Assessment of Instrument-Specific Variation between Measured and Calculated Bicarbonate

Article:
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Guests: Dr. Nga Yeung Tang is the director of Clinical Chemistry and Point-of-care testing at the University of Illinois, Chicago, where she also serves as an assistant professor. Dr. Qian (Katie) Sun is a board-certified clinical chemist at Corewell Health William Beaumont University Hospital in Michigan and an assistant professor at Oakland University William Beaumont School of Medicine.

Randye Kaye: Hello and welcome to this edition of *JALM* Talk from *The Journal of Applied Laboratory Medicine*, a publication of the Association for Diagnostics & Laboratory Medicine. I'm your host, Randye Kaye. Bicarbonate is an important analyte for clinicians to assess the acid-base status of their patients.

In the hospital setting, bicarbonate concentration is assessed by two main methods. One method is by measuring the total CO_2 on a clinical chemistry analyzer, where bicarbonate represents the majority of the total CO2 measured. The second method is by calculating the concentration of bicarbonate by the Henderson-Hasselbalch equation using measured components from a blood gas analyzer. If these two methods deliver conflicting results for a patient, this can put clinicians in a difficult situation trying to determine which is the more accurate result.

The May 2026 issue of *JALM* features a research article that dives into the comparison between the two methods, where the measured total CO_2 from three different clinical chemistry analyzer platforms was compared with the calculated bicarbonate from a radiometer blood gas analyzer. This study was a collaboration between three different institutions across the United States. Today we're joined by the article's two corresponding authors, Drs. Nga Yeung Tang and Qian Katie Sun. Dr. Nga Yeung Tang is currently the director of Clinical Chemistry and Point-of-Care Testing at the University of Illinois Chicago, where she also serves as assistant professor.

Dr. Qian Katie Sun is a board-certified clinical chemist at Corewell Health William Beaumont University Hospital in Michigan and assistant professor at Oakland University William Beaumont School of Medicine. She serves as the technical director of the Automated Chemistry and Urinalysis Labs at Corewell Health. Welcome, Drs. Tang and Sun. First, what made you interested in investigating this specific discrepancy between measured and calculated bicarbonate?

Qian Katie Sun: So in our institution, an issue of discrepant measured bicarbonate from the Abbott Architect chemistry analyzer and the calculated bicarbonate from the Radiometer blood gas analyzer was raised by a pediatric nephrologist. And this equipment measured and calculated bicarbonate were noticed in a few pediatric patients over a few months. For example, for one patient, the measured bicarbonate result will be 7, but the calculated bicarbonate result could be 14. Most of these patients were infants or under three years old and clinically unstable. This prompted us to further evaluate the agreement between the measured and the calculated bicarbonate from different chemistry analyzers using patient samples across three healthcare systems.

Randye Kaye: Thank you so much. Dr. Tang, what are the key findings of your investigation?

Nga Yeung Tang: Our findings suggest that there may be instrument-specific variation for the bicarbonate testing, even though all instruments from different vendors included in this study use the PEP carboxylase method to measure the bicarbonate spectrophotometrically. So we compared the calculated bicarb from Radiometer blood gas analyzer against the measured bicarbonate from multiple chemistry analyzers, which include the Abbott Architect, Siemens ADVIA, and Beckman AU680. And the comparison used a three-month data set from each institution. Note that each comparison was between the chemistry and the blood gas analyzers, but no direct comparison was done between the chemistry analyzers.

And a key finding was that the bicarb measured on the Abbott Architect was negatively biased by -2.6 mmol/L when compared with the calculated bicarb from the Radiometer blood gas analyzer. And this bias exceeds 50% of the total allowable error for bicarbonate testing, which is a range recommended by CLIA and CAP. And even though direct comparison between chemistry analyzers of multiple vendors were not possible, we were able to conclude that Siemens and Beckman and the Radiometer analyzers correlate well with each other, so the bias was always within 1 mmol/L. And the Abbott Architect analyzer is the exception.

Randye Kaye: Okay, thank you. Dr. Sun, what are the possible explanations for the observed instrument-specific variations?

Qian Katie Sun: Our findings are consistent with PT surveys from CAP, which suggests that Abbott Architect gave lower measured bicarbonate results compared to the other automated chemistry methods. Our findings are somewhat puzzling because all three methods, like Dr. Tang mentioned, were measured -- bicarbonate used the same testing method, and

all of them claim to be traceable to the same standard reference material, which is the NIST SRM 351. This difference can be due to a number of factors. It is possible that the reference material does not have optimal commutability to all measurement procedures. It was previously shown that the process of preparing reference materials, including freezing, cooling, may cause matrix effects. In addition, there might be differences in reaction temperature, incubation time, and absorbance measurement wavelength. However, confirming this difference can be pretty difficult for bicarbonate because of stability issue.

Randye Kaye: Does the Henderson-Hasselbalch equation make any assumptions that can impact the reliability stability of calculated bicarbonate, Dr. Tang?

Nga Yeung Tang: Yes, there is assumption. It is assumed that the pKa constant, which is the full name is the acid dissociation constant, in the Henderson-Hasselbalch equation works well for all patients, which is not the case. pKa is varied by ionic strength, temperature, pH, and the concentrations of urea, proteins, and electrolytes. One study found that there is poor agreement between measured and calculated bicarb in critically ill patients or patients with abnormally low bicarbonate. And another study that focused on pediatric patients demonstrated that the pKa cannot be considered a constant among pediatric and neonate patients.

Randye Kaye: So, it is common for reference intervals to be standardized for analytes within a hospital even if different methodologies are used. So what are the pros and cons of this practice, Dr. Sun?

Qian Katie Sun: So the benefits of using standardized reference intervals could be that it's easier for physicians to interpret the results, especially if they use this test in similar fashion for clinical diagnosis. For example, for our test here, physicians tend to use both measured and calculated bicarbonate to diagnose acid-base imbalance, kidney disorders, and assess ventilatory and oxygenation status in patients. On the other hand, having the same reference range would require that the test results compare well. In our case, we performed this study because of complaints from our pediatric nephrologist that our two methods would give different interpretation for the same patient.

Randye Kaye: Thank you. So, what actions do you suggest laboratorians take when instrument-specific variations are observed?

Nga Yeung Tang: So it depends on where the laboratory is at. If the instruments are already in service, we should still regularly assess the correlation between the two analyzers using different testing methodology or calculate and measure

methodology across the analytical measurement range. Even though CAP does not require comparison between measured and calculated analytes and as Dr. Sun mentioned, there are lots of benefits using the same reference interval when different testing methodologies are used.

However, if it turns out that there is a significant discrepancy between the two, the lab should consider using different reference intervals. We would rather flag the results correctly instead of letting conditions going unnoticed or providing unnecessary treatment. And if a laboratory is at the instrument selection phase, perhaps the lab could include agreement between the two platforms into their decision-making. Even if a demo instrument is unavailable, the CAP participant summary will be a good resource. And outside of the lab operation, laboratorian could advocate or participate in standardization or harmonization of laboratory testing.

Randye Kaye: Alright, thank you so much for joining us today. That was Drs. Nga Yeung Tang and Qian Katie Sun describing the *JALM* research article, "Assessment of Instrument-Specific Variation between Measured and Calculated Bicarbonate." Thanks for tuning in to this episode of *JALM* Talk. See you next time, and don't forget to submit something for us to talk about.