Validation of point-of-care devices measuring calcium (iCa), potassium (K^+), and sodium (Na^+) concentrations in whole blood of cattle and horses using general-purpose water quality testing equipment

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Abstract

To clarify whether commercially available handheld iCa, K^+, and Na^+ devices may be used clinically, precise and accurate evaluations were performed using the handheld analyser i-STAT 1 as the standard device. Point-paired whole blood samples were obtained from 45 cattle and 19 horses. Data obtained using LAQUAtwin Ca-11C, K-11, and Na-11 correlated with those using i-STAT 1. LAQUAtwin devices were 'compatible' with i-STAT 1 because the frequency of differences between measurements within ± 20% of the mean was 95.5% in cattle and 94.7% in horses for iCa, 92.7% in cattle and 92.9% in horses for K^+, and 100% in both for Na^+. No proportional bias was observed between i-STAT 1 and LAQUAtwin Ca-11C and K-11 because the 95% CI for the intercept and slope were 0 and 1, respectively. LAQUAtwin Na-11 showed a good correlation with i-STAT 1 measurements of Na^+ concentrations in the whole blood of cattle and horses; however, measured values were approximately 4 mM lower with the former. Therefore, the LAQUAtwin series may be applied as a simplified system for measuring iCa, K^+, and Na^+ concentrations in the whole blood of cattle and horses under field conditions; however, caution is required because Na^+ values were lower than those with i-STAT 1.

Bovine, electrolyte, equine

The addition of potassium and calcium to resuscitation fluids, such as Acetated Ringer's and Lactated Ringer's solution, is one of the most common veterinary practices for cattle and horses (Constable et al. 2020; Fielding et al. 2023). However, if the blood ionized calcium (iCa) and potassium (K^+) dynamics of an animal requiring fluid therapy for resuscitation are unknown, there is a risk of serious cardiac events due to excessive administration. Furthermore, hypokalaemia is common in lactating dairy cattle with abomasal displacement, clinical mastitis, and retained placenta as well as in heifers and horses with a low feed intake (Megahed et al. 2019). Therefore, when adding calcium and/or potassium to fluids for resuscitation purposes in clinical practice, accurate information on iCa and K^+ concentrations in the whole blood of animals is essential. Before the administration of fluid therapy for cattle and horses, infusion fluids need to be selected based on electrolyte concentrations in whole blood and sequential changes in electrolyte concentrations in whole blood also need to be monitored during and after infusions (Wenge-Dangschat et al. 2020; Marcom et al. 2024; Wilms et al. 2024). Melo et al. (2022) suggested the importance of monitoring the blood gas and electrolyte balance in horses with food restriction under nutritional support or prolonged fluid therapy in order to promptly correct for any changes (Melo et al. 2022).

Blood iCa, K^+, and Na^+ concentrations are generally measured using conventional and handheld blood gas analysers in diagnostic laboratories and teaching animal hospitals, which are not suitable for farm animal practice fluid therapy often performed under on-

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farm conditions. i-STAT 1 (Abbott Point-of-Care, Abbott Laboratories, Chicago, IL, USA) is a popular point-of-care (POC) analyser for bovine practice (Bleul and Gotz 2014; Ro et al. 2022) and out-of-hours primary care (Hayward et al. 2020) that measures blood gases and several electrolytes. Although i-STAT 1 is an excellent portable blood gas and electrolyte measuring device (Oyaert et al. 2018), due to the cost of cartridges, it is not economically feasible for frequent and repeated measurements in clinical practice with economic animals, such as cattle on farms. LAQUAtwin meters (LAQUAtwin Ca-11C, HORIBA Advanced Techno, Kyoto, Japan) are handheld direct ion-selective electrode meters for general-purpose water quality testing, and have become available for the measurement of iCa, K, and Na concentrations and electrical conductivity in biological fluids (Goulet et al. 2017; Goulet and Baker 2017; Kandeel et al. 2019; Megahed et al. 2019). Therefore, the present study evaluated the optimized ion-selective electrode Ca, K, and Na module devices, the LAQUAtwin Ca-11C (iCa), K-11 (K^+), and Na-11 (Na^+) measuring devices, respectively, as potential cow and horse-side devices for electrolyte measurements in whole blood within the broad ranges expected for electrolyte abnormalities. The accuracy of the LAQUAtwin series was assessed using i-STAT 1 as the gold standard method.

