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Evaluation of 2 portable ion-selective electrode meters for determining whole blood, plasma, urine, milk, and abomasal fluid potassium concentrations in dairy cattle

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ABSTRACT

Two low-cost ion-selective electrode (ISE) handheld meters (CARDY C-131, LAQUAtwin B-731; Horiba Ltd., Albany, NY) have recently become available for measuring the potassium concentration ($[K^+]$) in biological fluids. The primary objective of this study was to characterize the analytical performance of the ISE meters in measuring $[K^+]$ in bovine whole blood, plasma, urine, milk, and abomasal fluid. We completed 6 method comparison studies using 369 whole blood and plasma samples from 106 healthy periparturient Holstein-Friesian cows, 138 plasma samples from 27 periparturient Holstein-Friesian cows, 92 milk samples and 204 urine samples from 16 lactating Holstein-Friesian cows, and 94 abomasal fluid samples from 6 male Holstein-Friesian calves. Deming regression and Bland-Altman plots were used to characterize meter performance against reference methods (indirect ISE, Hitachi 911 and 917; inductively coupled plasma-optical emission spectroscopy). The CARDY ISE meter applied directly in plasma measured $[K^+]$ as being 7.3% lower than the indirect ISE reference method, consistent with the recommended adjustment of +7.5% when indirect ISE methods are used to analyze plasma. The LAQUAtwin ISE meter run in direct mode measured fat-free milk $[K^+]$ as being 3.6% lower than the indirect ISE reference method, consistent with a herd milk protein percentage of 3.4%. The LAQUAtwin ISE meter accurately measured abomasal fluid $[K^+]$ compared to the indirect ISE reference method. The LAQUAtwin ISE meter accurately measured urine $[K^+]$ compared to the indirect ISE reference method, but the median measured value for urine $[K^+]$ was 83% of the true value measured by inductively coupled plasma-optical emission spectroscopy. We conclude that the CARDY and LAQUAtwin ISE meters are practical, low-cost, rapid, accurate point-of-care instruments suitable for measuring $[K^+]$ in whole blood, plasma, milk, and abomasal fluid samples from cattle. Ion-selective electrode methodology is not suitable for measuring $[K^+]$ in bovine urine.

Key words: hypokalemia, point-of-care

INTRODUCTION

Hypokalemia is common in lactating dairy cattle with abomasal displacement or volvulus, developing in response to alkalemia secondary to sequestration of chloride in the gastrointestinal tract (Constable et al., 1991; Rohn et al., 2004). Low feed intake, obligatory loss of potassium in milk (1.4 g of K/L of milk), hyperglycemia, and hypovolemia are also considered main predisposing factors (Constable et al., 2013). Hypokalemia is also common in lactating dairy cattle with abomasal impaction (Wittek et al., 2005), clinical mastitis (Ohtsuka et al., 1997; Smith et al., 2001), and retained placenta (Hashem and Amer, 2008). Lactating dairy cattle with hepatic lipidosis and cattle receiving multiple injections of isoflupredone acetate as part of the treatment of ketosis are more susceptible to hypokalemia (Neff et al., 1960; Kalaitzakis et al., 2010; Sattler and Fecteau, 2014). The development of optimal treatment protocols for hypokalemic dairy cattle requires accurate, rapid, and repeated measurements of whole blood, plasma, or serum potassium concentration ($[K^+]$) because the clinical signs of hypokalemia are nonspecific (Radostits et al., 2007; Sattler and Fecteau, 2014) and excessive potassium administration can be fatal (Constable, et al., 2014).

Hypokalemia is most commonly defined in adult cattle as serum $[K^+]$ <3.9 mEq/L (Radostits et al., 2007; Constable et al., 2013). Plasma $[K^+]$ is approximately 0.4 mEq/L lower than serum $[K^+]$ because intracellular potassium is released from platelets during clotting (Hartland and Neary, 1999); consequently, plasma is

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preferred to serum for the accurate measurement of blood [K^+]. Plasma [K^+] is widely accepted to accurately reflect intracellular potassium stores in euglycemic or hypoglycemic animals with a blood pH within the reference range; however, it is generally believed that in severe alkalemia, plasma [K^+] must be <2.5 mEq/L for clinically significant intracellular potassium depletion to be present (Burnell and Scribner, 1957).

