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Analysis of intraosseous blood samples using an EPOC point of care analyzer during resuscitation

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ABSTRACT

Background: In the early phases of resuscitation in a critically ill patient, especially those in cardiac arrest, intravenous (IV) access can be difficult to obtain. Intraosseous (IO) access is often used in these critical situations to allow medication administration. When no IV access is available, it is difficult to obtain blood for point of care analysis, yet this information can be crucial in directing the resuscitation. We hypothesized that IO samples may be used with a point of care device to obtain useful information when seconds really do matter.
Methods: Patients presenting to the emergency department requiring resuscitation and IO placement were prospectively enrolled in a convenience sample. 17 patients were enrolled. IO and IV samples obtained within five minutes of one another were analyzed using separate EPOC® point of care analyzers. Analytes were compared using Bland Altman Plots and intraclass correlation coefficients.
Results: In this analysis of convenience sampled critically ill patients, the EPOC® point of care analyzer provided results from IO samples. IO and IV samples were most comparable for pH, bicarbonate, sodium and base excess, and potentially for lactic acid; single outliers for bicarbonate, sodium and base excess were observed. Intraclass correlation coefficients were excellent for sodium and reasonable for pH, pO2, bicarbonate, and glucose. Correlations for other variables measured by the EPOC® analyzer were not as robust.
Conclusion: IO samples can be used with a bedside point of care analyzer to rapidly obtain certain laboratory information during resuscitations when IV access is difficult.

1. Introduction

Emergency physicians are often called upon to resuscitate critically ill patients with very little background information. In this situation, a key laboratory value such as a critically high potassium, low pH or high/low sodium can be invaluable in guiding immediate therapy. Point of care testing has been an important technological advancement allowing rapid laboratory assessment [1-4]. A blood sample must still be rapidly procured, however, and in many critically ill patients this can be a particular challenge. In fact, the patients with the most difficult venous access (dialysis patients, intravenous drug users, and the very old or very young, for example) are also often the sickest patients, requiring rapid resuscitation. Intraosseous line placement has become a widely accepted and invaluable method of obtaining access for medication delivery during the resuscitation of critically ill patients with difficult venous access [5-12].

Studies in animals and in hemodynamically stable, healthy or relatively healthy, children and adults have provided evidence of correlation between intraosseous blood samples and venous blood samples for some laboratory values; however this study seeks to investigate whether this correlation would remain consistent in critically ill patients [13-17].

2. Methods

IRB approval was obtained for this study in an expedited manner and informed consent was waived. The authors have no financial disclosures. A dedicated research EPOC® was purchased with a local research grant (Central California Faculty Medial Group), and was used exclusively for study purposes.

17 convenience sampled patients were prospectively enrolled over a period of eight months (8/2015-3/2016). All enrolled patients presented in cardiac arrest from non-traumatic causes or as critically ill patients requiring immediate resuscitation. Enrollment criteria were 1) intraosseous line placement clinically required for resuscitation, 2) a marrow sample could be obtained, and 3) venous blood was available for analysis within 5 min of the marrow sample. Infants under the

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age of 1 year and prisoners and persons in police custody were excluded from the study.

Intraosseous lines were placed using standard techniques when clinically indicated, as determined by an attending physician. All IO lines were placed in the anterior tibia or proximal humerus. Marrow samples were drawn from the intraosseous line in a 10 cc syringe prior to infusion of any saline or medications. Marrow samples were run on an EPOC® point of care analyzer (Alere, Waltham, Massachusetts) using the appropriate single use test cards (EPOC® BGEM cards). All samples were run on the same analyzer, which is dedicated for research purposes. Care providers did not review or make any clinical decisions based on marrow results and these results were not available in the electronic medical record. Venous samples were obtained separately via venipuncture for clinical indications and were run on a separate EPOC® point of care analyzer designated for clinical purposes using identical single use test cards. These results were made available to care providers for clinical decision making and were recorded in the electronic medical record, according to our current practice.

Laboratory values for intraosseous and venous samples for each patient were evaluated for agreement using Bland Altman (Tukey mean difference) plots. Bias was estimated by mean difference. 95% limits of agreement were calculated as plus or minus 1.96 times the standard deviation. Absolute agreement was assessed via intraclass correlation coefficient. Data were analyzed using Excel (Microsoft 2016) and SPSS (SPSS Inc., version 23.0).

