GUIDELINE FOR THE MANAGEMENT OF RHABDOMYOLYSIS

I. Background

Rhabdomyolysis is a clinical syndrome characterized by skeletal muscle destruction and release of intracellular muscle contents into the bloodstream, causing systemic complications. Trauma, including crush injuries or entrapment, is a leading cause of rhabdomyolysis. The syndrome is characterized by muscle pain, weakness, dark tea colored urine, and marked elevations of serum creatine kinase (CK) levels. There is no universal definition of rhabdomyolysis, though often used definitions include CK levels 5 times above normal. The most common systemic complication of rhabdomyolysis is the development of acute renal failure secondary to hypovolemia from fluid sequestration in the extracellular space and toxic effects of myoglobin on the nephron both directly and through its breakdown products, such as free iron. Myoglobin itself causes renal toxicity through renal vasoconstriction, formation of intra-tubular casts, and direct toxicity of myoglobin to kidney tubular cells. The most important principle in the management of rhabdomyolysis is the identification and release of compartment syndrome. The treatment for rhabdomyolysis otherwise remains controversial with respect to the amount of intravenous fluid resuscitation and the use of additional medical therapies such as bicarbonate and mannitol. The goal of any treatment is to improve renal blood flow to minimize ischemia, increase urine flow rate to wash out obstructing casts, minimize the cytotoxic effects of myoglobin, and relieve any ongoing muscle compression such as compartment syndrome.

II. Clinical Guideline

a. Diagnosis should be made with urinalysis demonstrating myoglobinuria and/or CK levels exceeding 5x the normal limit
    a. Either the presence of myoglobin in urine, or a urinalysis positive for heme in the absence of red blood cells can be used to detect myoglobinuria
b. Initiate treatment for CK levels >10,000 U/L:
    a. Intravenous fluid replacement should be initiated to achieve urine output of 1-2 mL/kg/hr (ideal body weight) until CK levels trend below 10,000 or myoglobin clears from the urine
        i. If CK remains elevated and total fluid volume exceeds 3L in a 24-hour period, consider early Nephrology consult for initiation of renal replacement therapy
            1. Fluid replacement should be discontinued once CRRT is initiated
        ii. Isotonic fluids (i.e. lactated ringers, normal saline) should be used for fluid replacement and electrolytes should be monitored closely
        iii. Interval CK values should be followed until a peak concentration is reached (typically at 24–72 hours), and discontinued once the CK is reliably downtrending
    b. Bicarbonate to maintain a urinary pH >6.5 has not been shown to reduce the incidence of ARF and should not be used
    c. The use of mannitol to increase urine output does not convey any additional benefit beyond adequate hydration and should not be used

III. References

1. Bywaters EG, Beall D. Crush Injuries with Impairment of Renal Function. Br Med J, 1941;1(4185):427-432.
2. McMahon GM, Zeng X, Waikar SS. A risk prediction score for kidney failure or mortality in rhabdomyolysis. JAMA Intern Med, 2013;173(19):1821-1828.

3. Scharman EJ, Troutman WG. Prevention of kidney injury following rhabdomyolysis: a systematic review. Ann Pharmacother, 2013;47(1):90-105.
4. Chavez LO, Leon M, Einav S, Varon J. Beyond muscle destruction: a systematic review of rhabdomyolysis for clinical practice. Crit Care, 2016;20(1):135.
5. Petejova N, Martinek A. Acute kidney injury due to rhabdomyolysis and renal replacement therapy: a critical review. Crit Care, 2014;18(3):224.
6. Sever MS, Vanholder R, Disasters RoIWGoRftMoCViM. Recommendation for the management of crush victims in mass disasters. Nephrol Dial Transplant, 2012;27 Suppl 1:i1-67.
7. Better OS, Abassi ZA. Early fluid resuscitation in patients with rhabdomyolysis. Nat Rev Nephrol, 2011;7(7):416-422.
8. Brochard L, Abroug F, Brenner M, et al. An Official ATS/ERS/ESICM/SCCM/SRLF Statement: Prevention and Management of Acute Renal Failure in the ICU Patient: an international consensus conference in intensive care medicine. Am J Respir Crit Care Med, 2010;181(10):1128-1155.
9. Brown CV, Rhee P, Chan L, et al. Preventing renal failure in patients with rhabdomyolysis: do bicarbonate and mannitol make a difference? J Trauma, 2004;56(6):1191-
1196.
13. Ioannidis K, Papachristos A, Athanassa Z, et al. Safety and effectiveness of the combination acetazolamide and bicarbonates to induce alkaline diuresis in patients with rhabdomyolysis. Eur J Hosp Pharm, 2015;22(6):328.
14. Nielsen JS, Sally M, Mullins RJ, et al. Bicarbonate and mannitol treatment for traumatic rhabdomyolysis revisited. Am J Surg, 2017;213(1):73-79.
15. Ron D, Taitelman U, Michaelson M, et al. Prevention of acute renal failure in traumatic rhabdomyolysis. Arch Intern Med. 1984;144(2):277-280.
16. Eneas JF, Schoenfeld PY, Humphreys MH. The effect of infusion of mannitol-sodium bicarbonate on the clinical course of myoglobinuria. Arch Intern Med, 1979;139(7):801-805.
17. Homsi E, Barreiro MF, Orlando JM, Higa EM. Prophylaxis of acute renal failure in patients with rhabdomyolysis. Ren Fail. 1997;19(2):283-288.
18. Ward MM. Factors predictive of acute renal failure in rhabdomyolysis. Arch Intern Med. 1988;148(7):1553-1557.
19. Yang B, Xu J, Xu F, et al. Intravascular administration of mannitol for acute kidney injury prevention: a systematic review and meta-analysis. PLoS One, 2014;9(1):e85029.
23. Manis T, George-Varghese B, Kashani J. Rhabdomyolysis - Go big or go home. Am J Emerg Med. 2019;37(12):2194-2196.
26. Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. N Engl J Med. 2009;361(1):62-72.
29. Michelsen J, Cordtz J, Liboriussen L, et al. Prevention of rhabdomyolysis-induced acute kidney injury - A DASAIM/DSIT clinical practice guideline. Acta Anaesthesiol Scand, 2019;63(5):576-586.