

PEARLS OF LABORATORY MEDICINE

www.traineecouncil.org

TITLE: Intraosseous Blood Analysis

PRESENTER: Anna K. Füzéry

Slide 1: Title Slide

Hello, my name is Anna Füzéry. I am a clinical chemist with Alberta Health Services and an Assistant Clinical Professor of Laboratory Medicine at University of Alberta. Welcome to this Pearl of Laboratory Medicine on “Intraosseous Blood Analysis”

Slide 2: A Real World Example

I'd like to begin this Pearl with a real world example. An 85-year-old female with a decreased level of consciousness is brought to the emergency room where she is found to be in hypovolemic shock. The clinical team resorts to intraosseous vascular access after difficulties in establishing an intravenous line. An intraosseous blood sample is sent to the lab for a comprehensive metabolic panel, phosphate, magnesium, lactate dehydrogenase, troponin, and B-type natriuretic peptide. The picture on the left illustrates the sample's unusual appearance after centrifugation. There is a layer of fat at the top of the sample and the plasma-like layer is visibly hemolyzed. Also noteworthy is the fact that the separator gel did not properly rise to separate the cellular content from the plasma-like portion. What would you do next with this sample? Would you put it on your analyzer and report the results? Or would you cancel it and ask for a redraw?

Slide 3: IO Vascular Access

In 1922 Drinker and Doan independently demonstrated for the first time the adequacy of the bone marrow for infusion of fluids in animals. Interest in their findings did not pick up until the 1940s though when a series of well-controlled animal studies showed that the injection of glucose solutions, blood, and dyes into the bone marrow of the tibia resulted in their effective and immediate absorption into the general circulation. A flurry of publications followed that related clinical cases where fluids were administered by the intraosseous route to human patients with minimal complications. Academic and clinical interest continued into the early 1950s but declined thereafter because of the increasing popularity of venous cannulation. The practice of intraosseous vascular access began to revive again in the mid-1980s following improvements in devices for rapid fluid delivery. Today clinicians resort to intraosseous access

when patients are in a state of cardiovascular collapse or when vascular access is made difficult by chronic disease or past IV drug abuse. While the main purpose of such access is the rapid delivery of drugs and fluids, blood is also sometimes collected for laboratory analysis.

Slide 4: IO Vascular Access

Before diving further into intraosseous blood analysis, let's take a quick look at the structure of long bones and the mechanism of intraosseous vascular access.

The outer shell of long bones consists of compact bone. This layer contains few spaces and provides protection and support to the bone. This layer is also filled with a vast system of blood vessels, called Haversian canals and Volkmann's canals, that rapidly delivers blood and other fluids to and from the systemic circulation. In contrast to the peripheral vascular system, these blood vessels are non-collapsible due to the hardness of the surrounding compact bone and the presence of bone spicules.

Beneath this compact layer of bone is a honeycomb like structure called spongy bone that is filled with bone marrow and blood vessels. These vessels get their blood supplies from the Haversian and Volkmann's canals.

Intraosseous cannulas are typically inserted into the proximal and distal ends of long bones using one of a number of commercially available drill-like devices as illustrated in the top left image. Because the cannula is placed into the spongy bone, any sample drawn by this route will contain a mixture of blood and bone marrow.

Slide 5: IO Blood Sample Quantity & Quality

While the delivery of fluids and medications by intraosseous vascular access is relatively straightforward, the laboratory analysis of intraosseous blood is fraught with difficulties. Intraosseous blood samples are often limited in volume, making extensive testing difficult. For example, the authors of a 2010 study were unable to draw more than 6 to 8 mL of whole blood following an initial marrow discard from healthy adult volunteers. A 2014 publication suggested that available sample volumes may be even less in emergent pediatric patients. A second problem arises from the fact that the separator gel may not rise properly as shown in the photograph on the left. This leads to incomplete separation of cellular content from the plasma-like portion of the sample and may lead aspiration of the former into reaction vessels. This may be a particular problem for laboratories that use front-end laboratory automation and thus do not visually inspect centrifuged samples prior to running them on an analyzer. A third problem with intraosseous blood samples is that their quality tends to be poor as well. Hemolysis is seen in roughly 10% of all samples, clotting in 13% of all samples, and excessive fat in 6% of samples. The picture to the left illustrates a centrifuged sample that exhibits both hemolysis and excessive fat content. Owing to the nature of intraosseous blood collection, such samples may also contain small slivers of bone, called bone spicules that can clog and damage laboratory instrumentation.

Slide 6: Assay Validation

In the event that a laboratory is able to secure high quality intraosseous samples of adequate volume, its next challenge is to ensure that all of its assays report reliable results. Intraosseous blood is typically not included among the acceptable sample types in manufacturers' claims for assay performance. Therefore, it is up to individual laboratories to validate assays for this non-standard body fluid. The Clinical and Laboratory Standards Institute, or CLSI for short, published a guidance document in 2007 entitled "Analysis of body fluids in clinical chemistry". While most parts of this document do not apply to intraosseous blood, laboratory directors may find section 7.5 entitled "Clinically unique samples" of some use. For results that are within the analytical measurement range of the assay, this section suggests that a 1:2 and a 1:4 mixture of the body fluid with the diluent specified for use with an assay should be used to assess for interferences. If observed dilution ratios and variability compare well to an already validated sample type, then there is a reduced probability of an interfering substance affecting the neat result. For results that are below the analytical measurement range of the assay, the body fluid should be used as the diluent for a routine patient sample with a higher measurable concentration. There is a reduced probability of the neat body fluid result being due to an interfering substance if the observed dilution ratios and variability are comparable to the routine dilution of a standard patient sample. However, as mentioned previously, it is often difficult to get sufficient volumes of intraosseous blood so laboratories may be challenged to perform even these relatively simple studies.