3. Results

3.1. Demographics

17 patients were enrolled in this study, ages ranging from 12 to 93 years (median age 67 years). 15/17 (88%) of patients were male. All but one patient arrived in the ED in cardiac arrest (16/17, 94%). 7/15 patients died in the ED (47%), and total inpatient mortality was 13/17 (76%).

3.2. Data

Fig. 1 shows Bland Altman Plots of Analytes, with 95% agreement lines and mean difference or bias line horizontally.

Table 1 shows the intraclass correlation of the absolute agreement between intraosseous and intravenous samples (reasonable agreement is generally considered to be >0.6, with excellent agreement >0.8).

Based on the Bland Altman plots, there was reasonable agreement between IV and IO values for pH, bicarbonate, sodium and base excess, and moderate agreement for lactic acid. There were single outliers beyond 95% limits of agreement for bicarbonate, sodium, base excess and lactic acid. After removal of single outliers, the average difference for bicarbonate, sodium, base excess and lactic acid did improve substantially, to −0.78 for bicarbonate, 0.2 for sodium, −0.07 for base excess, and −0.22 for lactic acid.

Table 1
Intraclass correlation.

Analyte	Intraclass correlation	95% confidence interval
pH	0.75	(0.30–0.92)
pCO2	0.36	(−0.35–0.74)
pO2	0.73	(0.24–0.90)
HCO3	0.75	(0.30–0.92)
BE	0.53	(−0.39–0.84)
Na+	0.85	(0.57–0.95)
K+	0.37	(−0.26–0.75)
Glucose	0.75	(0.32–0.91)
Lactic acid	0.45	(−0.67–0.81)

The intraclass correlation co-efficient was excellent for sodium and reasonable for pH, pO2, bicarbonate and glucose. After removal of single outliers for bicarbonate, sodium, base excess and lactic acid the intraclass correlation co-efficient remained excellent for sodium and improved to excellent for bicarbonate and reasonable for lactic acid (Table 2).

4. Discussion

Previous studies have begun to establish the feasibility of obtaining clinical information from bone marrow samples with point of care devices. Veldhoen et al. introduced the idea of using point of care testing to evaluate bone marrow samples in humans, though previous studies had investigated the concept in animals [18], and found no technical difficulty in doing so [14]. Miller et al. took samples from 10 healthy volunteers and found good correlation between intraosseous and venous values for hemoglobin, glucose, blood urea nitrogen and creatinine, but not for sodium, potassium, bicarbonate or calcium [15]. Ummenhofer et al. took similar samples from 30 healthy children and found high correlation between values for hemoglobin, sodium, chloride, glucose, creatinine, pH and bicarbonate [16]. Similar studies done in pediatric oncology patients also found significant correlations between values [14,17].

Additionally, animal studies have evaluated bone marrow versus venous samples in the setting of hypothermia, low flow states, or prolonged resuscitations, similar to critically ill patients in the emergency department. Voelckel et al. found that intraosseous samples from pigs correlated well with venous samples with respect to pCO2 and pH but not to lactate [13]. Kissoon et al. found no significant differences between pH, pCO2, and bicarbonate values between intraosseous and venous samples in piglets during a low flow state [19]. Finally, Abdelmoneim et al. found no difference between intraosseous and venous pH and pCO2 during the first 15 min of CPR [13].