Materials and Methods

All procedures were performed in accordance with the Guide for the Care and Use of Laboratory Animals of the School of Veterinary Medicine at Rakuno Gakuen University (Approved #: VH22C7). The health status of the cattle and horses tested animals was normal.

In the present study, i-STAT 1 (Abbott Point-of-Care, Abbott Laboratories, Chicago, IL, USA) was used to evaluate the accuracy and clinical usefulness of general-purpose electrolyte measuring devices as POC for bovine and equine blood iCa, Na^+, and K^+ concentrations. A portion of blood samples was used for immediate determination of blood K^+, Na^+, and Cl concentrations using the i-STAT equipped with EC8+ cartridges. The EC8+ cartridges were stored in a refrigerator (4–8 °C) and the cartridges were used before the expiration date. Each cartridge was allowed to warm for 10 min in the ambient temperature before using. The i-STAT control solutions were administered to 2 cartridges out of each cartridge batch. The i-STAT and auto-analyser were calibrated and used in accordance with their manufacturers' specifications.

The commercially available general-purpose electrolyte measuring ion-selective electrode handheld devices used to measure iCa, Na^+, and K^+ concentrations in the whole blood of cattle and horses in this study were LAQUAtwin Ca-11C, Na-11, and K-11 (Horiba Advanced Techno, Co., Ltd., Kyoto, Japan), respectively (Plate I, Fig. 1A).

Whole blood obtained from 30 Holstein beef steers (147.7 ± 14.9 days old; mean ± standard deviation [SD]) at a commercial farm and 9 riding horses (15.0 ± 4.5 years old, 2 geldings and 7 mares) at a horse-riding club were used for precision and accuracy control testing of the POC devices. The whole blood of 30 steers was directly measured for iCa, Na^+, and K^+ concentrations using i-STAT 1 and LAQUAtwin on-farm condition. In addition, an equal volume of saline (Nihon Zenyaku Kogyo Co., Ltd., Fukushima, Japan) or 1/2 Ringer's solution (Nihon Zenyaku Kogyo Co., Ltd.) was added to whole blood samples randomly collected from 7 and 8 steers to change electrolyte concentrations. Therefore, 45 point-paired samples were prepared from 30 steers. Electrolyte concentrations in the whole blood of 9 riding horses at the horse-riding club were directly measured using POC devices with the same approach. Saline and 1/2 Ringer's solution were added to whole blood samples from 5 horses to vary electrolyte concentrations. Therefore, 19 point-paired samples were prepared from 9 horses.

Whole blood samples were collected via jugular vein venipuncture using an 18-gauge regular bevel needle and 5 ml syringe (Terumo Co., Ltd., Tokyo, Japan). Heparin sodium solution (AY Pharma, Co., Ltd., Tokyo, Japan) was added to the syringe to a final concentration of 10 IU/ml when filled with 5 ml of blood (50 µl of 1,000 IU/ml heparin sodium solution/syringe). The appearance and operation of the LAQUAtwin devices are shown in Fig. 1B and 1C (Plate I). The details are as follows: Immediately prior to measurements of electrolyte concentrations by these devices, a drop of blood (> 0.3 ml) from a syringe was applied directly to the end of a test strip for LAQUAtwin. The MEAS button was pressed after closing the light cover of LAQUAtwin, and results immediately appeared on the display. The duration from the initiation of the calibration to results being displayed was less than 3 min. Whole blood iCa, Na^+, and K^+ measurements by LAQUAtwin devices were performed in duplicate, and mean values were used in statistical analyses.

