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### Emergency Intraosseous Access: Novel Diagnostic and Therapeutic Possibilities and Limitations



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The intraosseous needle is an essential tool in emergency settings when initial vascular access is difficult to achieve. This paper focuses on possible biochemical analyses on blood from emergency intraosseous needles, suggesting principles of use as well as pointing out advantages and shortcomings.

Intraosseous (IO) access has been used since 1922 as a method for delivering fluids and medications when conventional vascular access is difficult to achieve. The method was extensively used during the second world war (Wayne 2006). Today, both the European Resuscitation Council and American Heart Association guidelines state that IO access should be the first alternative when IV access is unsuccessful (European Resuscitation Council 2015; American Heart Association 2015). Pediatric Advanced Life Support (PALS) (American Heart Association n.d.) and Advanced Trauma Life Support (ATLS) (American College of Surgeons n.d.) now recommend placement of an IO line if adequate IV access cannot be established within three attempts or 90 seconds, whichever is sooner. Use of multiple IO needles is also an opportunity, for example in combat injuries (Sarkar and Philbeck 2009). The use of IO access in medical emergencies has recently been reviewed by Weiser et al. (2012).

Given that the indication for intraosseous access is the lack of other access to the circulation, blood from such an access could aid diagnostics in life-threatening conditions. However, potential damage to laboratory equipment, as IO aspirates may contain bone marrow particles, has been suggested (Nicoll and Rochester 2008). When analysing whole blood, bone fragments might lodge in the narrow tubings in modern laboratory analysers. This is feared by laboratory managers, who may be reluctant to analyse IO samples unless appropriately labelled (Salter and Maconochie 2008). Analysing IO samples labelled as venous samples in cell counters may cause delays, as the samples will contain immature cells. When the laboratory finds immature cells they will normally perform manual microscopy of the samples. This will cause delays in the reporting of test results. It is important to respect both the clinician that wants quick test results and the laboratory that does not want to damage their instruments. It is therefore essential to find ways of circumventing this problem and avoid unnecessary conflicts. This scenario has now changed, since point-of-care technology (POCT) with single-use cartridges allows rapid analysis of samples in a separate cassette, where blood or IO aspirates are never in contact with the analysis device. This further strengthens the choice of POCT as the analysis modality, since POCT, in contrast to conventional laboratory equipment, provides test results within a few minutes. The main difference is the elimination of the transportation time of the samples to the centralised laboratory.

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IO access in combination with POCT could allow acute laboratory analyses even in remote conditions or during the ambulance transport of the patient.

### **Validation of IO Blood Gases by POCT**

It would not be ethically appropriate to compare IO and IV access in critically ill humans without having performed initial animal studies. Utilising a model where healthy anaesthetised pigs were cannulated with a 15 Gauge IO needle, IO aspirates were taken and analysed by POCT hourly during a 6-hour experimental period. This instrument was not only suitable for analyzing the samples without technical difficulties, but aspiration of IO samples was usually easily obtained. This was especially the case with the first sample, which probably is of the greatest clinical interest (Strandberg et al. 2012).

In the emergency situation, rough estimates on haemoglobin, PCO<sub>2</sub> and bicarbonate, indicating acidosis/alkalosis of metabolic or respiratory origin, and electrolytes, may guide initial treatment. Arterial oxygen partial pressure and oxygen saturation were poorly reflected in IO samples. Biomarkers that are substantially different in venous and arterial blood are likely to be difficult to analyse adequately in IO samples. Evaluation of oxygenation may be performed utilising other mobile monitoring equipment, i.e. pulse oximeter. In a subsequent study, IO access and evaluation of blood gases, using POCT, was studied in children according to a similar protocol. IO and IV samples of children scheduled for diagnostic bone marrow aspiration were analysed using POCT. Similar to our results, IO samples did not differ considerably from IV, and may be clinically acceptable alternatives in an emergency. POCT analysis of intraosseous aspirates may thus be a useful guide for treatment (Veldhoen et al. 2014).

