFA) of the Rural Federal University of Pernambuco (UFRPE). The rats were kept in boxes (height 14 cm, width 34 cm, and length 41 cm) with a maximum capacity for six animals, in a controlled environment (21 ± 2 ºC and 50% RH), with light-dark cycle (12 / 12 h), receiving commercial feed and water *ad libitum* for two months.

For the blood collection, the animals fasted for eight hours without water restriction. They were placed in a plastic container suitable for the species and the area to be punctured was cleaned (70% alcohol). Then, the puncture of the lateral caudal vein was performed with the aid of a nº. 24 venous catheter. A sample of blood (0.5 ml) was collected and placed in a 2 ml sterile Eppendorf tube, identified for each animal. The blood glucose reading was performed immediately after collection, using portable glucometers.

For the reference test (laboratory test), blood samples (2.0 ml) were also collected by lateral caudal venipuncture and placed in a Vacuette® plastic tube with a coagulation activator. Then, the samples were centrifuged at 2500 rpm during 15 minutes to obtain the serum, which was collected with a pipettor and immediately used for the determination of blood glucose through the enzyme endpoint test (Kit Labtest Diagnóstica SA, Minas Gerais, BR), by absorption spectrophotometry with colorimetric reaction. The reading was performed in triplicate at 505 nm, following the manufacturer's recommendations, using a spectrophotometer Agilent® 8453 (Agilent, California, USA).

Statistical analysis

The data were organized into 3 groups (reference test, Accu chek performa and Accutrend plus) submitted to the Shapiro-Wilk's test, then the Friedman test was used since the reference test group did not follow a normal distribution. Friedman´s test allowed us to compare the glycemic values of the rats obtained by those different methods. To check the agreement between the reference test and each device, the Bland-Altman test was used. All the analyses were performed using the GraphPad Prism software (version 8.4.3, California, USA).

RESULTS

The blood glucose levels of male Wistar rats subjected to an eight-hour fast without water restriction and assessed by a laboratory reference test and two portable devices are shown in table 1. The blood glucose range of the laboratory test was 80 to 167 mg/dl. The Accu chek performa device had a range in blood glucose levels of 81 and 142 mg/dl, while the Accutrend plus device showed a range of 78 to 143 mg/dl. The data variation coefficients were 21.52%, 16.21%, and 15.64% for the reference test, Accu chek performa, and Accutrend plus, respectively. The Friedman test showed that there was no difference among the tests and there was also no difference among rats´ glucose values ($p = 0.6$). Then, there was no difference among plasma glucose values obtained for reference test, Accu chek performa and Accutrend plus.

Table 1. Glycemic values (mg/dl) of male Wistar rats in 8 h of fasting obtained by portable devices (Accu chek performa and Accu trend plus) and laboratory reference method.

Sample	Reference test* (mg/dl)	Accutrend plus (mg/dl)	Accu chek performa (mg/dl)
1	80	83	107
2	80	132	106
3	80	120	92
4	82	108	85
5	82	110	97
6	84	107	117
7	86	102	124
8	86	105	85
9	90	108	93
10	90	117	119
11	93	106	135
12	97	81	78
13	102	129	91
14	103	131	108
15	105	92	96
16	107	100	98
17	108	124	106
18	109	85	83
19	113	103	112
20	121	86	118
21	127	141	113
22	128	106	132
23	128	109	114
24	134	109	115
25	135	137	124
26	135	84	84
27	136	111	110
28	138	84	109
29	139	106	130
30	167	143	142

*For the reference method, the mean of the triplicates of each analyzed sample was used.

Bland-Altman analysis (agreement verification) was done by classifying the results obtained by the reference method in glycemic values less than 100 mg/dl and equal to or greater than 100 mg/dl in relation to the evaluated portable devices (Fig. 1), based on the criteria established by ISO 15193: 2013.