The i-STAT 1 was used at a temperature range of 17 to 30 °C, while the LAQUAtwin devices were used beside both steers and horses regardless of the outside temperature. Therefore, measurements of blood iCa, Na^+, and K^+ concentrations by i-STAT 1 and LAQUAtwin were performed beside both steers and horses when the outside air temperature ranged between 17 and 30 °C.

Whole blood iCa, Na^+, and K^+ measurements by LAQUAtwin devices were performed in duplicate, and mean values were used in statistical analyses.

Statistical analysis

Data were analyzed by a Deming regression analysis and Bland-Altman plots using a commercial statistical software program (MedCalc ver 22.030, MedCalc Software Ltd., Ostend, Belgium). The Kolmogorov-Smirnov test was performed to assess whether the data population was normally distributed, and a non-normal distribution was ruled out when $P \geq 0.05$. In the present study, the ratio of the difference between paired measurements to the mean was defined as the 'relative error (RE)'. If the number of measurements with RE of ±10% or less was within 75% of the total number of measurements, it was considered to be 'compatible' (Critchley and Critchley 1999). The significance of differences was set at $P < 0.05$.

Results

Data are plotted with LAQUAtwin Ca-11C (Plate I, Fig. 2), K-11 (Plate II, Fig. 3) and Na-11 (Plate II, Fig. 4) on the y-axis and i-STAT 1 as a reference method on the x-axis under field conditions for steers and horses, respectively.

iCa

The Deming regression analysis of steers revealed an intercept = −0.0162 (95% CI = −0.0600 to 0.0276) and slope = 0.9990 (95% CI = 0.9604 to 1.0376). The Deming regression analysis of horses revealed an intercept = −0.0374 (95% CI = −0.2014 to 0.2763) and slope = 0.9089 (95% CI = 0.7621 to 1.0556). These results suggested that there was no proportional bias between i-STAT 1 and LAQUAtwin Ca-11C under field conditions because 95% CI for the intercept and slope were 0 and 1, respectively. Concordance correlation coefficients in cattle and horses were 0.9863 (95% CI = 0.9750 to 0.9925) and 0.9636 (95% CI = 0.9059 to 0.9862), respectively, which indicated almost perfect performance.

Based on the Kolmogorov-Smirnov test, the accuracy of LAQUAtwin Ca-11C was similar to that of i-STAT 1, which is a POC device with a confirmed accuracy ($P \geq 0.05$). Overall, 100 and 94.7% of observations in cattle and horses were between 95% CI in the Bland-Altman plot, demonstrating good agreement. In addition, LAQUAtwin Ca-11C was 'compatible' with i-STAT 1 because the frequency of differences between measurements within ± 20% of the mean was 95.5% in cattle (44/45, > 75%) and 94.7% in horses (18/19, > 75%).

K^+

The Deming regression analysis of steers revealed an intercept = 0.0156 (95% CI = −0.2620 to 0.2932) and slope = 0.9502 (95% CI = 0.8859 to 1.0145). The Deming regression analysis of horses revealed an intercept = −0.1729 (95 %CI = −0.8170 to 0.4713) and slope = 1.0102 (95% CI = 0.8357 to 1.1847). These results suggested that there was no proportional bias between i-STAT 1 and LAQUAtwin K-11 under field conditions because the 95% CI for the intercept and slope were 0 and 1, respectively. Concordance correlation coefficients in cattle and horses were 0.9450 (95% CI = 0.8986 to 0.9705) and 0.9923 (95% CI = 0.9751 to 0.9976), respectively, which indicated almost perfect performance. Based on the Kolmogorov-Smirnov test, the accuracy of LAQUAtwin K-11 was similar to that of i-STAT 1, which is a POC device with confirmed accuracy ($P \geq 0.05$). Overall, 95.0 and 93.3% of observations in cattle and horses, respectively, were between the 95% CI in the Bland-Altman plot, demonstrating good agreement. In addition, LAQUAtwin K-11 was 'compatible' with i-STAT 1 because the frequency of differences between measurements within ± 20% of the mean was 92.7% in cattle (37/40, > 75%) and 92.9% in horses (14/15, > 75%).