However, a more clinically relevant question is whether IO aspirates reflect arterial blood gas values during shock. Previous studies have demonstrated acceptable agreement between IO and central venous measurements of pH and PCO<sub>2</sub> during cardiopulmonary resuscitation (Kissoon et al. 1997). We studied blood gas and acid base parameters in a porcine septic shock model. This experiment, for obvious reasons, could not be performed in humans. Endotoxaemic shock, frequently used to mimic septic shock, was induced by a continuous infusion of *E. coli* endotoxin during the entire 6-hour experimental period.

IO pH levels were approximately 0.1 units lower in IO samples than in arterial ones. Base excess was lower in IO versus arterial blood. The PCO<sub>2</sub> levels in IO samples were clearly higher than those seen in arterial blood, with the venous levels on an intermediate level. IO lactate was also higher in IO samples than in arterial blood. Haemoglobin was somewhat lower and glucose was clearly lower in the IO aspirate than in arterial and venous samples, but still seems close enough to diagnose severe hypoor hyperglycaemia. Since there was consistency regarding these differences, the direction of bias can be predicted (Strandberg et al 2014).

There are some limitations that should be borne in mind regarding IO blood gases. Most important is the fact that IO aspirates are a mixture of arterial and venous blood. In the event of a severely compromised circulation, one might assume that IO blood gases more resemble venous ones. Also, a POCT instrument is a prerequisite for such analysis. Arterial oxygenation cannot be evaluated by IO blood gases. Still, especially in an emergency situation, IO blood gases may add useful information to the clinical picture.

### **IO Administration of Antibiotics During Shock**

It has been demonstrated previously in animal models that IO administration of a number of antibiotics results in plasma concentrations equivalent to those seen after intravenous administration (Jaimovich et al. 1991; Pollack et al. 1991). However, this has not been demonstrated in a setting of circulatory shock. In the patient with an acute life-threatening infection, timely administration of parenteral antibiotics may increase the probability of survival (Dellinger et al. 2013), and IO administration may be considered as an alternative when IV access is not available. We therefore studied plasma concentrations of cefotaxime and gentamicin after IO and IV administration in a porcine model, using endotoxin infusion to simulate septic shock. At the onset of clinical shock, or alternatively after 3 hours of endotoxaemia, 75 mg/kg of cefotaxime and 7 mg/kg of gentamicin were randomly administered either IO or IV. Plasma concentrations of both antibiotics were then repeatedly measured in central venous samples. AUC (mg x h L<sup>-1</sup>) for cefotaxime was 108.1 ± 19.5 after intraosseous and 116.5 ± 11.1 after intravenous administration; ratio 0.93, (95% CI 0.71 - 1.19). AUC for gentamicin was 28.1 ± 6.8 for intraosseous and 32.2 ± 3.5 for intravenous administration; ratio 0.87 (95% CI 0.62 - 1.19). The peak value of IO-administered gentamicin was clinically equivalent to that of IV administration, and this value is essential for the action of aminoglycosides. Thus, in an emergency, intraosseous administration of these antibiotics may be considered to reduce the time to initiation of treatment (Strandberg et al. 2015).

### **Monitoring Creatinine and Troponin I via IO Access**

Early monitoring of renal function is of crucial importance in the critically ill patient. In septic shock, early treatment with antibiotics increases the probability of survival (Kumar et al. 2006). Many broad-spectrum antibiotics are eliminated via the kidneys, and some antibiotics may harm renal function. Furthermore, shock, irrespective of origin, may cause acute kidney injury. In order to evaluate the progress of such deterioration, the Risk-Injury-Failure-Loss-End stage kidney disease (RIFLE criteria), based on creatinine measurements and/or urine output, may be an aid when determining when and how to intervene in order to prevent further renal damage.