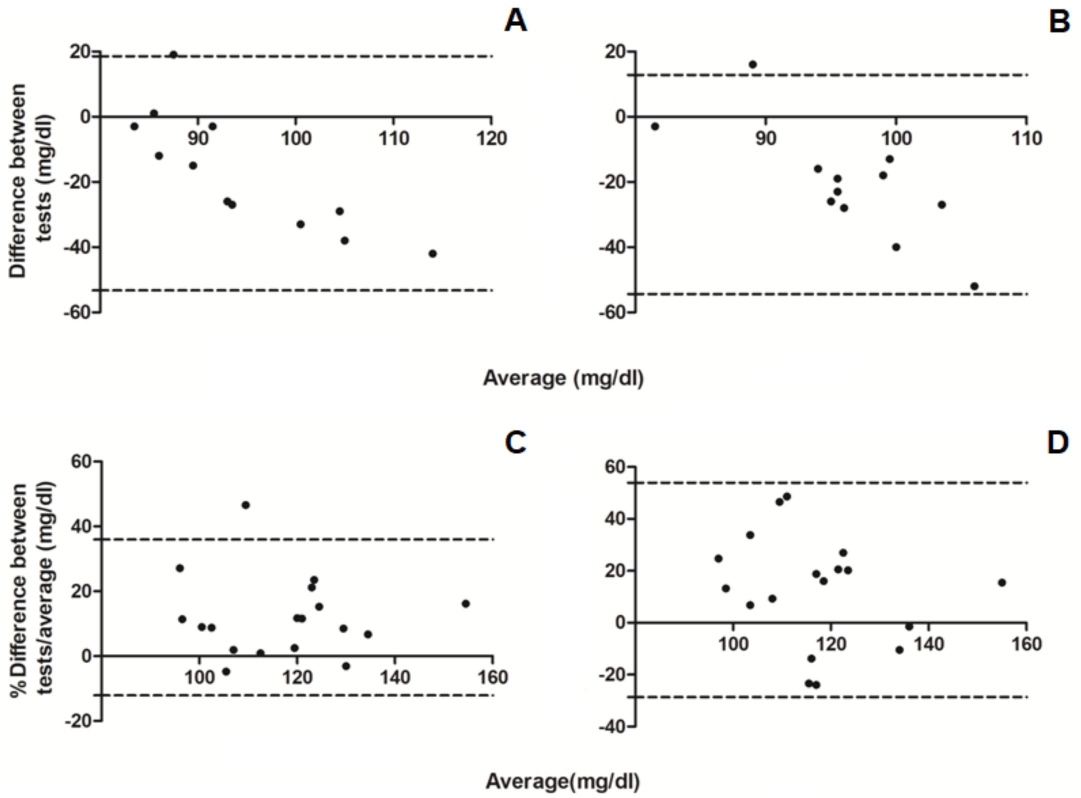

Figure 1. Bland - Altman graphs representing the average difference between the reference test and portable devices for blood glucose values <100 mg / dl (A - Accu chek performa and B - Accutrend plus) and percentage difference in relation to the reference test for values blood glucose> 100 mg / dl (C - Accu chek performance and D - Accutrend plus). On the x-axis are the mean blood glucose values, plotted against absolute (A and B) or percentage (C and D) errors for each corresponding value. The dashed lines represent the confidence limits for the test indicating that values above the upper line exceed acceptable limits (95%) according to the International Organization for Standardization (ISO) 15197: 2013 revised in 2018.

In the reference test, only 20 samples were within the normoglycemia range considered for the specie, while 26 samples were found to be normoglycemic in the analyzes performed by Accu chek performa device, and 24 samples by the Accutrend plus device. None of the samples were classified as hypoglycemic for the methods used, while indexes considered hyperglycemic were 10, four, and six samples for the reference method, Accu chek performa and Accutrend plus, respectively.

DISCUSSION

Based on the literature that seeks to establish normoglycemia reference values for Wistar rats, the data obtained vary in the present study. Dantas et al. (2006) and Melo et al. (2012) obtained values of 104 ± 17.2 and 108 ± 17.4 mg/dl, respectively, from male rats, clinically healthy, and subjected to an eight-hour fast. While Reis et al. (2011) obtained mean values of 141.2 ± 9.1 mg/dl in animals under the same conditions. Marques et al. (2016) showed that the mean of the rats´ glycemic values by the laboratory test was 129.2 ± 7.6 mg/dl, while by the Accutrend plus portable device it was 115.8 ± 4.2 mg/dl.

