BENDING THE VALUE CURVE

Getting Burned by Lactic Acid

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A 13-year-old boy with a history of moderate, persistent asthma was transferred to our facility from an outside hospital with shortness of breath and cough of 2 days' duration. In the emergency department at the other facility, initial vitals were temperature, 98.9°F; heart rate, 120 beats per minute; respiration rate, 40; pulse oxygen saturation, 87% on room air; and blood pressure, 191/63 and 128/41 upon repeat. Screening laboratory tests were performed: the complete blood count was within reference ranges, serum chemistry was notable for a bicarbonate concentration of 29 mEq/L, and peripheral venous lactate was 2.8 mmol/L. Chest x-ray showed central peribronchial cuffing consistent with viral infection.

Because of persistent wheezing and moderately increased work of breathing, the patient was placed on continuous nebulized albuterol (20 mg/h) and given 125 mg intravenous methylprednisolone, 250 mg oral azithromycin, and 1 g intravenous magnesium sulfate. Symptoms significantly improved per their report. Given the elevated lactate on the initial laboratories, he was given a 1-L bolus of intravenous crystalloid. Multiple repeat point-of-care capillary lactate levels were obtained: 7.2, 7.5, and 7.9 mmol/L. The persistently elevated lactate levels triggered additional fluid boluses and order for blood culture. The treatment team believed the patient was ready to be discharged from the hospital on intermittent albuterol and steroids, but the outside emergency department requested transfer to our pediatric ward given the persistently elevated lactate level. The transfer request was accepted.

Upon arrival, the patient appeared well, and there was no evidence of distress. Vital signs were within normal limits, other than sinus tachycardia to 120. His exam was notable for mild conversational dyspnea, diffuse expiratory wheezing, and prolonged expiratory phase. He was tapered to four puffs of albuterol metered-dose inhaler every 4 hours and was discharged home after a short period of observation. His peripheral perfusion was excellent, and his urine output was normal during the brief hospitalization. A clinic visit 3 days after discharge confirmed that he continued to do well with his prescribed regimen.

APPLYING MANDATES TO THE WRONG POPULATION: ONE TEST TO RULE THEM ALL

It is often joked about, though frequently there lies much truth in jest: be careful what you look for, because you just might find it. This patient presented for respiratory distress secondary to an exacerbation of known asthma. There were no clinical signs of shock or sepsis other than tachycardia, which in this case was attributable to increased work of breathing and pharmacologic agents. Therefore, the indication for the venous lactate measurement in the first place is unclear but likely stemmed from increasing national efforts and mandates for sepsis screening protocols.[1] These protocols are well established in adult medicine to identify occult sepsis; however, their utility in pediatric patients is unclear. Indeed, the American College of Critical Care Medicine recommends identifying pediatric sepsis with clinical parameters rather than laboratory tests.[2] The initial lactate was mildly elevated,

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prompting the treating team to obtain a repeat level to ensure normality. The increase in the lactate level was unexpected and belied the patient's otherwise reassuring response to asthma therapy. The elevated lactate levels triggered additional fluids, laboratory tests, and ambulance transfer to our facility.

WHEN ABNORMAL IS EXPECTED: HARD WORK, METABOLISM, AND AEROSOL

Elevated lactate in the setting of asthma exacerbations is a well-described phenomenon, with proposed mechanisms that involve both the disease process and pharmacotherapy.[3–8] Posited disease-based mechanisms of increased lactate in asthma involve overuse of respiratory muscles coupled with hypoxemia, decreased cardiac output due to increased intrathoracic pressure from dynamic hyperinflation, and decreased lactate metabolism by the liver.[6] Challenging this muscle metabolism–based mechanism is the observation of lactic acidosis in intubated, sedated, and paralyzed patients with status asthmaticus.[5]

In addition, β-adrenergic agents used to relieve asthma symptoms are well known to elevate plasma lactate, although this elevation is not related to poor tissue perfusion.[4,5,7] β-Adrenergic receptor stimulation leads to an increase in gluconeogenesis, glycogenolysis, glycolysis, and lipolysis, all of which increase serum lactate levels. β-Agonists (eg, albuterol, terbutaline) increase intracellular cyclic adenosine monophosphate, which stimulates enzymes involved in glycogenolysis. Glycogen breakdown to glucose increases intracellular pyruvate by way of glycolysis. The enzyme lactate dehydrogenase is bidirectional; an increase in pyruvate will favor the formation of lactate, according to Le Chatelier's principle. In addition, β-agonism on adipose cells stimulates lipolysis. Free fatty acids inhibit pyruvate oxidation via pyruvate dehydrogenase, thus favoring pyruvate-to-lactate formation by lactate dehydrogenase.[5,6] This mechanism is congruent with the type B lactic acidosis observed by Meert et al. in a cohort of asthmatic children admitted to the ICU.[7] Type B lactic acidosis is seen with normal oxygen delivery but excessive β-adrenergic stimulation, preserving a normal lactate-to-pyruvate ratio of 10:1.[7]

MINDFULLY INTERPRETING: THE TOLL OF REACTION

Cellular respiration is a core concept in preclinical courses, learned by all but forgotten by most. In this case, however, an understanding of this physiology and pharmacology could have improved the value of our patient's care by preventing multiple unnecessary interventions and the associated costs. Our patient was subject to several potential harms. He had multiple venipunctures, which are a significant source of anxiety in children. He received several fluid boluses, which in some situations are indicated in asthma because of hypovolemia, but in a euvolemic patient can lead to pulmonary edema and worsening respiratory status. The high lactate level prompted a blood culture, which in this situation is much more likely to yield a contaminant that prompts administration of unnecessary antibiotics and can prolong hospital length of stay. Finally, the child was admitted to the hospital, which comes with multiple potential iatrogenic risks.

OVERDIAGNOSIS: HARMED BY THE BEST INTENTIONS

In summary, incidental—or even expectedly abnormal—test results have the potential for serious physical and emotional harm to patients and contribute to the high cost of medical care.[9] Hyperlactatemia, even lactic acidosis, is a common finding in asthma and is predominantly related to β-agonist therapy. There is no clear reason that lactate levels should be obtained routinely in asthma, and this case demonstrates how a seemingly mundane laboratory test can generate a cascade of low-value care. When physicians are confronted with abnormal laboratories, even laboratories that in retrospect should not have been obtained, it can be extremely difficult—psychologically, culturally, and perhaps legally—not to react. It is imperative to understand the clinical condition in the setting of any abnormal laboratory result before reacting. Additionally, one should always be cautious of applying recommendations for the adult population to pediatric patients without established evidence. As hospitals, emergency rooms, and clinics strive to detect and treat sepsis in a timely fashion, close attention should be paid to these potential unintended consequences.

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