Slide 7: Human Studies – Methods

Since the mid 80s, clinicians and laboratorians alike have sought to better understand the clinically useful information that may be hidden in intraosseous blood. The first human study on intraosseous blood analysis was reported in 1991 by Grisham and colleagues. The authors recruited 15 pediatric patients from the hematology-oncology division of Children's Hospital in Oakland, California. Blood gases, electrolytes, calcium, glucose, and hematocrit were compared between intraosseous blood and peripheral venous blood and good agreement was seen for glucose and base excess. This encouraged other researchers to embark on similar studies with the most recent one published in 2014. Studies have used anywhere from 9 to 30 patients with some recruiting solely children and others solely adults. The tests examined these studies included CMP, complete blood count, blood gases, lactate, and typing and screening. Older studies tested centrifuged blood samples in the central laboratory while two recent reports performed testing at the bedside with i-STAT devices. The one commonality to all studies was that participants were hemodynamically stable and had normal acid-base status which is in stark contrast to the target patient population for this type of laboratory testing.

Slide 8: Human Studies – Findings

Despite the encompassing nature of these studies, only the few analytes listed here showed consistently strong or moderate correlation between intraosseous and venous blood. The remaining analytes showed little or no correlation between the two sample types. You may wonder what I mean by a strong correlation or a moderate correlation; unfortunately there is no simple answer to this. The strength of correlation was assessed differently from one study to the next: for example, two studies used the Pearson correlation coefficient while a third study used

the ratio of venous to intraosseous results. For this reason I encourage you to examine these studies in more detail so that you can decide for yourself if you agree with the author's definitions of strong, moderate, and weak correlations.

Before describing the limitations of these studies, I also want to point out that the analytes listed here form only a small fraction of the labs that would be requested for a patient in distress.

Slide 9: Human Studies – Limitations

You have probably realized already that these studies have significant limitations. I already mentioned the small study sizes and the fact that findings may not be directly extrapolatable to hemodynamically compromised patients, patients with abnormal acid-base status, and patients with other acute pathological conditions. An additional drawback is that the volume of bone marrow discarded prior to sample draw may have an impact on the measured lab results. For example, Miller and colleagues found in their 2010 study that disposing of 2 mL versus 6 mL of intraosseous blood sample prior to collection for lab analysis significantly altered the white blood cell count and platelet count, along with sodium, potassium, and calcium concentrations. A further limitation of these studies is that intraosseous access was established at varying sites. While it's assumed that the composition and tissue blood flow is similar in all of these locations, there is no concrete evidence to support this assumption.

Slide 10: Animals Studies - Methods

Owing to the difficulties I just mentioned, animal models have become popular for exploring the potential of intraosseous blood analysis. The first such study was published in 1986 and evaluated the correlation between intraosseous and intravenous chemistry profiles and complete blood counts in five healthy domestic pigs. Subsequent animal studies have closely mirrored human studies in terms of participant size, measured analytes, and measuring devices but have also included hemodynamically unstable states such as cardiovascular arrest, cardiopulmonary resuscitation, and shock.

Slide 11: Animal Studies – Results

Animal models have yielded mixed results. Studies in general have observed positive correlations for intraosseous versus venous mean pH and pCO₂. Such correlations may be misleading though. Kissoon and colleagues examined 14 piglets in 1994 and revealed clinically significant intra-individual differences that were masked by the analysis of mean values. While Bland-Altman plots of their data showed small average biases between intraosseous and central venous values, the range of variability associated with these values was large. For example, two standard deviations for pH corresponded to 0.1 units and to 10 mmHg for pCO₂.

Animal models for other blood chemistries have generally yielded discordant results. The applicability of all such findings to humans remains unclear.

Slide 12: Summary

Taken together, minimal compelling evidence exists for laboratory analysis of intraosseous blood samples. Sample volume is often insufficient for extensive laboratory investigations and poor sample quality jeopardizes laboratory instrumentation and result accuracy. Only a small number of human studies exist and they show limited correlation between intraosseous and venous blood results. The applicability of these findings to hemodynamically unstable patients remains unclear.

Slide 13: A Real World Example

To finish up my presentation, I'd like to revisit the real world example that I showed at the beginning of my talk. While we were deciding what to do with the intraosseous blood sample that we had received in the laboratory, the emergency room notified us that they were able to establish a central venous line in the patient and were sending a venous sample to the laboratory.

We therefore canceled the intraosseous sample but, out of curiosity, went ahead analyzed it offline for four of the requested analytes. Similarly to the previously published human studies, we found relatively good agreement with the subsequent venous sample for creatinine, urea, and random glucose. The potassium result was much higher, however, which was not completely surprising given the strong pink color of the sample.

Slide 14: References

Slide 15: Disclosures

Slide 16: Thank You from www.TraineeCouncil.org

Thank you for joining me on this Pearl of Laboratory Medicine on "Intraosseous Blood Analysis."
I am Anna Füzéry.