Conventionally, blood glucose measurement is performed using serum or blood plasma by the enzymatic method, with oxidase or hexokinase, in which the values obtained can be up to 15% higher when compared to those measured in venous blood (Briggs & Cornell, 2004; Brito-Casillas et al. 2014; Johnson & Baker, 2001; Oliveira et al. 2015). Portable glucometers frequently use capillary blood. Generally, the results of capillary glycemia are slightly higher than venous glycemia and this fact is related not only to the time required for changes in venous blood to reach capillary blood levels but also to the type of sample used (Borges & Andrade, 2009; Cordova et al. 2009). In our work, only venous blood samples were used.

Monteiro et al. (2015), in research involving humans, compared the glucose levels of normal and diabetic individuals obtained by means of a portable glucometer (capillary glucose) with a standard laboratory method (venous glucose), verifying through Spearman's correlation test and the Bland-Altman graph a strong agreement between the two glucose assessment methods. In a research with dogs, Ferreira et al. (2013) demonstrated that the method using a portable glucometer is accurate and consistent with enzymatic laboratory tests, in which capillary glycemic levels were compared with the venous levels analyzed by both methods. These results are corroborated with those obtained in a previous assay performed by Neto et al. (2011), in which one of the equipment described in our research (Accutrend Plus) was used, with no significant difference when compared to the reference laboratory test for checking blood glucose in horses.

However, the scientific literature is not unanimous regarding the coherence between the results obtained through portable devices in relation to the reference analysis methods. A study related to human patients pointed out a significant difference between the capillary blood sample analyzed by the portable glucometer and the venous blood analyzed by the laboratory process (Cordova et al., 2009). Neves et al. (2017) demonstrated that the performance of two portable devices in determining glucose was sample-dependent when compared to a standard test; while one of them got better results with venous blood samples, the other one got better performance with capillary blood samples.

Often a statistical analysis of the different methods used to measure the same variable, especially some clinical measure that is quantifiable as blood glucose, is not always suitable as the simple analysis of central tendency and dispersion measures, which can lead to mistaken conclusions in relation to the results obtained (Hirakata, Carney, 2009; Giavarina, 2015). However, there is a statistical evaluation that aims to estimate the agreement between the studied methods known as the Bland-Altman test (1999). In this test, a scatter plot is obtained in which the dependent variable shows the difference between the two paired measurements, while the independent variable represents the average of these measurements.

According to the International Organization for Standardization (ISO) 15197: 2013 revised in 2018, portable glucometers should have a maximum variation of ± 15 mg/dl when the glycemic value is less than 100 mg/dl. In samples with values equal to or greater than 100 mg/dl obtained by the reference tests, this variation should not exceed ± 15%. Taking this criterion, none of the devices was found to meet the standards, which requires caution in their use in experimental protocols. In the comparative analysis performed between serum samples of rats submitted to eight-hour fasting with blood glucose lower than 100 mg/dl obtained through the reference test (n = 12; mean ± standard deviation = 85.83 ± 5.61 mg/dl) and those obtained in the Accu chek performa device measured in venous blood samples differed by up to 54.34 mg/dl below and 12.84 mg/dl above in relation to the reference test, exceeding the established confidence limit (Fig 1A). In relation to Accutrend plus, these differences were 53.22 ml /dl below and 13.17 ml /dl above that obtained in the laboratory test, and also for this device the confidence limit was exceeded, as can be seen in Fig. 1B. When we analyze, for example, sample number 10 (Table 1, line 11), while for the reference test the value is within the normoglycemia range (90 mg/dl), the same sample evaluated by portable devices showed a value that would lead to classify it as a prediabetes condition (variation of 27 mg/dl and 29 mg/dl when Accu chek performa and Accutrend plus were used, respectively), according to the SBD guidelines (2019).

