

Evaluation of four point-of-care meters for rapid determination of blood lactate concentrations in dogs

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Objective—To determine whether blood lactate values determined in dogs with 4 commercially available point-of-care meters were in agreement with values determined with a critical care laboratory blood analyzer.

Design—Prospective study.

Animals—50 dogs evaluated for emergency treatment.

Procedures—Blood samples were collected at initial evaluation and processed on 4 point-of-care meters and on a critical care laboratory blood analyzer.

Results—All 4 point-of-care lactate meters generated measurements that were in agreement with the hospital's critical care analyzer. Values for agreement (bias) between the 4 point-of-care meters and the critical care analyzer were -0.652 (limits of agreement [LA], -1.958 to 0.654), -0.670 (LA, -2.110 to 0.769), -0.096 (LA, -2.071 to 1.879), and -0.498 (LA, -2.616 to 1.620), respectively.

Conclusions and Clinical Relevance—Despite its prognostic and therapeutic relevance, blood lactate measurement in dogs has been hampered by the inability to perform the test in a timely fashion. Results of the present study indicated that several handheld point-of-care lactate meters provided results that were in agreement with a laboratory critical care blood analyzer. (*J Am Vet Med Assoc* 2007;230:1315–1318)

High blood lactate concentration has been used as an indirect measure of systemic hypoperfusion and tissue hypoxia in critically ill humans and other animals.¹⁻³ In addition, some conditions, such as sepsis, have been associated with increases in blood lactate concentration resulting from disordered cellular metabolism rather than from absolute hypoxemia.^{3,4} Measurement of blood lactate concentration has prognostic as well as therapeutic value. In human studies,⁵ the survival rate of patients with shock decreases from 90% to 10% as blood lactate concentration increases from 2.1 to 8.0 nmol/L. In veterinary medicine, blood lactate concentrations are prognostic in some canine diseases,⁵ as well as in the general population of critically ill dogs.⁶

The inability to obtain lactate values in a timely, cost-effective manner has made use of this blood analyte problematic. Treatment decisions in critically ill patients with hypoperfusion are time sensitive and often require serial lactate measurements to evaluate the patient's response to treatment.⁷⁻¹⁰ Measurement of lactate concentration traditionally involves sending blood to a central laboratory for analysis. Transporting blood samples to an outside laboratory for lactate analysis is not practical because of the time required to obtain results and the effect of the delay between sample acquisition and analysis.^{1,2} The inconvenience and cost associated with obtaining statim blood test results have limited the use of

ABBREVIATIONS

POC	Point-of-care
LA	Limits of agreement
NAD ⁺	Nicotinamide adenine dinucleotide

lactate measurements in critically ill patients even at those hospitals that have laboratories that can measure blood lactate concentration.

Recently, 3 commercially available handheld POC lactate measuring devices (A,^a B,^b and C^c) have become available. These handheld units are simple to operate, inexpensive to maintain, and require only a single drop of blood. The units were originally designed for use by high-performance athletes who use blood lactate concentrations as a mechanism to monitor and adjust workouts, and the units are calibrated for use with capillary blood. At this time, none of these units have been validated for use with venous blood in companion animals. A medical-grade POC analyzer (D^d) is also commercially available.

The purpose of the study reported here was to determine whether lactate values obtained from 4 commercially available POC meters were in agreement with those obtained with a critical care laboratory blood analyzer.^e

Materials and Methods

Animals—Fifty dogs that were evaluated at the hospital's emergency service during a 2-month period were admitted to the study. The only selection criteria used for recruitment of dogs were that blood would otherwise have to be drawn for testing purposes and no

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fluids containing lactate had been given IV in the past 24 hours. No attempt was made to screen dogs on the basis of age, sex, and type of disease or severity of illness. Owners provided written informed consent. The School of Veterinary Medicine Clinical Study Protocol Review Committee approved the protocol for this study.

Blood samples—A blood sample was collected into a syringe via direct venipuncture and minimal restraint or via IV catheter. The blood sample was divided, and 1.0 mL was placed in a lithium heparin tube and taken to the laboratory for immediate processing by trained technicians on the critical care blood analyzer. The remainder of the sample was used for the POC meters. All meters were calibrated in accordance with the manufacturer's specifications and were operated by individuals trained in their use.

