Ready for Prime Time? Biomarkers in Sepsis

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KEYWORDS

• Biomarkers • Lactate • Procalcitonin • Troponin • Proadrenomedullin • Sepsis

KEY POINTS

- Clinical biomarkers should be used in association with clinical gestalt, but they cannot replace the bedside clinician.
- Lactate has many uses in sepsis including assessment of severity, screening for disease, and as a marker for resuscitation but it is not always elevated in sepsis and can be elevated for other reasons.
- Procalcitonin is a marker used to distinguish bacterial from viral infection and has been studied in de-escalation of antibiotics in intensive care unit populations; however, its use in the emergency department for antibiotic use and resuscitation monitoring requires further study.
- Besides myocardial infarction, troponin can be elevated in many other conditions and is associated with worse prognosis in sepsis.
- New biomarkers include endothelial activators, acute-phase reactants, B-type natriuretic peptide/N-terminal B-type natriuretic peptide, and proadrenomedullin.

INTRODUCTION

Sepsis is a common cause of death in patients presenting to the emergency department (ED), and the condition results from the host response to the presence of infection.[1] Current diagnosis relies on physiologic criteria and suspicion of a source of infection using history, physical examination, laboratory studies, and imaging studies. Diagnostic uncertainty often results with the patient who presents with systemic inflammatory response syndrome (SIRS) criteria and suspected sepsis, but a source of infection has not been discovered.[1–4]

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Biomarkers are laboratory assessments used to detect and characterize diseases and improve clinical decision making. Numerous laboratory markers have been used to assist decision making, including complete blood cell count, troponin, creatine kinase, lactate, C-reactive protein, and myoglobin. Some have argued the use of these biomarkers shows a lack of history and examination skills, whereas others have argued these tests have the potential to supplant physical examination and history taking. A reliable biomarker for sepsis should assist with earlier diagnosis, improve risk stratification, or improve decision making for care in sepsis patients.[4–8]

LACTATE

Causes of Elevated Lactate Level

Lactate has numerous uses in sepsis, particularly in resuscitation and categorization of illness severity. Lactate is produced from all body tissue with the metabolism of pyruvate and Nicotinamide adenine dinucleotide (NADH), with normal production of 20 mmol/kg/d. Traditionally, lactate production with acidosis was thought to be caused by anaerobic metabolism or impaired hepatic metabolism. Elevated lactate can be broken into several categories, shown in **Table 1**. Of note, lactate elevation may be caused by endogenous epinephrine-stimulating β-2 receptors, which produce excess pyruvate during aerobic glycolysis and circulation of inflammatory mediators and liver disease.[8–12]

Screening

Serum lactate measurement is recommended as a screen for severe sepsis by the Surviving Sepsis Campaign.[1] Many studies evaluating lactate in sepsis support its use to evaluate and prognosticate for sepsis, with an initial elevated lactate

Table 1
Lactate elevation

Type A	Type B1 Associated with Disease	Type B2 Drugs and Toxins	Type B3 Associated with Inborn Errors of Metabolism
Tissue Hypoperfusion	Leukemia	Phenformin	Pyruvate carboxylase deficiency
Anaerobic muscular activity	Lymphoma	Metformin	Glucose-6-phosphatase deficiency
Reduced tissue oxygen delivery	Thiamine deficiency	Epinephrine	Fructose-1,6-bisphosphatase deficiencies
	Pancreatitis	Norepinephrine	Oxidative phosphorylation enzyme defects
	Hepatic or renal failure	Xylitol	
	Short bowel syndrome	Sorbitol	
		Lactate-based dialysate fluid	
		Cyanide	
		β-agonist	
		Alcohols: methanol, ethylene glycol	
		Salicylates	
		Nitroprusside	
		Isoniazid	
		Fructose	
		Paracetamol	
		Biguanides	
		Antiretroviral agents	

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