A variety of analytical procedures have been developed to measure the total or ionized [K^+] in blood and other biological fluids, and these procedures have distinct advantages and disadvantages (Fogh-Andersen et al., 1984; Maas et al., 1985; Burnett et al., 2000; D'Orazio et al., 2000; Buzanovskii, 2015). Ion-selective potentiometry has become the dominant methodology for the analysis of ionized [K^+] in many biological fluids because it is accurate, rapid, and inexpensive (Burnett et al., 2000; D'Orazio et al., 2000). Ion-selective electrode (**ISE**) methods have 3 main components: (1) a polyvinyl chloride membrane containing the antibiotic valinomycin that provides a selectively permeable barrier to potassium ions; (2) an internal filling solution with a weak fixed concentration of potassium ions that is separated from the test solution by the selectively permeable membrane; and (3) an internal reference electrode with a known potassium ion activity (Kimura et al., 1979; Anker et al., 1983). Following application of the test solution to the sensor, potassium ions rapidly diffuse through the selectively permeable membrane, and at equilibrium, the difference in potassium ion activity between the test solution and internal filling solution generates an electrical potential that is compared with the reference electrode. The potassium ion activity in the test solution is then calculated using the Nernst equation (Oesch et al., 1986).

The clinical application of ISE technology uses 2 approaches: direct ISE, which uses an undiluted sample, and indirect ISE, which uses a diluted sample. Direct ISE technologies, which measure the electrolyte activity in the water phase of a fluid, are widely used in point-of-care devices. Consequently, when direct ISE methods are applied to whole blood or milk, the measured electrolyte activity is not affected by the plasma protein concentration and packed cell volume or the fat and protein percentage, respectively. In contrast, indirect ISE technologies are extensively used in clinical pathology laboratories because they require a low volume of sample and provide a larger analytical range, which permits measuring electrolyte activity in fluids other than plasma or serum, such as urine, milk, saliva, and sweat (Dimeski et al., 2012). However, the extensive sample dilution in indirect potentiometry means that changes in the volume of the nonaqueous portion of the sample (such as a change in the protein concentration in whole blood, plasma, and serum from the assumed reference value of 70 g/L or the presence of hyperlipidemia) results in underestimated plasma or serum [K^+] in hyperproteinemic and hyperlipidemic samples and overestimated potassium concentrations in hypoproteinemic samples (D'Orazio et al., 2000; Dimeski and Barnett, 2005; Dimeski et al., 2006; Jain et al., 2009). As a consequence, whole blood, plasma, and serum [K^+] values measured by indirect ISE should be increased by 7.5% (1/[1 − 0.070]) (D'Orazio et al., 2000). A second analytical issue is the application of ion-selective potentiometry to urine, which is a complex matrix with variable pH, ionic strength, and cation–anion concentration. Initial studies of ISE methodology in undiluted human urine indicated the presence of anion interference (Jenny et al., 1980; Oesch et al., 1986), which was satisfactorily addressed by diluting the urine sample before analysis (Ladenson, 1979; Jenny et al., 1980). A subsequent study indicated that dilution of urine from cattle, sheep, horses, and cats failed to remove the anionic interference, resulting in underestimation of urinary [K^+] in these species (Brooks et al., 1988). The interference was attributed to the presence of a low molecular weight anionic or zwitterionic compound in urine that electrostatically bound potassium, thereby making potassium ions unavailable for measurement by ISE methodology (Brooks et al., 1988).

Two handheld meters (CARDY C-131 and LAQUAtwin B-731; Horiba Ltd., Albany, NY) have recently become available for the measurement of [K^+] in biological fluids. The meters use the same direct ISE technology, but they differ in external design in that the LAQUAtwin meter can be dipped directly into the solution. The meters are not currently approved for medical use by the US Food and Drug Administration. The low cost ($260 for the CARDY; $350 for the LAQUAtwin) and portability of the meters make them potentially useful for on-farm measurement of [K^+] in whole blood, milk, and other fluids from dairy cattle. We therefore hypothesized that the Horiba handheld ISE meters would provide an accurate and practical method for measuring [K^+] in whole blood, plasma, milk, and abomasal fluid but not urine from cattle. The objective of this study was therefore to determine the analytical performance of the Horiba portable ISE meters in measuring [K^+] in bovine whole blood, plasma, urine, milk, and abomasal fluid samples.

MATERIALS AND METHODS

All methods were evaluated and approved by the Purdue Animal Care and Use Committee.