British Inherited Metabolic Disease Group

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This protocol has 4 pages

GLUTARIC ACIDURIA TYPE 1 –ACUTE DECOMPENSATION

(Glutaryl CoA dehydrogenase deficiency, GCDH deficiency)

(standard version)

- **Please read carefully. Meticulous treatment is very important as there is a high risk of neurological complications.**
- **TREATMENT IS URGENT. DO NOT DELAY.**
- **If the instructions do not make sense or a problem is not addressed you must discuss your concerns with the consultant on call.**

1. Background

Glutaric aciduria is an inherited disorder of the breakdown of certain amino acids, notably lysine. Any metabolic stress can lead to serious illness, with encephalopathy - a reduced level of consciousness and other neurological abnormalities. Following these episodes, patients often have severe permanent neurological disability, particularly a movement disorder. However with early aggressive treatment neurological complications can be prevented. The damage results from the accumulation of glutaric acid and other toxic metabolites. Patients under 6 years of age are at most risk of neurological damage so treatment of the children must be very careful. Treatment aims to minimise the accumulation of toxic metabolites by preventing protein breakdown and to promote their excretion by the use of carnitine.

Decompensation is often triggered by metabolic stress such as any febrile illness, particularly diarrhoea and vomiting, or fasting, but an obvious cause is not always apparent. The early signs of decompensation may be subtle, such as minor changes in tone. Vomiting and diarrhoea are common and should always be taken seriously. However, the signs may be difficult to assess such as irritability or just ‘not right’. Always listen to parents carefully as they probably know much more than you do.

2. Admission

Almost all patients who present to hospital will require admission. Only allow the child home if you and the family are entirely happy and you have discussed the problems with the consultant on call. The family must have a clear management plan and be prepared to return if the child does not improve.

- **If there is any doubt at all, the child must be admitted, even if only necessary for a short period of observation.**

3. Initial plan and management in hospital

⇨ If the child is shocked or clearly very ill arrange for admission to ITU/High dependency unit.

⇨ If admitted to metabolic/general ward make a careful clinical assessment including blood pressure and even if the patient does not appear encephalopathic enter a Glasgow coma score (for details click here). This will help other staff to detect any deterioration, particularly around the time of a change of shifts.

The following tests should be done:

BLOOD:	pH and gases
	Urea and electrolytes
	Glucose (laboratory and bedside strip test)
	Full blood count
	Blood spot acylcarnitines
	Blood culture
URINE	ketones

4. Management

Treatment is urgent. Do not delay. Unless you are very confident and certain, treat with intravenous fluids.

A. ENTERAL.

Enteral treatment should only be used occasionally and with caution.

The emergency regimen should be used. This may be given as regular drinks or through a naso-gastric tube but if the patient is at risk of vomiting or is nauseated fluid should be given either continuously or as small boluses more frequently.

Click here for information about the emergency regimen for a child with Glutaric Aciduria Type 1, including amino acid composition.

Electrolytes should be added to the drinks if vomiting and/or diarrhoea is a problem using standard rehydration mixtures following manufacturer's instructions, but substituting glucose polymer solution for water

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Amino acids: As soon as available, the lysine-free amino acid mixture should be added to the glucose polymer drinks and initially given at the rate of 1g/kg/d. If this is not tolerated, the quantity can be reduced to 0.5 g/kg/d but for as short a period as possible. Do not delay giving drinks if the amino acid mixture is not immediately available. There is now laboratory evidence that arginine alone may be effective but at present its use should be part of a research project.

Fever. It is important to control fever. Ibuprofen (5-10 mg/kg per dose, up to 3 doses daily) or paracetamol (used at standard doses of 15mg/kg, up to 4 doses daily) can be given, especially if body temperature rises above 38.5°C (101°F).

- Treat any infection

Medicines Carnitine should be given 200 mg/kg/24h in 4 divided doses.

B. INTRAVENOUS.

This route should be used in most circumstances.