Na^+

The Deming regression analysis of steers revealed an intercept = −24.552 (95% CI = −31.9724 to −17.1315) and slope = 1.145 (95% CI = 1.0901 to 1.1998). The Deming regression analysis of horses revealed an intercept = −20.595 (95% CI = −33.4481 to −7.7420) and slope = 1.1215 (95% CI=1.0271 to 1.2160). These results suggested that there was proportional bias between i-STAT 1 and LAQUAtwin Na-11 under field conditions because the 95% CI for the intercept and slope were not 0 or 1, respectively. On the other hand, concordance correlation coefficients for cattle and horses were very high at 0.9866 (95% CI = 0.9756–0.9927) and 0.9919 (95% CI = 0.9785–0.9969), respectively, which indicated almost perfect performance. A plot of residuals between LAQUAtwin Na-11 and i-STAT 1 results against their means revealed that LAQUAtwin Na-11 readings were 4.6129 and 3.9651 mM lower on average in cattle and horses, respectively. Based on the Kolmogorov-Smirnov test, the accuracy of LAQUAtwin Na-11 was similar to that of i-STAT 1, which is a POC device with confirmed accuracy ($P \geq 0.05$). Overall, 97.8 and 94.7% of observations in cattle and horses were between the 95% CI in the Bland-Altman plot, demonstrating good agreement. In addition, LAQUAtwin Na-11 was 'compatible' with i-STAT 1 because the frequency of differences between measurements within ± 10% of the mean was 100% in cattle (45/45 > 75%) and 100% in horses (19/19, > 75%). LAQUAtwin Na-11 showed a good correlation with i-STAT 1 measurements of Na^+ concentrations in the whole blood of cattle and horses; however, measured values were approximately 4 mM lower with the former.

Discussion

The LAQUAtwin series are reliable and provide a similar degree of accuracy to more expensive analysers as general-purpose water quality testing equipment; however, interunit measurement errors remain unknown. In this precision and accuracy-controlled study conducted at a farm and horse-riding club, blood obtained from cattle (steers) and horses was assessed and compared using commercially available ion-selective electrode handheld iCa (LAQUAtwin Ca-11C), K^+ (LAQUAtwin K-11), and Na^+ (LAQUAtwin Na-11) meters and the handheld analyser i-STAT 1. Based on these results, LAQUAtwin Ca-11C and K-11 may be applied as a simplified system to measure iCa and K^+ concentrations in bovine and equine whole blood under field conditions.

Based on comparisons of the methods, it may be concluded that results are 'compatible' when the degree of agreement between the new method and standard method is good. In the present study, the ratio of the difference between paired measurements to the mean was defined as RE. If the number of measurements with RE of ± 10% or less is within 75% of the total number of measurements, it is considered to be 'compatible' (Critchley and Critchley 1999).

Clinical trials conducted cow-side in the farm environment and horse-side in the horse-riding club environment revealed that the high accuracy of whole blood iCa, K^+, and Na^+ measurements by the LAQUAtwin devices was similar to that of i-STAT 1 as the reference device. The results obtained suggested that there was no proportional bias between i-STAT 1 and LAQUAtwin Ca-11C and K-11 under field conditions because the 95% CI for the intercept and slope were 0 and 1, respectively. Although LAQUAtwin Na-11 also showed a good correlation with i-STAT 1 measurements of Na^+ concentrations in the whole blood of cattle and horses, measured values were approximately 4 mM lower with the former. It was not unclear why the LAQUAtwin Na-11 device measured the sodium concentrations lower than the i-STAT 1 by approximately 4 mM. It is possible for a systematic error to occur. Therefore, we can diagnose the clinical relevance for veterinary use. Based on these results, the LAQUAtwin series may be applied as a simplified system for measuring iCa, K^+, and Na^+ concentrations in the whole blood of cattle and horses under field conditions; however, caution is required because Na^+ values are lower than those with i-STAT 1. Therefore, LAQUAtwin may be beneficial for dairy practitioners as a screening tool for subclinical hypocalcaemia and/or hypokalaemia because no other low-cost method is currently available in the out-of-hours clinical field, and it represents a significant advance in the dairy and horse industries.

