Scottish Muscle Network

Management of Acute Rhabdomyolysis in Adults

NOTE

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined based on all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

Introduction

Rhabdomyolysis is a potentially life-threatening condition caused by the rapid breakdown of damaged muscle with the release of the intracellular muscle contents, including myoglobin, creatine kinase and various electrolytes, into the bloodstream and extracellular space. Clinically, patients complain of myalgia and muscle weakness and the creatinine kinase is elevated (5X the normal range i.e. >1000 IU/L).

Rhabdomyolysis can be mild, or severe and recurrent.

Initial Assessment & Management

1) **Airway, Breathing, Circulation – including urgent ECG**

2) **Disability, Exposure – rapid examination for signs of trauma / compartment syndrome**

3) **Check temperature and assess for infection / sepsis**

4) **Obtain iv access, send urgent bloods and blood gas. Frequent monitoring of U&Es and/or gases will be required**

5) **Catheterise and monitor urine output**

One of the most important treatment goals in rhabdomyolysis is to avoid acute kidney injury (AKI). This is multifactorial: myoglobin released by damaged muscle is nephrotoxic, and fluid sequestration in damaged muscle leads to relative hypovolaemia. **Aggressive fluid replacement can prevent AKI.**

Electrolyte disturbance is common as potassium and phosphate are released from damaged muscle, and both potassium and phosphate accumulation is exacerbated by acute kidney injury. Calcium first fluxes into cells and binds to phosphatidylinositol (leading to low serum calcium) but then effluxes from damaged muscles (leading to high calcium levels) and is slow to clear if there is muscle injury.

Detailed management

1) **Correct hyperkalemia and protect the heart:** Mild hyperkalaemia can be corrected with increased diuresis from aggressive fluid replacement. If potassium is moderately elevated (>6.0) and/or with accompanying ECG changes, follow standard emergency management guidelines for hyperkalaemia. In brief, consider using calcium gluconate for cardiac protection and iv insulin / dextrose and/or nebulised salbutamol to reduce the potassium. Haemodialysis may be required if there is no response to these measures.

Salbutamol works on ATP pumps which are compromised in rhabdomyolysis, as well as potentially causing a tachycardia, so should be used with caution.

Calcium containing agents such as calcium gluconate should also only be used if there is cardiac instability, as calcium may aggravate muscle injury and lead to delayed-

onset hypercalcemia. Haemodialysis will correct electrolyte disturbances but does not remove circulating myoglobin.

2) **Correct hypovolemia:** Fluids should be given at a rate of 1.5L/h aiming for a urinary output of 200-300 ml/h, with urinary pH of >6.5 and plasma pH of <7.5. Monitor fluid status carefully to avoid pulmonary or peripheral oedema. Avoid giving 0.9% saline exclusively (as multiple volumes may lead to hyperchloraemic metabolic acidosis, which can reduce urinary clearance of myoglobin). Mannitol and loop diuretics should be avoided. In elderly patients or those with pre-existent cardiac disease, fluid resuscitation will need to be cautious, and carefully monitored to avoid fluid overload.

1.26% Sodium bicarbonate solution can be used as part of the fluid regime, but monitor serum calcium levels carefully as sodium bicarbonate may exacerbate hypocalcemia.

3) **Hyperphosphatemia:** usually corrected by diuresis above.

4) **Calcium:** Avoid replacement unless symptomatic, as serum calcium is likely to rise later in the condition. Hypercalcaemia is managed with forced diuresis.

5) **Temperature:** If the episode is temperature-related then active cooling or warming should be initiated.

6) **Infection:** Screen for infection and treat accordingly.

7) **Disseminated intravascular coagulation:** This usually occurs later as a result of thromboplastin release and thrombotic microangiopathy. Monitor coagulation screen at all times. If deranged, treat with fresh frozen plasma.

8) **Drugs:** A careful drug history is vital. If on statins discontinue. Other possible culprits include colchicine, anti-malarials, zimovudine, neuroleptic agents, nonsteroidal anti-inflammatory agents and diuretics. Alcohol and recreational drugs, especially cocaine could be potential triggers. Ask about use of supplements e.g. for weight loss, or creatinine for body-building, and herbal remedies. Stop or reduce the dose of any drugs that may exacerbate hyperkalaemia (e.g. ACE inhibitors, angiotension II inhibitors, potassium sparing diuretics etc). Selective serotonin reuptake inhibitors, particularly sertraline, may cause rhabdomyolysis. Please also see document titled ‘Late-onset multiple-acyl-CoA-dehydrogenase deficiency and acquired causes’.

9) **Compartment syndrome:** This occurs after traumatic or ischemic muscle damage to muscle groups sheathed in noncompliant fascia. Muscle swelling increases intracompartmental pressures. The crushed muscle becomes oedematous and engorged with blood, compromising lymphatic drainage and then arteriolar perfusion. This, in turn, causes further muscle necrosis. Suspected compartment syndrome should be referred immediately to orthopaedics or plastic surgeons for consideration of surgical fasciotomy.

10) **Anaesthetic agents:** This is relevant if fasciotomy is indicated. Nitrous oxide and propofol are generally safe. Succinylcholine should be avoided as should ketamines.

11) **Consider investigation of underlying cause:** If there is no clear precipitant, or the degree of rhabdomyolysis is out of keeping with the trigger, additional investigations should be sent. These include **acyl carnitine profile, urine organic acids, a full hepatitis screen, HIV, thyroid screen, ANA and double stranded DNA.** Blood should be sent to genetics for DNA to be extracted and stored. If patients are on statins, send their serum to be tested for HMG CoA reductase antibodies.

12) **Muscle biopsy:** This should be avoided in the acute phase as the muscle is necrotic and the biopsy is unlikely to be diagnostic. If diagnostic uncertainty remains a muscle biopsy can be considered at least 1 month, and up to 6 months, after the rhabdomyolysis episode.

13) **Consider riboflavin supplements:** If the acyl carnitine profile shows abnormalities in keeping with Multiple Acyl CoA Dehydrogenase Deficiency (MADD) riboflavin supplementation should be started immediately, pending further genetic confirmation. Start riboflavin 100mg 8 hourly, warning the patient that urine and other bodily fluids may turn bright orange. Also see document ‘Late-onset Multiple Acyl-CoA-Dehydrogenase Deficiency and Acquired Causes’.

14) **Referral:** Any patient with an abnormal acyl carnitine profile and/or urine organic acids should be discussed with a neurologist or metabolic physician (see document Clinicians with Expertise in Rhabdomyolysis and Metabolic Myopathy). An acquired cause should be considered in the first instance (see document Late-onset Multiple Acyl-CoA-Dehydrogenase Deficiency and Acquired Causes).