Clinical Chemistry

Investigating interferences of a whole blood point-of-care creatinine analyzer: Comparison to plasma enzymatic and definitive creatinine methods in an acute care setting.

Bob Barrett: This is the podcast from Clinical Chemistry. I am Bob Barrett. Point of care testing has been one of the fastest growing sectors of the clinical diagnostics industry.

Small handheld devices allow for the rapid analysis of a single drop of blood, because the result is generated immediately, point of care has the potential to allow for immediate decision making or medical intervention. Many people are familiar with glucose meters used in both homes and hospitals to support patients with diabetes. However, many other types of handheld testing devices are now available and provide testing related to respiration, cardiac function, jaundice and other conditions.

A paper published in the November issue of Clinical Chemistry evaluated the accuracy, precision, and potential interferences of a point of care analyzer for creatinine. The authors investigated the performance of the point of care analyzer in comparison to traditional creatinine methods used in most laboratories. Joining us in this podcast is the lead author Dr. Joely Straseski, Assistant Professor in the Department of Pathology at the University of Utah and a Medical Director at ARUP Laboratories in Salt Lake City, Utah.

Dr. Straseski what are some of the applications of creatinine measurement at the point of care, when is that type of information useful?

Joely Straseski: So there is a variety of clinical settings in which a rapid creatinine result might be beneficial.

There are creatinine values that can be useful for determining the Estimated Glomerular Filtration Rate or the EGFR that people are familiar with, that's used to classify or monitor kidney disease in the renal clinic setting. It can also be helpful prior to administering chemotherapeutic agents that are known to be nephrotoxic. Creatinine points of care measurements are also becoming much more common for patients that are undergoing imaging such as a CT or an MRI. Some contract agents that they use for these scans can cause renal and other organ damage in patients that already have a limited renal filtration.

So that's referred to sometimes as contrast induced nephropathy or nephrogenic systemic fibrosis. Point of care measurement is an efficient way to confirm adequate renal function in these patients prior to administering contrast, particularly in imaging areas which are really reliant on getting patients through in a very timely fashion. An elevated creatinine or a decreased EGFR value would alert the imaging folks to possibly use less contrast or a different

contrast agent or they might just forgo contrast all together in those patients.

Bob Barrett: That sounds like a good application of point of care technology, are there any disadvantages to its use?

Joely Straseski: Well, one issue that might be of concern is the way that modern point of care analyzers actually report their values. Direct sensors measure the activity of an analyte as it relates to molality, and that's referred to as the amount of analyte per unit of water mass. For example something like millimoles per kilogram.

However it's conventional to actually report in units of morality or the amount of analyte per volume of sample, another example millimoles per liter. The relationship or the conversion between molality and molarity is actually dependent on the sample matrix. So in plasma for example there is very little discrepancy between the two. Any differences are caused by water displacement, by plasma proteins, and lipids.

In the case of whole blood, which is of course used by these point of care finger stick devices, the difference between molality and molarity is much greater, and that's primarily due to the presence of hemoglobin, because that just takes up a greater volume. The conversion factors that have been set up to accommodate for these differences in sample matrix, some people might be familiar with the 1.1 factor that is used by many glucose monitors.

That assumes one very important fact, that the plasma water mass, the red blood cell water mass, and the hematocrit is "normal". The mathematical formulas that were derived several years ago now, those are based on halthy values for each of these parameters. As we all know not every patient that comes into our clinics or our hospitals or our imaging suites are actually healthy.

So deviating from these normal values could affect the results that we get from these types of meters.

Bob Barrett: What types of methods did you choose to compare for this study?

Joely Straseski: We compared a commercially available point of care analyzer that was currently in use in our institution to two different creatinine methods. First we compared results to a definitive creatinine method that developed in-house. This was an isotope dilution mass spectrometry method that was traceable to serum based NIS calibrators. So that allowed us to assess whether or not any bias was present.

Additionally we wanted to compare the point of care results to method that would be much common in a routine clinical laboratory. So, we also included an enzymatic assay that's performed on a large automated chemistry analyzer. The point of care method obviously uses whole blood, while the others use plasma.

Bob Barrett: Can you describe the patient group that you used for this valuation?

Joely Straseski: Sure. We aimed to include a random sampling of over 100 hospital inpatients. Additionally we included a sub-population of oncology inpatients to make sure there wasn't a difference in that sub-population. It's important to note that we didn't just focus on renal patients but we included all types of diagnoses.

