Recurring SEVERE RHABDOMYOLYSIS with no Diagnosis

Priority patient: must not wait in A&E

Label

The patient has presented one or several episodes of rhabdomyolysis with 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 (RM)

1 EMERGENCY WORKUP

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 STARTED URGENTLY, without waiting for test results:

A- Management in all cases

- 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** for **at least 12 to 24h** even if initially normal CPK (objective: prevent rhabdomyolysis).
  - 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 it is not possible to infuse the patient and clinical signs are reassuring: await the CPK. If CPK >6 000 U/L, install NG tube for hydration (infusion solute above given at same flow rate). If CPK<6 000 U/L, test again at H4.
- Initiate specific treatment for potential intercurrent infection.

B– Adjustment depending on CPK

- **If CPK stable <6 000 U/L at H0 and H4** and serum potassium normal: infusion with polyionic 10% glucose possible (reintroduce K+), **to be continued for 12 to 24h.**
- **If CPK falls between 6 000 U/L and 20 000 U/L:** continue hydration described above 2L/m²/d WITHOUT POTASSIUM.
- **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, after agreement from reanimator:
  - 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
- **Specific treatments to be discussed:**
  - **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.

3 SEVERITY SIGNS = Consult / transfer to Intensive Care

- **CPK > 20 000 IU/L** (after installation of above infusion)
  - **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 degree of 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. Monitoring of cardiac function (clinical and ultrasound).
- **Rhythm disorders, 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

- **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 **12 to 24 hrs with infusion** 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.
- If TANGO2 deficiency is suspected: many drug contraindications - see TANGO2 protocol

- 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.
- **If TANGO2 mutations (genetics in progress): many CIs - see TANGO2 protocol.**

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