Conflict of interest

None of the authors have any financial or personal relationships that may have inappropriately influenced or biased the content of the paper. The authors declare no off-label use of antimicrobials and no humane ethics approval was needed for this study.

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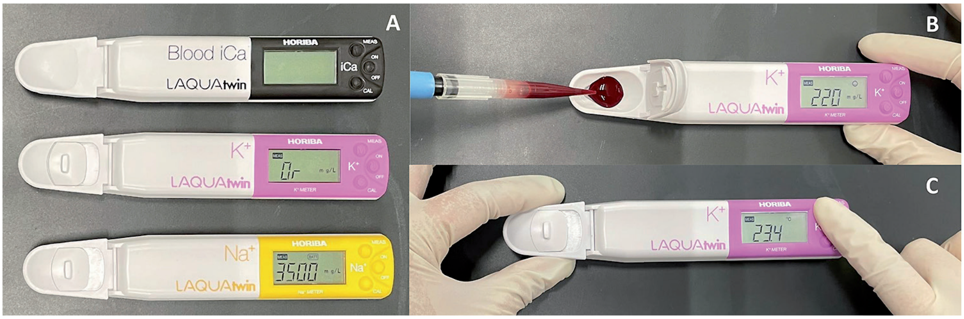

Fig. 1. The appearance and operation of the LAQUAtwin series used in this study

From top to bottom, LAQUAtwin Ca-11C, K-11, and Na-11, which measure iCa, K, and Na concentrations (A), respectively. Drop 0.3 ml or more of blood onto the sensor (B), close the light cover, and press the MEAS button to measure the iCa/K^+/Na^+ concentration and display the results (C). It takes less than 3 min from the initiation of the calibration to the display of results.

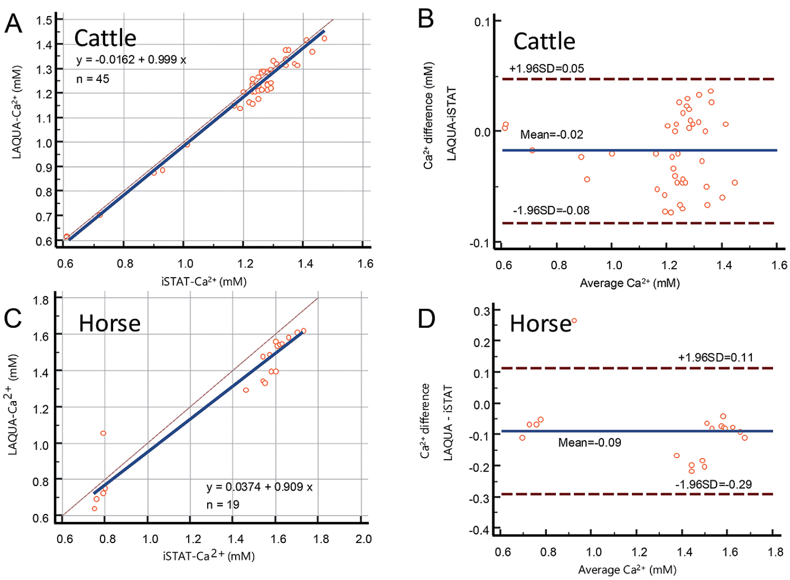

Fig. 2. A Deming regression analysis (left) and Bland-Altman plot (right) of whole blood ionized calcium (iCa) concentrations in cattle (top) and horse (bottom) among LAQUAtwin Ca-11C and i-STAT 1 under on-farm conditions. Totals of 45 and 19 paired-point whole blood samples were obtained from steers and riding horses. A and C: Brown and blue solid lines represent the line of identity (y = x) and the regression line with an intercept, respectively. B and D: The solid line represents the mean difference between the two methods and 95% confidence intervals are indicated by dashed lines.