Bob Barrett: Well, so how did the point of cure results for these patients compare to the other methods?

Joely Straseski: Overall the concordance between the point of care method and the enzymatic and IDMS methods actually look quite similar, they both had a slope of 0.88. Although there was a relatively small negative bias, overall there were clinically significant differences between the methods in a subset of patients.

We designed a significant discrepancy between methods at a difference of 0.5 milligrams per deciliter or more. And using that criteria, we found almost a quarter of samples were discrepant between the point of care and enzymatic methods. These patients had statistically significant higher creatinine values compared with a group of control patients that were matched by age, by gender and also by race.

When point of care methods were compared to both enzymatic and IDMS methods, the P value was actually less than 0.0001. Patients with creatinine values above 2 milligrams per deciliter were the ones that were most likely to show discrepancies. Not surprisingly there was better concordance between IDMS and the enzymatic methods than when those are compared to point of care method.

This points to a possible matrix issue - the plasma methods were comparable to each other but wider discrepancies exist when those are compared to whole blood samples.

Bob Barrett: Well, what type of interferences could possibly cause discrepancies in this subset of patients?

Joely Straseski: We looked at a wide variety of possible causes. To investigate these issues we identified a control group of patients, that I mentioned earlier, this is a group that was

matched by age, and gender, and race to those discrepant patients.

So those variables obviously didn't play a role in the discrepancies that we saw between the measurements because we were investigating a point of care measurement that actually relies on capillary flow and the production of current and we were also looking at an enzymatic assay that results in photometric product. We looked at the typical suspects for interference of those types of measurements.

We looked arterial pH, we looked at PO2, hematocrit both total and direct bilirubin and none of those showed any correlation with creatinine discrepancies. We also looked at the creatinine precursor creatine to see if that caused any interference, but it didn't. There was actually no difference at all in creatine concentrations between our discrepant population and the controls.

So we also reviewed the medical charts of both groups and we found no remarkable differences in the prescribed drugs between the groups. We looked at that because of the effects of oxidizing and reducing agents, certain drugs on amperometric assay such as the point of care measurement.

We did find differences in the diagnosis that were associated with the different groups. And you would expect from a higher creatinine value in the discrepant patients, the majority which is over three quarters had renal related diagnosis. The important thing to remember about these types of patients is the likelihood of additional interfering substances being present.

The inability of these patients to clear these compounds might be related to differences that we are seeing. Investigating these metabolites of course was outside the scope of the current study but it is certainly an area of interest.

I think it's also important to point out what didn't affect these point of care tests. All the factors I just outlined are the common culprits that we always think of when we encounter any issues with point of care tests, and our results show that in this circumstance at least with this analyzer and with this analyte, these factors actually didn't interfere with the assay at all.

Lastly we looked at whole blood matrix components to determine the role they might have played in all of this, since we realized the differences between the plasma and whole blood matrices which is what we've already discussed. We investigated plasma water and red blood cell water content and these are derived mathematically. The plasma

water content comes from the total of protein values and the red blood cell water content comes from the MCHC or the mean corpuscular hemoglobin concentration.

Multivariate analysis of these two factors and we also looked at hematocrit, all of that together explains 92% of the variants that we observed between the creatinine methods, that showed that whole blood matrix does contribute a small but significant influence on the point of care measurement.

Bob Barrett: So beyond the method comparisons, what are the overall implications of these results?

Joely Straseski: Well we certainly realized the benefit of point of care testing for creatinine in some but unfortunately probably not in all clinical settings.

This type of point of care testing device can be used as a general screen to quickly determine adequacy of renal function prior to getting contrast during an MRI or a CT. However if patients require highly accurate and precise measures of renal function, then this is probably not an appropriate tool.

For example in kidney disease patients, creatinine tests and estimates of glomerular filtration rate are best performed by central lab methods, and probably we would want to bypass point of care methods all together. Our data indicates that correcting for hematocrit, plasma water, and red blood cell water content in future point of care technologies might actually help improve the overall accuracy.

So someday this type of point of care testing device would be useful in all types of patients.

Bob Barrett: Dr. Joely Straseski is an assistant professor in the department of pathology at the University of Utah and a Medical Director at ARUP laboratories in Salt Lake City, Utah. She has been our guest in this podcast from Clinical Chemistry. I'm Bob Barrett, thanks for listening.