RECURRENT SEVERE RHABDOMYOLYSIS, undiagnosed
Priority patient: must not be kept waiting in the emergency department

Label

The patient has had one or more episodes of rhabdomyolysis with CPK > 6,000 U/L. A genetic cause is under investigation (mitochondrial fatty acid β-oxidation disorders have been excluded a priori). This patient is at risk of recurrence during stress or catabolic states. Strict and urgent care is required in the event of fever, vomiting, fasting, muscle pain or anaesthesia. No specific treatment ongoing. No specific diet.

If there is fever, vomiting, diarrhoea, muscle pain, or anaesthesia:
Risk of acute rhabdomyolysis (RM)

1 EMERGENCY ASSESSMENT

CPK, blood glucose, serum electrolytes, **potassium,** calcium, phosphate, urea, creatinine, blood gases, 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.

2 START TREATMENT URGENTLY, without waiting for test results:

A- Treatment in all cases

- If there are **signs of hypoperfusion, rehydrate** with Ringer's lactate or 0.9% NaCl at **10 mL/kg** (maximum 500 mL) in the absence of cardiac signs; reassess and repeat if needed.
- Infusion for **IV hydration** for **at least 12–24 hours**, even if CPK is initially normal (goal: prevention of rhabdomyolysis).
  - **10% glucose solution + NaCl 6 g/L WITHOUT POTASSIUM.** Intake **2L/m²/day** (maximum flow rate 150 ml/hr). **Do not use ready-made potassium-containing solutions** (balanced electrolyte solutions such as Glucidion, Bionolyte etc.) [BSA = (4W+7)/(W+90)].
  - If infusion is not possible and clinical condition is reassuring: wait for CPK results. If CPK > 6,000 U/L: insert an NG tube for hydration (administer the above solution for infusion at the same rate). If CPK < 6,000 U/L: check again at H4.
- Start specific treatment for any intercurrent infection.

B– Adjustment according to CPK

- **If CPK is stable at < 6,000 U/L at H0 and H4** and potassium is normal: infusion with 10% glucose solution and balanced electrolytes may be given (reintroduce K^+), **to be maintained for 12–24 hours.**
- **If CPK 6,000–20,000 U/L:** continue hydration as above, 2 L/m²/day WITHOUT POTASSIUM.
- **If CPK >20,000 U/L or immediately if myoglobinuria:** arrange **transfer to HDU/ICU** and, as soon as possible, start **aggressive IV hydration**, with approval from the intensive care doctor:
  - 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
- **Specific treatments to be considered:**
  - **Short-term corticosteroid therapy may be considered** (for the inflammatory component of rhabdomyolysis. In the absence of diagnosis, especially useful in rhabdomyolysis due to *LPIN1* mutation): **Methylprednisolone 1–2 mg/kg/day for 3–5 days.**
  - Consider **IV Dantrolene** if *RYR1* mutation suspected: history of rhabdomyolysis, malignant hyperthermia, general anaesthetic accident. Autosomal dominant inheritance.

3 SIGNS OF SERIOUS ILLNESS = Specialist opinion/transfer to intensive care

- **CPK > 20,000 IU/L** (after starting the above infusion)
  - **Consider renal replacement therapy if** serum potassium > 5 mmol/L despite aggressive IV hydration, any ECG abnormality, anuria/oliguria and positive fluid balances contraindicating continued aggressive IV hydration; renal impairment (creatinine results do not reflect the severity of the kidney impairment, as it is released by muscle breakdown; urea is more reliable).
  - **Monitoring in ICU:** blood glucose**,** Na and K every 2 hours during the first 24 hours, complete electrolyte panel with Ca, P, Mg, urea, creatinine, 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, hourly trace. Monitor cardiac function (clinical and echocardiographic).
- **Arrhythmia, ECG signs of** hyperkalaemia**, serum potassium > 7 mmol/L**
- **Oliguria/anuria, dark red urine, renal failure.**
- **Neurological disorder, prostration** (risk of hyperosmolar coma).

4 MONITORING (except for severe rhabdomyolysis CPK > 20,000 U/L in ICU)

- **CPK, serum electrolytes, calcium, phosphate, diuresis and urine colour every 4 h.** Adjust potassium supplementation according to serum potassium and renal function (if not included in the infusion there is also a risk of hypokalaemia).
- **Vital signs monitor, ECG every 4 hours if CPK > 6,000 U/L.**
- If CPK is normal**, keep the patient hospitalised** for **at least 12–24 hours with IV fluids** to ensure there is no secondary rise in CPK.

PATHOPHYSIOLOGY:

Acute rhabdomyolysis is the sudden destruction of skeletal muscle fibres, characterised by elevated CPK during acute episodes. It can be associated with acute cardiac involvement. The presence of myoglobinuria suggests CPK elevated to at least 15,000 U/L (normal range < 250 U/L).

In patients with a history of previous episodes, fatty acid β-oxidation disorder and endocrine causes have been excluded a priori, and the aetiological investigation is ongoing for metabolic causes (*LPIN1* mutations, disorders of glycogen metabolism, etc.), calcium channel abnormalities (including *RYR1*), inflammatory causes (myositis) or structural myopathies.

SITUATIONS WITH RISK OF DECOMPENSATION:

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

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

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

DRUG CONTRAINDICATIONS / GENERAL ADVICE:

- Treatments contraindicated during the acute phase of rhabdomyolysis: NSAIDs, all potassium-increasing drugs.
- 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 depressants), depolarising neuromuscular blocking agents (succinylcholine, promotes contraction), prolonged Propofol administration.**
- **If *RYR1* mutation (genetic testing in progress): Risk of malignant hyperthermia.**
  - Monitor capnography and core temperature.
  - Obtain the protocol for injectable Dantrolene (*RYR1* antagonist, see SFAR recommendation).

http://sfar.org/recommandations-dexperts-pour-le-risque-dhyperthermie-maligne-en-anesthesie-reanimation/

  - Monitor CPK before and after surgery.

Refer to the **Emergency section** on

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