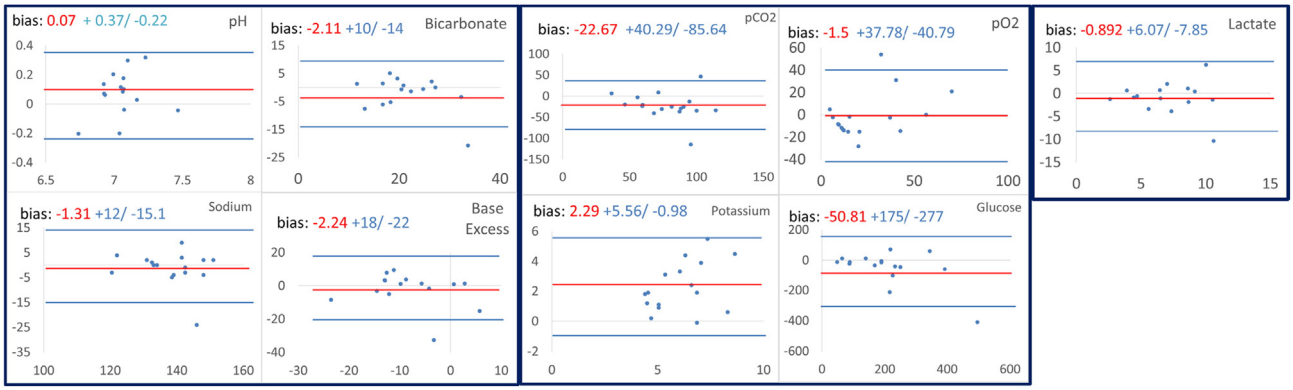

Fig. 1. Bland Altman Plots of Analytes.

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Table 2
Intraclass correlation after removal of single outliers.

Analyte	Intraclass correlation	95% confidence interval
HCO3	0.88	(0.70–0.97)
BE	0.56	(−0.24–0.86)
Na+	0.96	(0.88–0.99)
Lactic acid	0.74	(0.17–0.92)

Our study continues to demonstrate the potential of point of care testing from bone marrow samples and further serves to support the validity of this testing in critically ill patients. We found no significant technical difficulty in obtaining marrow samples in our study or in running them on the EPOC® analyzer. We found significant correlations between values obtained from IO and IV samples, even in a study population in which the majority of patients were undergoing active CPR.

When interpreting the Bland Altman plots, it is essential to consider whether the bias present would make a clinical difference or not. For sodium, for example, the bias of −1.3 is unlikely to represent a significant clinical difference. For potassium, on the other hand, the bias of 2.3 is likely to impact decision making as it would lead providers to conclude that hyperkalemia was present when potassium values may be within normal limits. Interpreting the plots in this manner, we conclude that the bias present is acceptable for pH, bicarbonate, sodium and base excess, and potentially for lactic acid as well. These results agree with the Ummenhofer study in which there was good correlation for sodium, pH and bicarbonate. We did not find as robust a correlation for glucose [16]. Our results were quite similar to the Veldhoen study in pediatric oncology patients, in that acidosis can be diagnosed using base excess and there is a difference in bicarbonate values that is clinically acceptable. We also found a clinically relevant difference in pCO2, pO2 and potassium [14]. This is likely to be a consistent finding in future studies, as these observations were made in very different patient populations using different point of care devices.

In our study, the intraclass correlation measurement was excellent only for sodium prior to the removal of any outliers. It was reasonable for pH and bicarbonate. However, given the small number of observations, our confidence intervals are broad. We feel firm conclusions regarding which analytes are clinically reliable and which are not should be established by a much larger study.

5. Limitations

The primary limitation in the study is the small number of observations. We noted single outliers in our data that, given the small number of observations, substantially impacted the results. After removal of single outliers, the average difference and intraclass correlation coefficients for bicarbonate, sodium, base excess and lactic acid did improve substantially. This speaks to the need for a larger study.

We found few barriers to obtaining values from IO marrow samples, however we did find that a significant number of patients did not survive long enough to have a venous sample drawn or did not have a venous sample obtained within an appropriate timeframe. These are the precise patients that could potentially benefit from this research. In addition, we initially set out to include a comparison with “standard” or core lab values. This turned out to be impractical, as more than half of the patients enrolled never had core labs obtained.

This research was conducted at a single site, and may not be generalizable. In addition, there are limitations to point of care testing in general. Some of the values for analytes were so far outside the normal range that the EPOC® point of care analyzer provided only an error result, and these values could not be interpreted. Furthermore, when there was variance between the IO and IV values, it is impossible to conclude which method was more accurate without comparison to core labs as a gold standard.

We were unable to test some analytes included in previous studies, the most important of which clinically is creatinine, as this assay was not available on the EPOC® BGEM cards at the time of the study (though it is our understanding that this is available now). We were obligated by practical reasons to use the point of care testing available at our institution.

6. Conclusion

It is technically feasible to obtain IO samples during resuscitation, and these samples can be used with a bedside point of care analyzer to rapidly obtain laboratory information when IV access is difficult. The information obtained using a point of care analyzer may have clinical utility in the management of critically ill patients during initial resuscitative efforts.

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