In comparison with serum samples with glycemia equal to or greater than 100 mg /dl obtained by the standard method (n = 18; mean ± standard deviation = 124.20 ± 17.12 mg / dl), the Accu chek performa device showed percentage variation of 28.60% below and 53.94% above the values obtained in the reference test when using venous blood samples, but still within the confidence limit established for the Bland-Altman test (Fig. 1C). On the other hand, for the Accutrend plus device the variations were 12.08% below to 35.94% above the reference values obtained in the laboratory test and exceeding the confidence limit established for the Bland-Altman test (Fig. 1D).

In general, based on what is established by ISO 15197: 2013 and the analysis made using the Bland-Altman difference test, the devices evaluated in this work showed a variation greater than recommended. When Accu chek was used, the variation was approximately twice less than the value obtained in the laboratory test. Although in Accutrend plus this variation is within the allowed, caution is also required in the use of this device for the purpose of establishing a diagnosis in experimental protocols.

When analyzing of our some samples, for example, for samples number 26 and 27 (Tab. 1, lines 27 and 28) the blood glucose values obtained would be classified as a condition of diabetes when evaluated by the reference test, while on portable devices, the samples would be classified as normoglycemic for sample 26 and prediabetes condition for sample 27 according to the SBD guidelines (2019).

The data found in the present study corroborate with a study performed by Brito-Casillas et al. (2014), who analyzed the efficiency and concordance of data obtained through nine portable glycemia monitoring devices developed for use in humans in relation to the reference test, verified the devices inability to reach the criteria established by ISO 15197: 2003 to analyze canine blood samples.

The results obtained in the present study and by other authors who analyzed the glycemia of different animal species, reinforce that the portable devices developed for monitoring blood glucose in humans are easy to use, provide quickness in obtaining the results and require less amount of sample used.

From Wistar rats, portable devices can serve as an alternative to laboratory tests, since there were no significant differences between the average value obtained in the reference test and the devices tested for analyzing blood samples. The evaluation of the agreement between the methods shows that for experimental purposes, the use of these devices must be well evaluated because the data obtained can lead to false-positive results in conditions of normoglycemia. The data obtained also can lead to false negatives in conditions of prediabetes and diabetes in a referred species used as an animal model to induce diabetes or other experimental protocols.

Although the average glycemic values of male Wistar rats submitted to an eight-hour fast obtained by two portable devices which are developed for humans, do not differ significantly from that obtained by the reference laboratory test, the use of the devices should be done by means of careful analysis, especially in conditions of high glycemia in which the data obtained may lead to incorrect results.

Aknowledgements

We thank to Coordination for the Improvement of Higher Education Personnel (CAPES) and the National Council for Scientific and Technological Development (CNPq).

Conflicts of interest

The authors state that there was no conflict of interest.

REFERENCE

ALEIXO, G.S.; COELHO, C.O.M.; TENÓRIO, A.P.M.; GUIMARÃES, A.L.N.; ANDRADE, M.B.; CAVALCANTI, H.B. Uso do glicosímetro portátil para determinar a concentração de glicose no sangue de cães. **Ciência Animal Brasileira,** v.11, p.537-545, 2010.< DOI:10.5216/cab.v11i3.3700>.

AMERICAN DIABETES. Association. Diagnosis and classification of diabetes mellitus. **Diabetes care,** v.33, p. S62-S69. <DOI: 10.2337/dc10-S062>.

ARAÚJO, L.C.R.; SOUZA, L.B.; NASCIMENTO, A.H. Estudo comparativo dos valores de glicemia venosa com glicosímetro versus dosagem laboratorial do laboratório Santa Clara, da cidade de Anápolis. **Ensaios e Ciência: Ciências Biológicas, Agrárias e da Saúde,** v.17, p.89-97, 2013. <DOI:10.17921/1415-6938.2013v17n5p%25p>.

ARGOLLO, A.P.B.; FAUSTINO, T.N.; FAUSTINO, T.N; PEDREIRA, L.C. Valores glicêmicos oferecidos pelo glicosímetro portátil, utilizando sangue de diferentes vias de coleta: estudo de validade**. Revista Brasileira de Terapia Intensiva**, v.22 , p.351-357, 2010. <doi: 10.1590/S0103-507X2010000400007>.