- Give Glucose 200 mg/kg **at once** (2 ml/kg of 10% glucose or 1ml/kg of 20% glucose) over a few minutes.
- Give normal saline 10 ml/kg as a bolus immediately after the glucose unless the peripheral circulation is poor or the patient is frankly shocked, give 20 ml/kg normal saline instead of the 10 ml/kg.. Repeat the saline bolus if the poor circulation persists as for a shocked non-metabolic patient.
- Continue with glucose 10% at 5 ml/kg/h **ONLY until next solution is ready– do not leave on this high rate longer than necessary**. – see below
- Quickly calculate the deficit and maintenance and prepare the intravenous fluids
    - Deficit: estimate from clinical signs if no recent weight available
    - Maintenance: Formula for calculating daily maintenance fluid volume (BNF for children) 100ml/kg for 1st 10kg then 50 ml/kg for next 10kg then 20ml/kg thereafter, using calculated rehydrated weight. Deduct the fluid already given from the total for the first 24 hours.
    - Give 0.45% saline/10% glucose (for instructions to make this solution click here).

- Having calculated the deficit and the maintenance, administer the appropriate rate of 0.45% saline/10% glucose to correct the deficit within 24 hours
- Recheck the electrolytes every 24 hours if still on IV fluids.

Aminoacids: If at all possible give the lysine free aminoacid mixture orally or via naso-gastric tube, as drinks or as a continuous infusion. Initially it can be given at the rate of 1g/kg/d. If this is not tolerated, the quantity can be reduced to 0.5 g/kg/d but for as short a period as possible. Do not delay giving other treatment if the mixture is not immediately available.

Click here for information about the amino acid regimen for a child with Glutaric Aciduria Type 1 requiring intravenous fluids.

- Carnitine should be given intravenously - 200 mg/kg/24h given either as 4 divided doses or as a bolus of 100 mg/kg in 30 minutes followed by a slow intravenous infusion of 4 mg/kg/h.

- Potassium can be added, if appropriate, once urine flow is normal and the plasma potassium concentration is known.

- Arginine. There is now laboratory evidence that arginine may be effective in reducing neurological damage but at present its use should be part of a research project.

- Hyperglycaemia can be a problem. If the blood glucose exceeds the 8 mmol/l, start an insulin infusion using the local diabetic protocol rather than reducing the glucose intake. **Strict supervision is essential.**

Fever. It is important to control fever. Ibuprofen (5-10 mg/kg per dose, up to 3 doses daily) or paracetamol (used at standard doses of 15mg/kg, up to 4 doses daily) can be given, especially if body temperature rises above 38.5°C (101°F).

- Treat any infection

5. Progress:

Monitoring: Reassess after 4-6 hours or earlier if there is any deterioration or no improvement
Clinical assessment should include Glasgow coma score (for details click here) and blood pressure.
Blood tests: Blood pH and gases
Glucose (laboratory): high values can occur due to insulin resistance
Urea & electrolytes

For intravenous fluids after 24 hours please refer to the previous section.

6. Re-introduction of enteral feeds: As many more calories can be given enterally safely, feeds should be introduced as early as possible. It is usual to give soluble glucose polymer initially 10% and increase this both volume and concentration as tolerated. It is also customary to delay the introduction of any protein or aminoacids but this will only prolong the period of catabolism so early re-introduction is recommended. Aminoacids should be given and increased to 2g/kg/d. If necessary, consult your local dietitian for more details.

7. Going Home: Only allow the child home if you and the family are entirely happy and you have discussed the problems with the consultant on call. The family must have a clear management plan and be prepared to return if the child deteriorates.

For further information please refer to:
Saudubray J-M, van den Berghe G, Walter JH. (editors) Inborn Metabolic Diseases. Diagnosis and treatment. 5th Edition. Springer 2012

Kölker S *et al*. Diagnosis and management of glutaric aciduria type I – revised recommendations J Inherit Metab Dis (2011) 34:677–694

For further information you can refer to the guidelines in: METABNET - scroll down to the long and shortened versions.