Meters—Presently, POC lactate meters use 1 of 2 methodologies. In the first methodology, which is used only by meter C, an unmeasured drop of blood (approx 25 μ L) is placed on a strip that comprises 4 layers.¹¹ The top layer is composed of a protective mesh where the blood is applied. The second layer is a glass-fiber layer that permits separation of blood cells from the serum. The serum diffuses to the next layer, where a chemical reaction with lactate oxidase occurs. This reaction results in color change, and the degree of change is dependent on the concentration of lactate in the serum. The bottom layer is a support layer that extends the entire length of the strip. Once a drop of blood is placed on the strip, the resulting color change in the third layer is measured by use of reflectance photometry. This is translated into a lactate value that is displayed on a liquid crystal display.¹¹

The more common methodology used by meters A and B involves an amperometric reaction. In these meters, 5 μ L of blood is automatically drawn from the syringe into the hollow portion of a test strip. The blood reacts with lactate oxidase and potassium ferricyanide to produce an anodic current. The meters measure the magnitude of the current and translate it into a lactate value that is displayed on a liquid crystal display.¹² Although collection of the blood sample is not automated, the medical-grade POC meter (D) uses a similar methodology, except that platinum is substituted for potassium ferricyanide.

The critical care laboratory blood analyzer is equipped with a lactate-specific electrode.¹³ The unit automatically draws 130 μ L of blood, and a membrane covering the electrode allows only serum to enter the probe. Membrane-bound lactate oxidase catalyses the conversion of lactate and oxygen to pyruvate and hydrogen peroxide. At a constant potential of 0.7 V, electroactive hydrogen peroxide is oxidized at the surface of a platinum electrode. The current generated by the flow of electrons at the surface of the platinum electrode is proportional to the lactate concentration of the sample. Once calculated, the blood lactate concentration is displayed on a screen and printed.^d

Statistical analysis—Agreement between each of the handheld POC meters and the laboratory blood

analyzer was determined by use of the Bland-Altman method. Bias was defined as the mean difference between 2 methods. Limits of agreement were defined as the bias \pm 1.96 \cdot SD. Statistical analysis was performed by use of a commercially available statistical program.^f

Results

Fifty dogs of 21 breeds were included in the study, including 8 Labrador Retrievers; 6 Golden Retrievers; 5 mixed-breed dogs; 4 Dachshunds; 3 Boxers; 3 Poodles; 2 Rottweilers; 2 Shih Tzus; 2 Weimaraners; 2 Doberman Pinschers; 2 Great Danes; and 1 each of Chihuahua, Catahoula Cattle Dog, English Bull Dog, French Bull Dog, Scottish Terrier, Greyhound, Border Collie, Schnauzer, Basenji, Pomeranian, and German Shepherd Dog. Dogs ranged from 1.5 months to 14.5 years of age (median age, 4.0 years). There were 23 males and 27 females. Dogs were evaluated at the emergency service, and tentative diagnoses included gastritis or pancreatitis ($n = 8$), seizure (6), renal failure (6), liver disease (3), laceration or wound (3), toxin exposure (3), intervertebral disk disease (2), heat stroke (2), anorexia (2), respiratory distress (2), hypoadrenocorticism (1), pseudohypoadrenocorticism (1), lung lobe torsion (1), hemoabdomen (1), hemothorax (1), ascities of unknown cause (1), snake bite (1), diabetic ketoacidosis (1), gunshot wound (1), vehicular accident (1), gastric dilatation and volvulus (1), heart failure (1), and lymphadenopathy (1).

Lactate concentrations as measured by the laboratory analyzer ranged from 0.9 to 15.0 mmol/L (mean, 3.4 mmol/L). Degree of agreement between meter A (Figure 1) and the laboratory analyzer (bias, -0.652 ; LA, -1.958 to 0.654) was highest, compared with the other POC lactate analyzers. Agreement between meter D (Figure 2) and the laboratory analyzer was similar (bias, -0.670 ; LA, -2.110 to 0.769). Meter C (Figure 3; bias, -0.096 ; LA, -2.071 to 1.879) and meter B (Figure 4; bias, -0.498 ; LA, -2.616 to 1.620) had less agreement, as indicated by the wider LA.