BLAND, J.M., ALTMAN, D.G. Measuring agreement in method comparison studies. **Statistical methods in medical research** v.8, p.135-160, 1999. doi: 10.1177/096228029900800204.

BORGES, B.C.; ANDRADE, T.C. Estudo comparativo entre os níveis de glicemia venosa e glicemia capilar. **Universitas: Ciências de Saúde.** v.7, p. 20-37, 2009.

BRIGGS, A.L.; CORNELL S. Self-monitoring blood glucose (SMG): now and the future. **Journal of Pharmacy Practice,** v.17, p.29-38, 2004. doi: 10.1177/0897190003261306.

BRITO-CASILLAS, Y.; FIGUEIRINHAS, P.; WIEBE, J.C.; LÓPEZ-RÍOS, L.; PÉREZ-BARRETO; MELIAN, C.; WÃGNER D. ISO-based assessment of accuracy and precision of glucose meters in dogs **Journal of Veterinary Internal Medicine** v.28, p.1405–1413, 2014. doi: 10.1111/jvim.12397.

BUSH, B.M. Interpretação de resultados laboratoriais para clínicos de pequenos animais. Rocca, São Paulo, 2004.

COHN, L.A.; MCCAW, D.L.; TATE, D.J.; JOHNSON, J.C. Assessment of five portable blood glucose meters, a point-of-care analyzer, and color test strips for measuring blood glucose concentration in dogs. **Journal of the American**

Veterinary Medical Association, v.216, p.198-202, 2000. doi: 10.2460/javma.2000.216.198.

CORDOVA, C.M.M.; VALLE, J.P.; YAMANAKA, C.N.; CORDOVA, M.M. Determinação das glicemias capilar e venosa com glicosímetro versus dosagem laboratorial da glicose plasmática. **Jornal Brasileiro de Patologia e Medicina Laboratorial,** v.45, p.379-384, 2009. doi: 10.1590/S1676-24442009000500006

FARIA, P.F. Diabetes Mellitus em cães. **Acta Scientiae Veterinariae** v.1: p.8-22, 2007.
doi: https://doi.org/10.21708/avb.2007.1.1.258

FERREIRA, P.A.; MUELLER, E.M.; FISCHER, E.C.; TILLMAN, M.T.; PERES, W.; NOBRE, M.O. Glicemia do sangue capilar e venoso de cães saudáveis: mensuração por método eletroquímico versus enzimático laboratorial. **Semina: Ciências Agrárias,** v.34, p.1287-1292, 2013. doi: 10.5433/1679-0359.2013v34n3p1287-1292

FOSTER, S.A.; GOODE, J.K.R.; SMALL, R.E. Home blood glucose monitoring. **The Annals of Pharmacotherapy,** v.33, p.355-363, 1999. doi: 10.1345/aph.17328

FUKUTA, H.; MORI, A.; URUMUHAN, N.; LEE, P.; ODA, H.; SAEKI, K.; KURISHIMA, M.; NOZAWA, S.; MIZUTANI, H.; MISHINA, S.; ARAI, T.; SAKO, T. Characterization and Comparasion of Insulin Resistance Induced by Cushing Syndrome or Diestrus against Healthy Control Dogs as Determined by Euglycemic-Hyperinsulinemic Glucose Clamp Profile Glucose Infusion Rate Using an Artificial Pancreas Apparatus. **J Vet Med Sci.** v.74, p. 1527-1530, 2012.

GIAVARINA, D. Understanding bland altman analysis. Biochemia medica v.25, p.141-151.
2015. doi: 10.11613/BM.2015.015

GILON, C.; GRAVES, T. Interpretation of laboratory tests for canine Cushing's Syndrome. **Top Companion Anim Med**. v. 26 (2). P. 98-108, 2011.

HESS, R. S. Insulin Resistance in Dogs. **Vet Clin North Am Small Anim Pract**. v. 40 (2), p. 309-316, 2010

HIRAKATA, V.N.; CAMEY, A.S. Análise de concordância entre métodos de Bland-Altman. **Revista HCPA** ,v.29, p. 261 – 268, 2009. https://seer.ufrgs.br/hcpa/article/view/11727 /7021.

