

Rhabdomyolysis (RM) due to *LPIN1* mutation

Priority patient: must not be kept waiting in the emergency department

Transport by ambulance to a University Hospital with an ICU, and start infusion at home at the first sign of RM

If there is fever, vomiting, diarrhoea, muscle pain, or anaesthesia:

Risk of Acute Rhabdomyolysis rapidly followed by life-threatening hyperkalaemia with arrhythmia and renal failure

1 EMERGENCY ASSESSMENT

CPK, blood glucose, electrolytes, potassium, calcium, phosphate, urea, creatinine, blood gases, ionised Ca, lactate, AST, ALT, GGT, PT - Factor V. ECG on admission. Note the colour of the urine (myoglobinuria). Further tests depending on the intercurrent illness triggering the episode.

Do not wait for results of tests before starting infusion.

2 START TREATMENT URGENTLY, without waiting for test results:

A- Treatment in all cases

- **Corticosteroid therapy** Start at home orally (Cortancyl®) then IV upon arrival: **Methylprednisolone 1 to 2mg/kg/day for 3 to 5 days**
- **Discontinue Plaquenil maintenance treatment**
- **If signs of hypoperfusion, rehydrate** with Ringer lactate or NaCl 0.9% at **10ml/kg** (maximum 500 ml) if no cardiac signs; reassess and repeat if necessary.
- **Infusion for aggressive IV hydration:**
 - Volume **3L/m²/day**
 - Preparation for 1 litre of solution: 200 mL/kg 30% glucose solution + 400 mL bicarbonate 14% + 400 mL NaCl 0.9%
No potassium or calcium
- **Always admit to HDU/ICU in the event of rhabdomyolysis (regardless of the degree of CPK elevation)**
- Start specific treatment for any intercurrent infection

B- Adjustment according to the subsequent evolution of CPK levels

- Infusion for **at least 24 hours** even if CPK is initially normal. If CPK remains normal, it is possible to switch to an infusion of **G10%** (10% glucose) + **NaCl 6g/L** with an intake of **2L/m²/day** (maximum flow rate 150 ml/hr). **Do not use ready-made solutions containing potassium during the first few hours, except if there is secondary hypokalaemia.** If there is no RM, reintroduce K⁺ and in line with the level of serum potassium.

3 SIGNS OF SEVERITY

- **CPK > 20,000 IU/L**
- **Arrhythmia, ECG signs of hyperkalaemia, serum potassium > 7 mmol/L**
- **Oliguria / anuria, port wine-coloured urine, kidney failure**
- **Neurological disorders, prostration** (risk of hyperosmolar coma)
- **Consider renal replacement therapy if:**
 - blood potassium level > 5mmol/L,
 - any abnormality of any kind in ECG,
 - anuria/oliguria, and positive fluid balances contraindicating continuation of aggressive IV hydration,
 - kidney injury (creatinine levels do not reflect the severity of kidney injury, as it is released by muscle breakdown; urea level is more reliable).



4 Initial MONITORING in HDU/ICU

- Blood glucose, Na, and K every 2 hours for the first 24 hours, adjusting potassium intake in line with potassium level and renal function (if there is no potassium in the infusion, there is also a risk of hypokalaemia if the rhabdomyolysis is not severe).
- Complete electrolyte panel with Ca, P, Mg, urea, creatinine, and CPK every 6 hours.
- Hourly monitoring of urine output > 2ml/kg/h, urine pH and urine specific gravity < 1005.
- Fluid balance assessment every 3 hours to adjust aggressive IV hydration.
- ECG in place with hourly tracings. Monitor cardiac function (clinical and echocardiographic).
- If CPK normal, **keep the patient in hospital for at least 24 hours on an infusion** to make sure that there is no secondary CPK elevation

PATHOPHYSIOLOGY:

Mutations of the *LPIN1* gene predispose patients to particularly severe and rapid acute rhabdomyolysis which can be life-threatening. This is mainly due to cardiac rhythm disorders due to hyperkalaemia (ventricular fibrillation or ventricular tachycardia), but also potentially from myocardial damage which can cause rhythm disorders either directly or by lowering the threshold of tolerance to hyperkalaemia. Acute episodes can occur in at-risk situations (e.g. fever, intercurrent infection, vomiting, diarrhoea, unusual physical activity, or in any fasting or catabolic state).

Some patients also suffer from chronic muscle pain or fatigability upon exertion, with moderately elevated CPK levels outside an acute setting. The CPK level may increase secondarily in at-risk situations.

Standard treatment, depending on the patient:

- Low-dose Plaquenil as maintenance treatment Treatment must be stopped during acute attacks of rhabdomyolysis
- Short-term corticosteroid therapy in all at-risk situations, to be started by the patient at home.

SITUATIONS WITH RISK OF DECOMPENSATION:

- Intercurrent infectious disease, fever, anorexia, vomiting or **any fasting or catabolic state** .
- Unusual physical exertion
- Surgery/Anaesthesia

CLINICAL SIGNS OF DECOMPENSATION: Do not wait for these signs!

- Muscle pain (may precede elevation of CPK level)
- Inability to walk, prostration
- Arrhythmias, heart failure
- Impaired consciousness
- Hypovolaemic shock
- Myoglobinuria (sign of severe rhabdomyolysis)

DRUG CONTRAINDICATIONS / GENERAL ADVICE:

- Treatments contraindicated during the acute phase of rhabdomyolysis: NSAIDs, all drugs which raise serum potassium
- Statins (increased risk of rhabdomyolysis)
- Some anaesthetic agents: see below

- All vaccinations are recommended (particularly influenza).

IF UNDERGOING GENERAL ANAESTHESIA:

- **Contraindicated anaesthetic agents: Halogenated agents (myocardial depression), depolarising neuromuscular blocking drugs (succinylcholine, induces muscle contraction), prolonged administration of Propofol**
- **CPK to be monitored pre- and post-operatively.**

NUMBERS AND MEDICAL SPECIALISTS

On-call telephone numbers for metabolic emergencies:

At night, only medical teams can call in emergency situations, and only if the emergency certificate has not been understood or if the clinical state or test results are worrying. Whenever possible, calls should be made before nightfall.

Secretarial issues must be dealt with via the medical secretariat during the week, or by email addressed to the patient's metabolic medicine specialist.

Certificate issued on

Dr