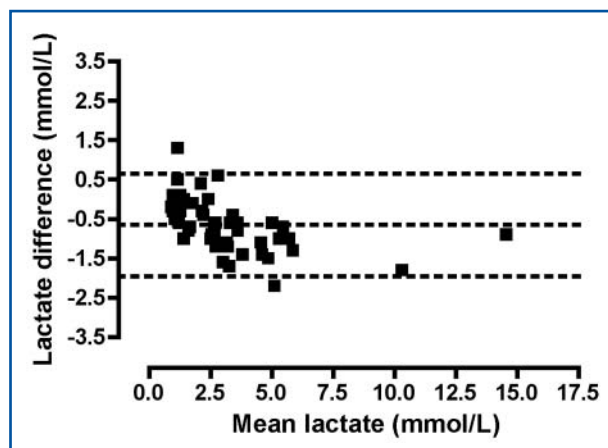


Figure 1—Bland-Altman plot of the differences between measurements of blood lactate values in 50 dogs obtained by use of 2 analyzers (analyzer A^a – critical care laboratory blood analyzer⁹) versus the mean of the values obtained by use of the 2 analyzers.

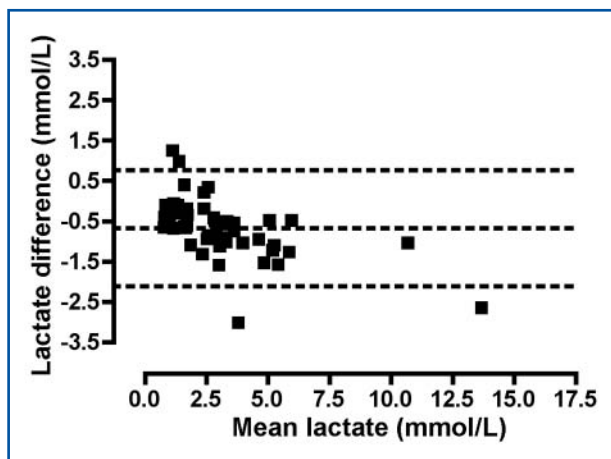


Figure 2—Bland-Altman plot of the differences between measurements of blood lactate values in 50 dogs obtained by use of 2 analyzers (analyzer D^d – critical care laboratory blood analyzer⁹) versus the mean of the values obtained by use of the 2 analyzers.

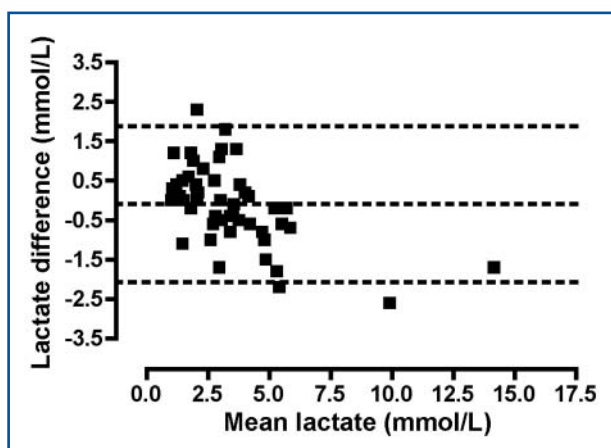


Figure 3—Bland-Altman plot of the differences between measurements of blood lactate values in 50 dogs obtained by use of 2 analyzers (analyzer C^c – critical care laboratory blood analyzer⁹) versus the mean of the values obtained by use of the 2 analyzers.

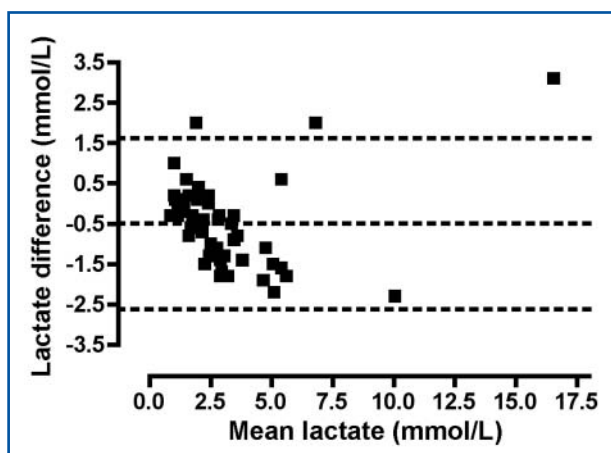


Figure 4—Bland-Altman plot of the differences between measurements of blood lactate values in 50 dogs obtained by use of 2 analyzers (analyzer B^b – critical care laboratory blood analyzer⁹) versus the mean of the values obtained by use of the 2 analyzers.

