KETOACIDOSIS from KETOLYSIS DISORDERS : SCOT - MAT - MCT1

(succinyl-CoA:3-oxoacid-CoA transferase / 3-ketothiolase / monocarboxylate transporter 1 deficiencies)

Patient Label

Priority patient: must not wait in A&E / ED

IN CASE OF VOMITING, DIARRHEA, FEVER, FASTING: RISK OF HYPOGLYCAEMIA, SEVERE KETOACIDOSIS, COMA

Do not wait for signs of decompensation, in all cases initiate management as set out below.

1 EMERGENCY WORKUP

Capillary glycaemia, blood and/or urinary ketones (positive if >0.8mmol/l or 1+), venous blood glucose, **electrolytes with bicarbonate**, **blood gases**, lactate, ammonemia, liver enzymes, PT, factor V. Must not delay treatment (see below).

2 TREATMENT TO BE STARTED URGENTLY, without waiting for lab results

- **If hypoglycaemia < 60 mg/dL (3.3 mmol/L):** Administer **1mL/kg of 30% glucose (dextrose) in water** (max. 30 mL) orally or enterally. **If enteral route impossible: administer 3mL/kg of 10% glucose in water by rapid IV** (30% glucose possible by central line or intraosseous route, some teams allow injection of 30% glucose via peripheral line for refractory hypoglycaemia).
- Check capillary blood glucose 5 minutes later. If still hypoglycaemic, administer a second dose of glucose and check 5 min later.
- If **hypovolaemia, expand** with 10mL/kg of Ringer's lactate or normal saline (max. 500mL), reassess and continue if necessary.
- Immediately start an infusion even if blood glucose levels have been corrected: Infusion using 10% glucose with standard electrolyte additions* (never pure glucose 10%)

Age	0-24 months	2-4 years	4-14 years	> 14 years / adult	**MAX INITIAL RATE**
Polyionic 10% glucose (glucose infusion rate)	5mL/kg/h (8mg/kg/min)	4mL/kg/h (7 mg/kg/min)	3.5mL/kg/h (6mg/kg/min)	2.5mL/kg/h (4mg/kg/min)	**120mL/h (3L/24h)**

e.g.: Bionolyte®, Glucidion®, etc. if no pre-made solution available, use 10% glucose in water + 4 to 6g/L NaCl (70 mEq/L) + 2g/L KCl (27 mEq/L)
If IV line is impossible => Nasogastric tube or gastrostomy: prepare the IV fluids listed above and pass them through the tube at the same rates.

Continue with the usual treatment, orally or IV

- **L-Carnitine (Levocarnil®, Carnitor®):** only for ketothiolase deficiency (MAT): usual dose *or* 100 mg/kg/day by continuous IV or qid (max 8g/day).

3 SEVERITY SIGNS = Consult / Transfer to Intensive Care

- **Comatose** or **worsening** of neurological clinical state, or **persistence** of neurological signs 3h after start of treatment.
- **Severe metabolic acidosis**, **pH< 7.1** from ketoacidosis without hyperlactataemia. Treatment with bicarbonate is not usually necessary. Beware of hyperkalaemia with acidosis, adjust KCl intakes.
- Signs of **severe liver failure:** Prothrombin ratio < 30%, factor V < 50%
- Disappearance of polypnea despite severe acidosis

4 MONITORING under treatment

- Electrocardioscope
- Capillary blood glucose q2h: if hyperglycaemia, adjust the glucose infusion rate (no lower than 50% of the initial rate). The acidosis may be corrected more slowly.
- Urinanalysis on every micturition and/or capillary blood ketones. Serum electrolytes and pH q3h then according to progress. Monitor ammonemia and liver function if initially abnormal.

PATHOPHYSIOLOGY

Patients with ketolysis disorders produce ketone bodies normally on **prolonged fasting**, but cannot metabolise them, hence creating a major risk of **hypoglycaemia** and **severe ketoacidosis** with rapid onset during prolonged fasting or **vomiting**, without a major increase in blood lactate levels. In addition, **3-ketothiolase deficiency** (MAT) also exposes patients to a risk of **intoxication by the products of protein degradation.**

Usual treatment is (depending on the patient):

- Oral **Carnitine** (Levocarnil®), to be given IV in case of fasting or food intolerance.
- Limitation of the fasting time**, hence continuous enteral feeding at night or uncooked cornstarch in the evening for some patients.**
- In 3-ketothiolase (MAT) deficiency: a low-protein diet may be offered, see "maintenance diet" sheet, and an "emergency diet" of carbohydrates without protein via NG tube or IV for situations **where there is a risk of increased catabolism**.

CIRCUMSTANCES WITH RISK OF DECOMPENSATION

- Intercurrent infectious disease, fever, anorexia, vomiting, surgery, or **any fasting state, insufficient caloric intake, weight loss or catabolic state.**
- **In all these cases, the patient is to be kept hospitalised. These are emergency situations:** do the workup on the patient in A&E before admitting them to a ward and implement the protocol described overleaf. **ACT QUICKLY** to prevent hypoglycaemia and/or severe acidosis, which can have serious and irreversible neurological sequelae.

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

- Signs of **hypoglycaemia, altered consciousness, vomiting, acidotic dyspnea.**
- Progression to **coma +/- status epilepticus**.
- **Liver failure**.

ASSISTANCE WITH PRACTICAL ADMINISTRATION OF DRUGS: verify with locally available brands

- LEVOCARNIL IV (vial 1g = 5mL), given neat or diluted in normal saline, using a Y infusion set
- LEVOCARNIL oral (vial 1g = 10mL), tid or qid

DRUG CONTRAINDICATIONS / GENERAL ADVICE:

Contraindication for **salicylic acid, valproic acid**

- All vaccinations are recommended (particularly influenza).
- Prolonged fasting is contraindicated, never leave the patient without a supply of carbohydrate (infusion or continuous enteral feeding) and their usual treatments
- Do not forget vitamins and trace elements when intake is exclusively parenteral for prolonged periods.
- Do not leave the patient without proteins for more than 3 days.

SURGERY:

WARNING: never leave the patient fasting without an infusion. Implement the emergency protocol with infusion as described overleaf, in preparation for surgery.

REFERENCE PHYSICIANS 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 the outpatient office during the week or by email addressed to the patient's referring metabolic physician.

Certificate issued on : Dr