Commentary

Lactate concentration gradient from right atrium to pulmonary artery: a commentary

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See related research by Gutierrez *et al*. in this issue [http://ccforum.com/content/9/4/R425]

Abstract

Inadequate myocardial performance is a common complication of severe sepsis. Studies in humans strongly argue against a decrease in coronary blood flow in the pathogenesis of this sepsis-induced cardiac injury. Moreover, regional myocardial ischemia may well be present in sepsis patients with coexistent coronary artery disease. Nevertheless, the diagnosis of myocardial ischemia remains difficult in patients with sepsis, since elevation of troponin in these patients can be the result of a variety of conditions other than acute myocardial ischemia. The use of the right atrium to pulmonary artery lactate gradient could perhaps help the clinician in detecting myocardial ischemia in patients with sepsis.

In this issue, Gutierrez *et al*. [1] compared simultaneous measurements of blood lactate concentrations in the right atrium and pulmonary artery in critically ill patients. They found decreases in both blood lactate concentrations and venous blood oxygen saturation in gradients from the right atrium to the pulmonary artery. These gradients are presumably produced by mixing right atrial blood with coronary venous blood, which has lower lactate concentrations and blood oxygen saturation. More interestingly, in this study, the lactate gradient was inverted in three patients, suggesting myocardial ischemia, a condition associated with lactate release by the heart.

Blood lactate levels are typically elevated in hypoperfusion states when pyruvate cannot enter the Krebs cycle as the cellular oxygen supply becomes insufficient. The pyruvate is shunted to lactate through the enzyme lactate dehydrogenase, producing only two molecules of energy-rich ATP for every two molecules of pyruvate (from one molecule of glucose), compared with 38 molecules of ATP for each glucose molecule through the aerobic mitochondrial process when sufficient oxygen is present. This causes the lactate to pyruvate ratio to increase (the normal value is around 10:1). Once molecular oxygen is again available, assuming that mitochondrial function is preserved, the excess lactate is rapidly metabolized back through pyruvate into carbon dioxide and water via the Krebs cycle. Lactate in the blood is metabolized mainly by the liver (50%) and kidney (20%). Liver function and liver blood flow can influence hepatic lactate clearance. Striated muscles, the heart and the brain can also metabolize lactate and, in some conditions, this clearance can be significant.

Traditionally, elevated blood lactate levels in hemodynamically unstable patients have been interpreted as reflecting acute circulatory shock. Elevated blood lactate levels have been correlated with mortality in all types of shock [2,3]. The speed at which lactate is cleared from the blood through vigorous resuscitation strongly correlates with ultimate outcome, including mortality and organ failure. The best chances of survival occur when resuscitation efforts result in lactate clearance to normal values within 12 to 24 h [4-6].

Blood lactate concentration represents a global marker of tissue oxygenation but does not reflect loco-regional tissue oxygenation. The venoarterial lactate gradient on both sides of an organ can be used to detect regional hypoxia. De Backer *et al.* [7] demonstrated that lung lactate production occurs in subjects with acute lung injury states but not in patients with normal lungs, cardiogenic pulmonary edema or pneumonia. Thus, lung lactate production requires a diffuse inflammatory process. Other organs can also produce lactate and experimental studies suggest that the gut can produce lactate in sepsis, which is probably from anaerobic metabolism as the portal lactate to pyruvate ratio is increased. The investigation of splanchnic lactate turnover in humans is much more complicated as access to the portal vein is not possible outside the operating room. Since the liver is usually able to clear this small amount of gut-produced lactate, splanchnic ischemia may go unsuspected. De Backer *et al.* [8] reported that hepatosplanchnic lactate release is uncommon in patients with severe sepsis and is not related to

arterial lactate concentrations, abdominal infection or signs of gut or liver dysoxia.

Inadequate myocardial performance, characterized by left ventricular systolic depression and diastolic dilatation, is a common and early complication of septic shock [9,10]. Several factors may contribute to the occurrence of myocardial damage during septic shock. A possible direct cardiac myocytotoxic effect of bacterial endotoxins or mediators (e.g. cytokines or reactive oxygen species) induced by the infectious process and produced by activated leukocytes, macrophages and endothelial cells [10] should be considered. Studies in humans [11,12] strongly argue against a decrease in coronary blood flow in the pathogenesis of this sepsis-induced cardiac injury. However, a dysfunctional microcirculation that produces regional flow disturbances and abnormal tissue oxygenation is a hallmark of septic shock, and may cause relative ischemia in various organs, including the heart [13,14]. Moreover, regional myocardial ischemia may well be present in sepsis patients with identifiable coronary risk factors or coexistent coronary artery disease. In this context, the diagnosis of myocardial ischemia remains difficult in sedated and mechanically ventilated patients with sepsis. Indeed, elevation of troponin can be detected in a variety of conditions other than acute myocardial ischemia, especially in critically ill patients with severe sepsis. The use of the right atrium to pulmonary artery lactate gradient reported by Gutierrez *et al*. in this issue [1] could perhaps help the clinician to detect myocardial ischemia in septic patients. However, the amplitude of the lactate gradients reported in this study [1] is close to the measurement error of blood lactate concentrations provided by many blood gas analyzers.

The present study is a preliminary observation. Further studies are needed to confirm these results and to study the usefulness of this lactate gradient in the detection of myocardial ischemia in critically ill patients.

Competing interests

The author(s) declare that they have no competing interests.

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