International Organization for Standardization. In vitro Diagnostic test systems – Requirements for blood-gulcose monitoring systems for self-testing in managing Diabetes Mellitus. **European Committee for Standardization (CEN)**, Brussels, ISO 15197. 2013. https://infostore.saiglobal.com/preview/98702766777.pdf?sku=857342_SAIG_NSAI_NSAI_2039529/.

JOHNSON, R.N.; BAKER, J.R. Error detection and measurement in glucose monitors. **Clinica Chimica Acta**, v. 307, p. 61-67, 2001.

KANEKO, J.; HARVEY, J.; BRUSS, M. Clinical biochemistry of domestic animals 5th ed. Academic press, San Diego, 1997.

LASSEN, E. D. Laboratory Evaluation of the Endocrine Pancreas and of Glucose Metabolism. In: THRALL, M. A.; BAKER, D. C.; CAMPBELL, T.W.; DENICOLA, D.; FETTMAN, M. J., LASSEN, E. D. (Eds) **Veterinary Hematology and Clinical Chemistry**. (2ªEd, pp 431-444). Blackwell Publishing. USA, 2006.

LOPES, R.D. Manual para coleta de sangue venoso em caninos e felinos. Trabalho de Conclusão de Curso (Especialização), Universidade de São Paulo, 2009.

LUPPI, M.M.; BASTOS, J.A.B.; MALTA, M.C.C.; COSTA, M.E.L.T.; PEREIRA, M.M. Estudo comparativo entre métodos de determinação da glicemia em macacos-prego (Cebus apella) mantidos em cativeiro. **Revista Portuguesa de Ciência Veterinária.** v.102, p.75-79, 2007. http://www.fmv.ulisboa.pt/spcv/PDF/pdf6_2007 /75-79.pdf

MARED, M.; CATCHPOLE, B.; KAMPE, O.; FALL, T. Evaluation of circulating concentrations of glucose homeostasis biomarkers, progesterone, and growth hormone in healthy Elkhounds during anestrus and diestrus. **Am J Vet Res**. v. 73 (2). p. 242-247, 2012.

MARQUES, A.C.R.; SCHIAVON, F.P.M.; TRAVASSOS, P.B.; EIK, V.F.; GODOY, G.; SCHAMBER, C.R.; BAZOTTE, R.B. Evaluation of the impact of orally administered carbohydrates on postprandial blood glucose levels in different pre-clinical models. **Brazilian Journal of Pharmaceutical Sciences**, v.52, p.761-769, 2016.

MATTIN, M.; O'NEILL, O.; CHURCH, D.; MCGREEVY, THOMSON, P. C.; BRODBELT, D. An epidemiological study of diabetes mellitus in dogs attending first opinion practice in the UK. **Vet. Rec.** v. 174 (14), p. 349, 2014.

MELO, M.G.D.; DÓRIA, G.A.A.; SERAFINI, M.R.; ARAÚJO, A.A.S. Valores de referência Hematológicos e Bioquímicos de Ratos (Rattus novergicus linhagem Wistar) provenientes do biotério central da Universidade Federal de Sergipe. **Scientia Plena** v.8, p.1 – 6, 2012.

METZGER, F. L.; REBAR, A. H. Clinical pathology interpretation in geriatric veterinary patients. **Vet Clin Small Anim.** v. 42 (4). p. 615-629, 2012.

MONTEIRO, S.C.M.; GOMES, E.; BELFORT, I.K.; AVELAR, M.F.; SAMPAIO, R.M. Análise comparativa da determinação de glicemia capilar e venosa com glicosímetro versus dosagem laboratorial/Comparative analysis of capillary and venous glycemia with glucometer versus laboratory dosage. **Revista de Pesquisa em Saúde** v.16, p.41-44, 2015

MORLEY, L.A.; GOMEZ, T.H.; GOLDMAN, J.L.; FLORES, R.; ROBINSON, M.A. Accuracy of 5 Point-of-Care Glucometers in C57BL/6J Mice. **Journal of the American Association for Laboratory Animal Science**, v.57, p. 44–50, 2018. PMCID: PMC5875097.

