Mitochondrial disease - Mitochondrial cytopathy

Patient monitored for:
Risk of:

1 PATHOPHYSIOLOGY

Deficiency in mitochondrial energy production, which can manifest as a range of disorders depending on the patient and the gene responsible. Each patient usually has one predominantly affected organ, but during decompensation other organs may be affected. **Hyperlactacidaemia** is usual, and not treatable, but it can be increased by high glucose intake; **by itself, it does not justify seeking a specialist opinion.**

2 CIRCUMSTANCES IN WHICH THERE IS A RISK OF

A- Circumstances creating a risk:
In general, any catabolic state: repeated vomiting, fasting, situations with a risk of dehydration, severe infection.

B– Signs of decompensation
Deteriorating general state, respiratory acidosis, acute neurological signs, life-threatening state, organ failure.

C– Tests to carry out
Capillary blood glucose +/- capillary ketones, venous blood glucose, serum electrolyte panel with bicarbonate, urea, creatinine, liver function tests, PT, CPK, lactate, blood ammonia, ABG. Urine dipstick (ketosis?) + other tests depending on context.

3 MANAGEMENT IN A&E:

A– Opt, if possible, for hydration orally or by CEF, with the patient's usual intakes

B- Infusion if enteral route not possible: in order to maintain hydration

- Avoid glucose overload (risk of exacerbating the hyperlactataemia).
  - → Infusion of bionolyte glucose 5% with electrolytes (bionolyte, polyionic, glucidion, B26, etc.), water volume adapted to the age and weight of the patient.
- If patient on ketogenic diet:
  - → Infusion of 2.5% glucose (e.g. for 1 litre of infusion, mix or put in a Y infusion set, a bag of 500 ml of 5% glucose and a bag of 500 ml of 0.9% NaCl at the same flow rates + electrolyte supplements according to the serum electrolyte results).
  - → Volume: depending on the clinical status, water volume adapted to the age and weight of the patient.
  - → If available: 20% lipids (Medialipids, smoflipids, ivelip, etc.): 1g/kg/day i.e. 0.2 ml/kg/h by continuous IV.
- **Blood glucose monitoring: If symptomatic hypoglycaemia** (capillary blood glucose < 3.5mmol/L): raise blood glucose with 10% glucose 2ml/kg by direct IV, then infusion of bionolyte 5% glucose.
- **If lactic acidosis (pH < 7.20 and/or lactate >10mmol/L):** stop glucose and infuse normal saline (0.09% NaCl). Monitor blood glucose Avoid Ringer's lactate.

C– Specific treatments

- **If acute neurological symptoms (psychomotor retardation, seizures, motor or visual neurological deficits, confusion, unusual headaches, coma) leading tosuspicion ofa stroke-like episode or Leigh syndrome (damage to the basal ganglia or brain stem). Admit to intensive care or intermediate care unit.**
  - EEG and brain MRI (Diffusion sequences, ASL and spectroscopy if possible) depending on the clinic.
  - Corticosteroid therapy if confirmed stroke-like episode or Leigh syndrome affecting the brain stem: Methylprednisolone orally or IV 2mg/kg/day with blood glucose monitoring. Duration to be assessed during working hours, with rapid reduction.
  - Consider arginine if stroke-like episode confirmed (cf dosage overleaf)
- **If status epilepticus**: distinguish between generalised tonic-clonic, focal (continuous partial epilepsy), and myoclonic seizures. Remember to consider status epilepticus without motor signs (coma, visual or sensory focal seizure, confusion) if alteration of consciousness and/or alertness.
  - Standard treatment: benzodiazepine IV, Keppra IV. Avoid barbiturates, intubation and Valproate.
  - Titrate the dose of antiepileptics if possible. With the experts: discuss treatment modifications and introduction of a ketogenic diet(during working hours).
  - Plan for an EEG to identify the nature of the epileptic state.
- **If symptomatic cardiac conduction disorder:** raise the heart rate (Isuprel, stimulation probe) and transfer to a surgical-medical cardiology service to install a pacemaker.
- **If rhythm disorders:** effective anticoagulation, do not use digoxin to lower the heart rate. Transfer to a cardiology service for specific treatment.

D– Other recommendations, irrespective of circumstances

- Continue usual treatment.
- If specific diet (ketogenic): continue if enteral route possible, if not infusion of normal saline or 2.5% glucose.
- Treat the cause of decompensation (infection, constipation, pain, anxiety, etc.) and the symptoms.

This emergency protocol is proposed by the G2M network working group. The protocol may be modified under the responsibility of the referring doctor. In no circumstances does it replace the responsibility of the doctor treating the patient in A&E.

DRUG CONTRAINDICATIONS / GENERAL ADVICE:

PROHIBITIONS: Acetylsalicylic acid (Aspirin), valproic acid (Depakin, etc.), Metformin, nucleoside reverse transcription inhibitors, tetracycline and chloramphenicol, zonisamide.

- **Vaccinations:** No contraindications. Influenza vaccine recommended every year. If poor tolerance of live vaccine, review the vaccination schedule with the patient's general practitioner.

IN CASE OF ANAESTHESIA:

- **Avoid succinylcholine and lactated Ringer's infusion.**
- Most anaesthetic drugs have depressive actions on mitochondrial function in vitro. However, general anaesthesia using intravenous anaesthetics or halogenated agents, as well as non-depolarising muscle relaxants, has been identified as safe.
- Partial overdose has been observed (especially with propofol), hence there is a need to **titrate the different anaesthetic agents and monitor their effects** (including for local anaesthesia).
- **Routine prevention of post-operative nausea and vomiting.** Following local protocols: Dexamethasone, Ondansetron (preferable in children 0.15 mg/kg), Droperidol (only in adults, at very low doses, 0.625 to 1.25 mg)
- **Maintain homeostasis** (Safe Tots): pay particular attention to ensuring normal blood glucose, blood volume and body temperature. Avoid prolonged use of tourniquets.
- **For minor surgery,** ketamine is a good alternative (ref = PNDS MELAS, accessible on the HAS site).
- **Prolonged fasting is contraindicated:** In case of surgery, always use infusion without glucose overload (see above)

ASSISTANCE WITH PRACTICAL ADMINISTRATION OF TREATMENTS:

- CORTICOSTEROID THERAPY: Methylprednisolone IV, 2mg/kg in a single dose (max 60mg)
- ARGININE: In a child, loading dose of 0.5g/kg (max. 6g) orally or slow IV over 1 to 2h (maximum perfusion rate 1g/kg/h) then 0.5g/kg/day (max. 12g) by continuous IV for 3 to 5 days. In an adult, loading dose 10g/m² orally or slow IV, then 10g/m²/day by continuous IV for 3 to 5 days (see PNDS Melas)

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