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The feasibility of creatinine analysis in IO aspirate was previously studied in healthy anaesthetised dogs (Orlowski et al. 1989).

We analysed creatinine in IO, central venous and arterial samples in a porcine model of septic shock, during a 6-hour period. Mean creatinine for all sampling sites increased from 70 micromol/L at 1 h to 104 micromol/L at the end of the experiment. Coefficient of variation for the mean of the sampling sites was 1.4% at 1 hour with a maximum value of 8.5% at 5 hours. The blunting of creatinine in IO samples collected at 5 hours may possibly be due to reduced bone marrow circulation during shock. Thus, IO creatinine reflects values in blood sufficiently well to be used as a glomerular filtration rate marker in an emergency situation (Strandberg et al. 2014).

Troponin I is a marker of myocardial damage. Elevated levels of this protein can be found in several conditions where cardiac injury occurs, e.g. myocardial infarction, cardiac trauma, sepsis, snake venom and other intoxications. Since the kinetics of troponin I in bone marrow aspirates were unknown, anaesthetised pigs were challenged with a 6-hour continuous infusion of *E. coli* endotoxin. IO and IV samples were taken hourly.

Endotoxaemic shock resulted in a marked decrease in left ventricular stroke work index. Troponin I increased, and at 1 hour the values in IO aspirates and venous samples were nearly identical. Troponin I in IO samples increased somewhat less than in venous samples until 3 hours, when the IO samples did not increase further, which was in contrast to venous samples. All samples were above the normal reference interval. Thus, IO analysis of troponin I reflects the values of troponin I in blood sufficiently well to give valuable information on acute myocardial damage in an emergent situation (Eriksson et al. 2015).

### **Use of IO Access in Acute Cardiac Care**

Induction of hypothermia after cardiac resuscitation using iced saline infusion in IO vs central venous access was evaluated in a swine model of prolonged ventricular fibrillation. The feasibility of inducing therapeutic hypothermia after resuscitation by giving iced saline IO vs IV was evaluated. There were no significant differences between IO and IV access with regard to decrease in core body temperature. Thus mild therapeutic hypothermia can be effectively induced in swine after successful resuscitation by infusion of iced saline through an IO needle (Mader et al. 2010). Thrombolytic agents may be administered intraosseously during spontaneous circulation, not only in myocardial infarction, but also in massive pulmonary embolism (Wenzel et al. 2006).

In a recent experimental study, tibial intraosseous access was compared with IV access in adult male swine, who received cardiopulmonary resuscitation (CPR) and defibrillation.

The animals were placed in cardiac arrest for 2 minutes before CPR was initiated. After 2 minutes of CPR, epinephrine was delivered and serial blood samples were collected. There were no significant differences between IV versus IO epinephrine in achieving return of spontaneous circulation. Thus epinephrine delivered via the IO route is a clinically relevant alternative to IV administration. When IV access cannot be immediately obtained in cardiac arrest patients, IO access should be considered (Wong et al. 2016).

### **Conclusion**

Although analysis of IO samples can provide valuable information, these answers must be interpreted with care. It should be remembered that the bone marrow not only is the site of platelet generation, but is also rich in leucocytes and contains mature as well as immature blood cells. Peripheral blood leucocyte count should not be determined from IO samples, as the immature cells most likely will lead to manual microscopy, causing delayed test results and may cause damage to automated cell counters. However, if haemoglobin is determined with a POCT instrument blood transfusions can be initiated and the determination of other peripheral blood counts can wait until an intravenous or intra-arterial route has been established. Taking this into consideration, IO samples may be a useful tool, helping us to guide initial therapy. The focus on IO testing should probably be on assays where the test result can be readily available with POCT. It should also be remembered that IO cannulation is not a long-time conventional vascular access, but may buy valuable time in an emergency.

### **Abbreviations**

**CPR** cardiopulmonary resuscitation

**IO** intraosseous

**IV** intravenous

**POCT** point-of-care technology