MOURA, L.P.; GURJÃO, A.L.D.; JAMBASSI FILHO, J.C.; MIZUNO, J.; SUEMI, C.; MELLO, M.A.R. Spirulina, exercício e controle da glicemia em ratos diabéticos. **Arquivo Brasileiro de Endocrinologia e Metabolismo,** v.56, p.25-32, 2012 doi: 10.1590/S0004-27302012000100005.

NETO, A.R.T.; BOTELHO, R.G.; SOUZA, K.E.; GOMES, J.L.; LIMA, E.M.M. Ineficácia do aparelho portátil Accutrend® Plus na clínica médica de equinos. **ARS Veterinária**, v.27, p.17-21, 2011.

OLIVEIRA, Y.S.G.; COSTA JÚNIOR, J.D.C.; SANTOS-LEONARDO, A.S.; MORAIS, K.S. Comparação entre os métodos laboratorial e portátil na análise da glicemia em felinos com amostras de sangue venoso central e capilar. **Revista Ciência Animal Brasileira** v.16, p.279-286, 2015. doi: 10.1590/1089-6891v16i231266.

PICA, C.Q.; MENEZES, J.R; ALBERTAZZI, J.A.; CAMIÑA, R.M. Avaliação comparativa de glicosímetros portáteis através de curva glicêmica induzida. **In: Anais do Congresso Brasileiro de Metrologia** 3, Recife, Brasil; pp. 1-7, 2003.

POLAKOF, S.; MOMMSEN, T.P.; SOENGAS, J.L. Glucosensing and glucose homeostasis: from fish to mammals. **Comparative Biochemistry and Physiology Part B: Biochemistry and Molecular Biology** v.160, p.123-149, 2011. doi: 10.1016/j.cbpb.2011.07.006.

REBAR, A. H. A Case Oriented Approach to Liver Laboratory Profiling in Dogs and Cats. **33rd World Small Animal Veterinary Congress**. Dublin. Irelanda, 2008.

REIS, T.A.; GOULART, P.F.P.; DE OLIVEIRA, R.M.E.; DE OLIVEIRA, L.; DE AREU, O.S. Parâmetros metabólicos de ratos wistar submetidos à dieta suplementada com estévia e açúcar. **Semina: Ciências Agrárias**, v.32, p.1477-1487, 2011. doi: 10.5433/1679-0359.2011v32n4p1477.

Sociedade Brasileira de Diabetes (2019) Posicionamento Oficial SBD nº 01/2019. Conduta Terapêutica no Diabetes Tipo 2: Algoritmo SBD. https://www.diabetes.org.br

/publico/images/pdf/sbd_dm2_2019_2.pdf/. Accessed 12 december 2019.

STEIN, J.E.; GRECO, D.S. Portable blood glucose meters as a means of monitoring blood glucose concentrations in dogs and cats with diabetes mellitus. **Clinical Techniques in Small Animal Practice,** v.17, p.70-72, 2002. doi: 10.1053/svms.2002.33041.

VANDRESEN, L.T.S.; SCHNEIDER, D.S.L.G.; BATISTA, M.R.; CROZATTI, M.T.L.; TEIXEIRA, J.J.V. Níveis glicêmicos de pacientes diabéticos segundo estudo comparativo entre duas técnicas **Revista de Ciências Farmacêuticas Básica e Aplicada,** v.30, p.111-113, 2009. http://files.bvs.br/upload/S/1808-4532/2009/v30n1/a014.pdf.

WESS, G.; REUSCH, C. Evaluation of five portable blood glucose meters for use in dogs. **Journal of the American Veterinary Medical Association**, v.216, p.203-209, 2000a. doi: 10.2460/javma.2000.216.203.

WESS, G.; REUSCH, C. Capillary blood sampling from the ear of dogs and cats and use of portable meters to measure glucose concentration. **Journal of Small Animal Practice,** v.41, p.60-66, 2000b. doi: 10.1111/j.1748-5827.2000.tb03164.x.