

RECURRENT MILD RHABDOMYOLYSIS, undiagnosed

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

Label

The patient has had one or more episodes of mild rhabdomyolysis with CPK < 6,000 U/L. It is not yet known whether this patient may develop severe myolysis (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.

In the event of fever, vomiting, diarrhoea, muscle pain or anaesthesia:
Risk of acute rhabdomyolysis

1 EMERGENCY

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 EMERGENCY TREATMENT TO BE IMPLEMENTED :

A- Management according to symptoms and initial CPK

- In the absence of muscle pain or myoglobinuria:
 - CPK normal on admission (< 500 IU/L): no systematic infusion, but monitoring and CPK test at H0 and H6.
 - Abnormal CPK: CPK 500–6,000 IU/L and normal potassium: infusion of 10% glucose solution with balanced electrolyte supplementation at 2 L/m²/day (not 10% glucose alone) for at least 24 hours, with CPK every 4 hours.
- If CPK 6,000–20,000 U/L and/or muscle pain:
 - If signs of hypoperfusion: rehydrate with Ringer's lactate or 0.9% NaCl at 10 mL/kg (max. 500 mL) in the absence of cardiac signs; reassess and repeat if needed.
 - Infusion for IV hydration: 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 IV infusion is not possible: insert nasogastric tube for hydration (above infusion at the same rate).
 - Start specific treatment for any intercurrent infection.
- If CPK > 20,000 U/L or immediately if myoglobinuria present: arrange transfer to HDU/ICU and start aggressive IV hydration as soon as possible (see paragraph below).

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

- CPK > 20,000 IU/L
 - 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
 - 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.
 - Consider renal replacement therapy if serum potassium > 5 mmol/L despite correctly administered 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 elevated > 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 6 h 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