Patient Label

KETOGENESIS DISORDERS

(3 HydroxyMethylGlutaryl (HMG)-CoA lyase / 3 HMG CoA synthase deficiencies)

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

IN CASE OF VOMITING, DIARRHEA, FEVER, FASTING : RISK OF HYPOGLYCAEMIA, HYPERAMMONEMIA, AND COMA

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

1 EMERGENCY WORKUP

Capillary and venous blood glucose, liver enzymes, PT, factor V, ammonemia, blood gases, electrolytes.
Must not delay treatment.

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

- **If hypoglycaemia < 60 mg/dL (3.3 mmol/L):** Administration of **1mL/kg of 30% glucose** (max. 30 mL) **orally** or enterally if conscious or **3mL/kg of 10% glucose IV** if unconscious (IV 30% glucose is also possible via central line or intraosseous route; some teams allow 10 mL of 30% glucose via peripheral venous 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.
- Immediately start an infusion even if blood glucose levels have been corrected: Infusion using 10% glucose (=dextrose) with standard electrolyte additions* (never pure 10% glucose)

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 + 4g/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 medicines orally or IV
  - **L-Carnitine (Levocarnil®):** usual dose or 100 mg/kg/day by continuous IV infusion 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.
- Signs of **liver failure:** Prothrombin ratio < 30%, factor V < 50%.
- **Hyperammonemia >100µM, administer "scavenger" treatments:**
  - **Continuous IV** sodium benzoate: Start with a **loading dose** of 250mg/kg over 2 hours (**max. 8g over 2h**) then 250-500mg/kg/24h (**max. 12g/24h**) (given orally via NG tube if no IV access). Draw another ammonemia blood sample before the loading dose, without waiting for the result.
- **Severe metabolic acidosis**, **pH < 7.1**, with hyperlactataemia. Treatment with bicarbonate is usually unnecessary.

4 MONITORING

- Electrocardioscope
- Capillary blood glucose q2h: If hyperglycaemia: adjust the glucose infusion rate (no lower than 50% of the initial rate).
- Tests: if initial results abnormal, monitor electrolytes, pH, blood ammonia and liver function tests.

PATHOPHYSIOLOGY

HMG CoA lyase and HMG CoA synthase deficiencies are **ketone body synthesis disorders** (ketogenesis deficiencies) which **mimic fatty acid oxidation disorders.** The risk is a deficit of energy production (**metabolic acidosis with hyperlactataemia, liver failure, hypoglycaemia**) that may occur during episodes of fasting, and for HMG-CoA lyase deficit a risk of toxicity from products of protein breakdown.

The usual oral treatments can be (depending on the patient):

- Oral **L-Carnitine** (Levocarnil®), to be given IV in case of fasting or food intolerance.
- Limited fasting time, with for some patients night-time continuous enteral feeding or supplements of uncooked cornstarch.
- In HMG-CoA Lyase deficiency: a low-protein diet may be offered, see the patient's "maintenance diet" sheet and it's "emergency diet" (carbohydrates without protein) via NG tube (or emergency IV infusion) for situations with 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 overleaf. **ACT QUICKLY** to prevent hypoglycaemia and/or severe acidosis and/or liver failure (intoxication in cases of HMG-CoA lyase deficiency), 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 orally (vial 1g = 10mL), to be given tid or qid
- SODIUM BENZOATE IV: vials of 1g = 10ml, to be diluted 1:1 by volume in 10% glucose. Contains 7 meq of sodium per gram of benzoate.

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) or 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 above, 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