

Discussion

Myoglobin is an approximately 17 kDa oxygen carrying protein. It is rapidly filtered by the glomeruli and the proximal tubule reabsorbs and degrades it. When renal capacity is exceeded it is excreted into the urine and is visible as a reddish to dark brown color. It is most commonly used clinically to assess for rhabdomyolysis.

Myoglobinuria may be found in a large number of clinical conditions including trauma, crush injuries, ischemia, thermal injury such as burns, lightning and electrical injury, extreme exercise, myositis, toxic conditions such as envenomations (snake bites), carbon monoxide poisoning, excessive alcohol ingestion, drugs of abuse such as cocaine, seizures, hypokalemia, malignant hyperthermia, hereditary syndromes such as McArdles, phosphorylase deficiency, or phosphofructokinase myopathies.¹ Any condition with excess myoglobin may cause renal failure. A number of mechanisms have been proposed for the pathophysiology of acute renal failure due to myoglobinuria. Tubular destruction from casts has been seen and pressure increases and mesangial changes may also contribute, due to toxicity to the renal tubule. Dehydration, hypotension, and nephrotoxic drugs may exacerbate risk of a patient developing renal failure.¹ In most normal patients urine myoglobin is undetectable but exercise may lead up to a 40-fold increase.² Patients with urine myoglobin >15 mg/L are thought to be at risk but values may overlap with the normal exercised population.¹

In a recent poll of CAP Proficiency participants 35.7% utilize ultrafiltration, 33.9% perform precipitation methods, and 21.4% reported no pretreatment with their methods. 8.9% reported “other” such as adjustment of pH or centrifugation pretreatment. The participants also were polled on the method used and 84.2 % utilized dipsticks, 8.8% performed immunoassays, and 7% reported “other” including POCT or immunoturbidometric methods. Interestingly, units used to report results also varied widely.

There is considerable debate in the literature as to the utility and reproducibility of urine myoglobin testing as well as pretreatment recommendations. Loun and colleagues investigated the utility of ultrafiltration/dipstick methodology that is most commonly reported and found that the concentration of myoglobin recovered with filtration was highly variable, independent from sample matrix or precentrifugation.³ Discrepancies existed particularly for samples with concentrations < 60 mg/L that could lead to a potential for false negative results.³ A study performed at Johns Hopkins University Medical Center with a sample of 673 cases found the microconcentration method to have only a 26.4% sensitivity and a specificity of 96.8%.⁴ The authors concluded that a microconcentration-based assay had a “poor and clinically inadequate sensitivity in the detection and diagnosis of rhabdomyolysis.”⁴

A recent review of the literature screened 1602 English language studies and included 52 studies published from 1980-the end of 2006. The review concluded that there is “inadequate evidence evaluating the use of urine myoglobin as a predicator of acute renal

failure in patients with suspected rhabdomyolysis.”⁵ This review found reported specificities of the assays to vary widely in the reports (15-88%) .⁵

In light of these data, it is worth noting that a serum CK is a much better test for making the diagnosis of rhabdomyolysis; levels of ~1000 U/L are commonly used for the diagnosis⁶ and levels >10,000 U/L are associated with severe rhabdomyolysis.⁴ In addition to its analytical superiority, it becomes elevated when myoglobinuria is present but it also remains elevated for many days after myoglobin has disappeared from the urine.

References

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