# Validation of the bovine blood calcium checker as a rapid and simple measuring tool for the ionized calcium concentration in cattle

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### Introduction

Hypocalcemia is a metabolic disorder in which homeostatic mechanisms fail to maintain normal blood Ca concentrations at the onset of lactation. Although the incidence of clinical milk fever in the United States is approximately 5%, as many as 50% of periparturient dairy cows may have subclinical hypocalcemia, with total blood Ca concentrations being between 1.38 and 2.0 mM. As intravenous 22.5% calcium borogluconate infusion immediately induces a state of hypercalcemia, followed by reduction of the whole blood ionized calcium (iCa) and serum total calcium (tCa) concentrations 24 hr later, it is difficult to maintain an ideal blood calcium level without monitoring the blood calcium level. Point-of-care (POC) devices that veterinary practitioners can use to easily and rapidly measure blood ionized calcium (iCa) levels in cows immediately after withdrawing a blood sample on the dairy farm are needed. The aim of present studies was to compare the commercially available ion-selective electrode handheld iCa meter (bovine blood iCa checker) with the benchtop blood gas analyzer GEM premier 3500 and handheld analyzer i-STAT 1.

#### Materials and methods

This series of studies consisted of two parts: (1) laboratory-level precision and accuracy control tests, and (2) clinical trials carried out in the northeast and southwest regions in Japan. Three non-pregnant, non-lactating, and multiparous cows (731  $\pm$  27 kg,  $7.0 \pm 0.9$ -year-old; mean  $\pm$  SD) were enrolled in this study. During the experiment, the cows were housed in a stanchion barn at the university. Three mature cows received aqueous solution containing 5% disodium ethylenediaminetetraacetate (Na2-EDTA, Wako Pure Chemical Industries, Osaka, Japan) intravenously (IV) at a flow rate of 1.2 mL/kg/hr. Blood samples were taken before and at 10 min intervals up to 3 hr after the initiation of Na2-EDTA infusion.

In the clinical trials, a total of 36 blood samples drawn from 6 and 3 commercial farms in the northern and southern regions, respectively, were used to measure the iCa concentration by the bovine blood iCa checker and i-STAT 1 portable analyzer. Results from laboratory-level precision study, the iCa measurement ability of the bovine blood iCa checker is markedly highly correlated and homologous when the GEM premier 3500 and i-STAT 1 are used as the reference methods. Therefore, the bovine blood iCa checker is a useful POC instrument to measure the iCa concentration, similar to i-STAT 1. In a clinical trial conducted in the northern region of Japan, a total of 16 Holstein dairy cows were enrolled and consisted of 6 cows immediately after calving, 6 cows being treated for hypocalcemia within 1 week after calving, and 4 healthy cows. In a clinical trial conducted in the southern region of Japan, a total of 20 Japanese

black beef cows were enrolled and consisted of 4 cows before expected calving within 1 week, 5 cows after calving within 5 days, and 12 cows that were patients but not hypocalcemic.

#### Results

The results using the bovine blood iCa checker correlated with those using the GEM premier 3500 and i-STAT 1. The bovine blood iCa checker was "compatible" with the GEM premier 3500 and i-STAT 1 because the frequency of differences between the measurements within  $\pm 20\%$  of the mean were 100% (65/65, >75%) and 90.8% (59/65, >75%), respectively. In the field trial, the blood iCa concentration measured by the bovine blood Ca checker was significantly positively correlated with that measured by the i-STAT 1 portable analyzer. The bovine blood iCa checker was "compatible" with the i-STAT 1 because the frequency of differences between the measurements within  $\pm 20\%$ of the mean was 100% (36/36, > 75%).

## Significance

This series of studies that consisted of laboratory-level precision and accuracy control tests, and clinical trials, were to compare the commercially available ion-selective electrode handheld iCa meter (bovine blood iCa checker) with the benchtop blood gas analyzer GEM premier 3500 and handheld analyzer i-STAT 1. In addition, the iCa measurements by the bovine blood iCa checker in the field were markedly highly correlated and homologous with those by the i-STAT 1 regardless of ambient temperature. Based on these findings, the bovine blood iCa checker may be applied as a simplified system to measure the iCa concentration in bovine whole blood. In conclusion, the bovine blood iCa checker and i-STAT 1 are useful POC analyzers that can be used safely, rapidly and simply in animal hospitals, ambulatory clinics and dairy farms to evaluate the blood iCa concentration in cows. Moreover, bovine practitioners can rapidly decide the treatment method for milk fever and hypocalcemia beside the cow because the bovine blood Ca checker can measure the iCa concentration regardless of ambient temperature.

