Recurring MILD RHABDOMYOLYSIS with no Diagnosis

Priority patient: must not wait in A&E

Label

The patient has presented one or several episodes of mild rhabdomyolysis with CPK < 6 000 U/L. We do not yet know if this patient may present severe myolysis (CPK > 6 000 U/L). These episodes are currently under investigation for a genetic cause (the fatty acid ß-oxidation deficiencies have been excluded a priori). This patient is at risk of recurrence during a situation of stress or catabolism. He/she requires strict and urgent treatment in case of fever, vomiting, fasting, muscle pain or anaesthesia. No specific ongoing treatment. No specific diet.

In case of fever, vomiting, diarrhoea, muscle pain or anaesthesia:
Risk of Acute Rhabdomyolysis

1 EMERGENCY

CPK, Blood glucose, serum electrolytes, **potassium**, calcium, phosphorus, urea, creatinine, blood gases, lactate, ASAT, ALAT, GGT, PT - **Factor V. ECG** on arrival**.** Note the **colour of the urine (myoglobinuria).** Tests depending on triggering intercurrent illness.

2 TREATMENT TO BE INITIATED AS AN EMERGENCY:

A- Treatment depending on symptomology and initial CPK

- **In the absence of muscle pain or myoglobinuria:**
  - **CPK normal on arrival (<500 IU/L)**: no systematic infusion but monitoring and CPK measurements at H0 and H6.
  - **Abnormal CPK: 500 IU/L < CPK < 6 000 IU/L** and normal serum potassium: Polyionic infusion 10% glucose at 2L/m²/d (not pure 10% glucose) to continue for at least 24h with CPK / 4h.
- **If CPK falls between 6 000 U/L and 20 000 U/L and/or muscle pain:**
  - If **signs of hypoperfusion, replenish** with Ringer's Lactate or 0.9% NaCl at **10 ml/kg** (maximum 500 ml) if no cardiac signs - reassess and continue if necessary.
  - Infusion for **IV hydration:** Serum Glucose **G10% + NaCl 6g/L WITHOUT POTASSIUM.** Intake **2L/m²/d** (maximum flow 150 ml/h). **Do not use pre-prepared solutes containing potassium** (polyionic, Glucidion, Bionolyte, etc.) [body surface area = (4P+7)/(P+90)].
  - If not possible to infuse the patient, install NG tube for hydration (infusion above given at same flow rate).
  - Initiate specific treatment for potential intercurrent infection.
- **If CPK >20 000 U/L or from the outset if myoglobinuria:** plan for transfer to **Continuous monitoring unit/Intensive care,** and start **hyperhydration** as soon as possible (*see paragraph below*).

3 SEVERITY SIGNS = Consult / transfer to Intensive Care

- **CPK > 20 000 IU/L**
  - **Hyperhydration:** Volume **3L/m²/day.**
    - Preparation for 1 litre of solute: 200 ml of G30% + 400 ml of Bicarbonate 14 ‰ + 400 ml of NaCl 0.9%
      No potassium, nor calcium
  - **Short corticosteroid therapy possible** (inflammatory component of rhabdomyolysis. In the absence of diagnosis, will be useful especially if *LPIN1* mutation): **Methylprednisolone 1 to 2mg/kg/d for 3 to 5 days.**
  - Consider **Dantrolene IV** if suspected *RYR1* mutation*:* history of RM, malignant hyperthermia, general anaesthesia accident. Autosomal dominant transmission.
  - **Consider extrarenal purification** if serum potassium > 5mmol/L despite appropriate hyperhydration, an ECG anomaly of any nature, anuria/oliguria and positive electrolyte panel contraindicating the continuation of hyperhydration, renal damage (the creatinine figures do not express the significance of the renal damage, since it is released by muscular necrosis, urea is more reliable).
  - **Intensive care monitoring:** Capillary blood glucose, Na, K/2h in the first 24h, Complete electrolytes with Ca, Ph, Mg, urea, creat, CPK / 6 hrs. Hourly urine flow monitoring > 2ml/kg/h, pHu and urinary density < 1005. Electrolyte panel / 3h to adjust hyperhydration. ECG in place, trace/h. Echocardiography.
- **Rhythm disorder, ECG signs** of hyperkalaemia, **hyperkalaemia > 7 mmol/L.**
- **Oligo/anuria, "port wine" red coloured urine, renal failure.**
- **Neurological disorders, exhaustion**, (risk of hyperosmolar coma)

4 MONITORING (excluding severe rhabdomyolysis > 20 000 U/L in intensive care)

- **CPK, electrolytes, calcium, phosphorus, diuresis, and urine colour** every 4 hrs. Adjust the potassium intake to the serum potassium and renal function (in the absence of intake via the infusion, there is also a risk of hypokalaemia).
- **Electrocardioscope, ECG/4h if CPK > 6 000 U/L.**
- If normal CPK, **keep the patient in hospital** for **at least 6 hrs** to ensure the CPK does not increase secondarily.

PATHOPHYSIOLOGY:

Acute rhabdomyolysis is the sudden breakdown of skeletal muscle fibres, characterised by an increase in CPK during the acute attack. It can be associated with acute cardiac impairment. The presence of myoglobinuria indicates an increase in CPK of at least > 15 000 U/L (N <250 U/L).

In a patient who has already had an attack, a fatty acid ß-oxidation disorder and endocrine causes have been excluded a priori, and the aetiological investigation is underway: metabolic causes (*LPIN1* mutations, glycogen metabolism errors, etc.), calcium channel anomalies (including *RYR1*), inflammatory causes (myositis), or structural muscular causes.

CIRCUMSTANCES IN WHICH THERE IS A RISK OF DECOMPENSATION:

- Surgery / Anaesthesia
- Intercurrent infectious disease, fever, weight loss, vomiting, **or any fasting or catabolic state**.
- Unusual physical exercise.

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

- Muscle pains (can precede the increase in CPK).
- Unable to walk, exhaustion.
- Cardiac rhythm disorders, heart failure.
- Impaired consciousness.
- Hypovolemic shock.
- Myoglobinuria (sign of severe rhabdomyolysis).

DRUG CONTRAINDICATIONS / GENERAL ADVICE:

- Treatments contraindicated in the acute phase of rhabdomyolysis: NSAID, all hyperkalaemia-inducing drugs.
- Statins (increased risk of rhabdomyolysis).
- Some anaesthetic agents: see below.

- All vaccinations are recommended (particularly influenza).

IN CASE OF GENERAL ANAESTHESIA:

- **Contraindicated anaesthetic agents: Halogens (myocardium depressor), depolarising curares (succinylcholine, promotes muscle contraction), prolonged administration of propofol.**
- **If *RYR1* mutation (genetics ongoing): Risk of malignant hyperthermia.**
  - Ensure capnography and core temperature monitoring.
  - Retrieve the injectable dantrolene protocol (*RYR1* antagonist, see SFAR recommendations)

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

  - CPK monitoring pre- and post-surgery.

Consult the **Emergency page** on

REFERENCE DOCTORS AND CONTACT DETAILS

On-call telephone numbers for metabolic emergencies of:

At night, only the 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. As far as possible make calls before night time.

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

Certificate issued on Dr