Discussion

Two cellular pathways are used in the generation of ATP. The first pathway, which is composed of glycolysis, the citric acid cycle, and the electron transport chain, is a highly efficient, but relatively slow, aerobic pathway that can generate 36 moles of ATP for each mole of glucose that is oxidized to carbon dioxide and water.¹⁴ In this pathway, glycolysis produces pyruvate and reduces NAD⁺. In the presence of oxygen, the citric acid cycle metabolizes the pyruvate and recycles the NAD⁺.^{14,15} The second pathway for generating ATP is based only on glycolysis.¹⁴ It is a substantially less complex, faster process that can proceed in the absence of oxygen. This pathway generates only 2 moles of ATP for each mole of glucose.^{2,14,15} As in anaerobic metabolism, glycolysis produces pyruvate and reduces NAD⁺. For anaerobic metabolism to continue, NAD⁺ must be recycled. Therefore, cells dispose of the excess pyruvate and recycle NAD⁺ by converting pyruvate to lactate.^{2,14,15} The resulting accumulation of lactate is sometimes referred to as the oxygen debt. Later, when oxygen conditions improve, most lactate is converted back to pyruvate and oxidized by the citric acid cycle.¹⁴

Hyperlactatemia is the result of lactate production that proceeds at a rate that is faster than its metabolism. This can be caused in 1 of 3 ways: tissue hypoxemia causing a shift from aerobic to anaerobic cellular metabolism,³ a defect in cellular metabolism resulting in failure of the citric acid cycle to accept pyruvate at an acceptable rate,⁴ or relative rather than absolute hypoxemia.² Increases in blood lactate concentration associated with sepsis have been attributed to disordered cellular metabolism which results in glycolysis preceding at a rate faster than the citric acid cycle.⁴ Relative hypoxemia often occurs with exercise and seizures. Racing Greyhounds can generate a serum lactate concentration of 30 mmol/L, whereas animals with seizures often have lactate concentration in the 6 to 10 mmol/L range.² Clinically, the most important cause of hyperlactatemia is tissue hypoxia, as occurs with hypoperfusion or reduced arterial oxygen content.

Although relevant studies in veterinary medicine are limited, reports^{9,16} in the human literature indicate that in critically ill patients with hypoperfusion, serial lactate concentration measurements can be used to estimate the response to treatment and to provide treatment end points. In some diseases, increases in lactate concentration that decrease in response to appropriate resuscitative therapy are associated with a better prognosis than are lactate concentrations that fail to respond.^{10,16} Persistent increases in serial lactate concentrations have also been associated with increased mortality rates in cardiac patients⁸ and patients with acute renal failure undergoing hemofiltration.¹⁷ Results of these studies suggest that in the critical care setting, measurement of lactate concentration can provide meaningful insight into the adequacy of treatment as well as prognosis. Studies in veterinary medicine have already revealed the prognostic value of single-measurement lactate concentrations in dogs with gastric dilatation-volvulus,¹⁸ as well as the prognostic value of serial lactate measurements in dogs with babesiosis.¹⁹ Addi-

tional studies are needed to determine whether lactate measurement has usefulness in determining response to treatment and prognosis in other diseases associated with hypoperfusion or disordered cellular metabolism. Such studies would undoubtedly be aided by the availability of reliable POC meters.

The present study was limited to a small number of patients; however, studies^{1,20} in the human medical literature with similar sample sizes have been used to validate the use of lactate POC meters in critical care and neonatal medicine. Examination of the Bland-Altman plots revealed that the POC meters often overestimated serum lactate concentration when concentrations were low, and underestimated serum lactate concentration as concentrations increased; however, for clinical purposes, the differences were small. This was especially true for meters A and D. The minor differences in agreement between the POC meters and the critical care blood analyzer were probably attributable to variations in the methodologies used.

The prognostic value of measuring blood lactate concentrations has been confirmed by studies in the human and veterinary literature. Time, cost, and the inconvenience associated with lactate measurement have prevented widespread use of this important blood analyte. The commercially available POC meters studied here bring the promise of nearly instantaneous cage-side lactate measurement. In addition, the POC meters are inexpensive to operate and simple to maintain. Results indicated that all 4 POC lactate meters produced results that were in agreement with the hospital's critical care blood analyzer, although the degree of agreement did vary among analyzers.

- a. Lactate Pro, Arkray Inc, Kyoto, Japan.
- b. Lactate Scout, SensLab GmbH, Leipzig, Germany.
- c. Accutrend, Roche Diagnostics, Basel, Switzerland.
- d. iSTAT, Abbott Point of Care, Abbott Laboratories, Abbott Park, Ill.
- e. Stat Profile Critical Care Xpress, Nova Biomedical, Waltham, Mass.
- f. GraphPad Prism, version 4.0 for Macintosh, GraphPad Software Inc, San Diego, Calif.

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