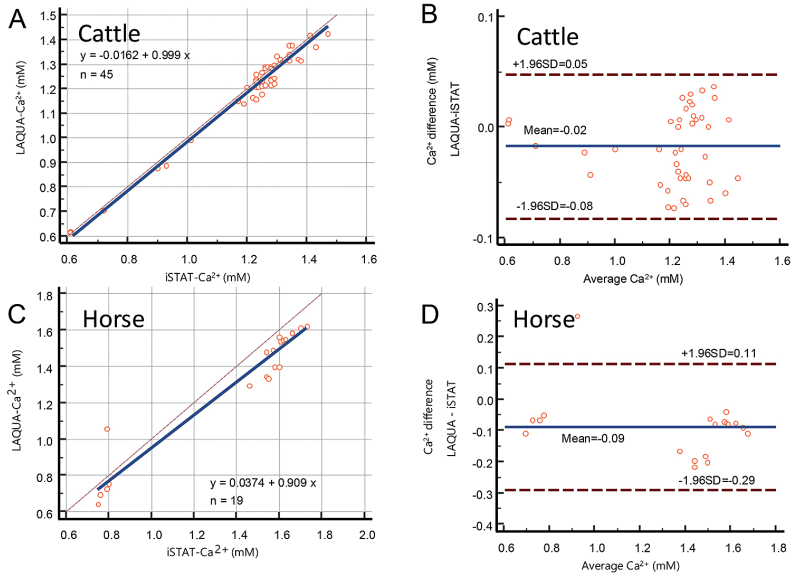

Fig. 3 A. Deming regression analysis (left) and Bland-Altman plot (right) of whole blood potassium ion (K^+) concentrations in cattle (top) and horse (bottom) among LAQUAtwin K-11 and i-STAT 1 under on-farm conditions. Totals of 45 and 19 paired-point whole blood samples were obtained from steers and riding horses. A and C: Brown and blue solid lines represent the line of identity (y = x) and the regression line with an intercept, respectively. B and D: The solid line represents the mean difference between the 2 methods and 95% confidence intervals are indicated by dashed lines.

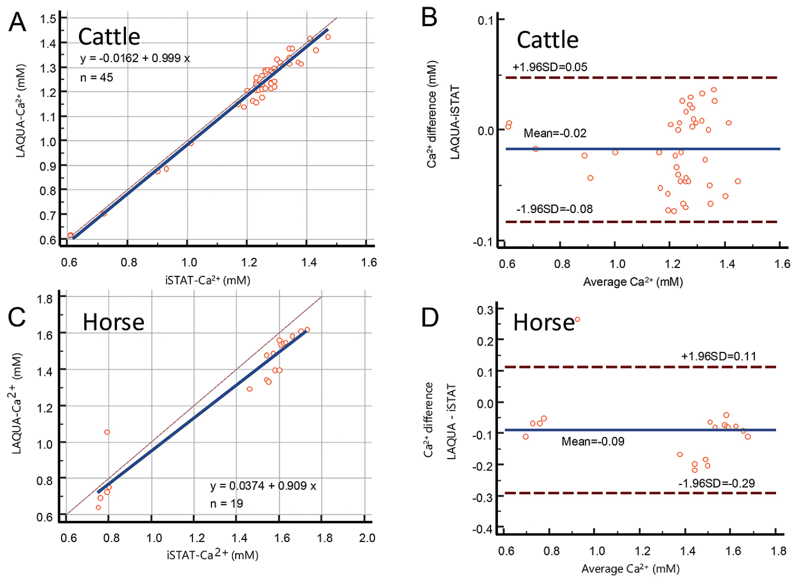

Fig. 4. A Deming regression analysis (left) and Bland-Altman plot (right) of whole blood potassium ion (Na^+) concentrations in cattle (top) and horse (bottom) among LAQUAtwin Na-11 and i-STAT 1 under on-farm conditions. Totals of 45 and 19 paired-point whole blood samples were obtained from steers and riding horses. A and C: Brown and blue solid lines represent the line of identity (y = x) and the regression line with an intercept, respectively. B and D: The solid line represents the mean difference between the 2 methods and 95% confidence intervals are indicated by dashed lines.