BIMDG

British Inherited Metabolic Disease Group

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This protocol has 4 pages

DEFECTS OF KETONE METABOLISM- ACUTE DECOMPENSATION

(standard version)

(SCOT - succinyl CoA oxoacyl CoA transferase deficiency; 3-oxothiolase deficiency - also called β-ketothiolase deficiency, mitochondrial acetoacetyl-CoA thiolase or T2deficiency)

- **Please read carefully. Meticulous treatment is important as there is a high risk of serious complications.**

- **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

Ketone bodies are formed as part of the normal response to fasting. Two enzymes are necessary for their utilisation - Succinyl-CoA 3-oxoacid CoA transferase (SCOT) and 3- oxothiolase deficiency, often commonly called β-ketothiolase deficiency. Patients with these disorders are well most of the time without intervention. They can, however, develop severe ketoacidosis if fasted for a prolonged period or during minor illnesses (particularly if there is diarrhoea or vomiting). This complication can be prevented by maintaining a high carbohydrate intake, enterally or intravenously. If patients become severely acidotic, they will also require intravenous sodium bicarbonate, with frequent monitoring of blood gases and electrolytes.

The early signs of decompensation may be subtle but particularly look for tachypnoea. Always listen to parents carefully as they probably know much more than you do. As hypoglycaemia only occurs at a relatively late stage, intervention should take place whilst the blood glucose is normal.

2. Admission

Most patients who present to hospital will require admission as they are likely to have been having treatment already at 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 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.

⇨ If admitted to metabolic/general ward make a careful clinical assessment including blood pressure and a Glasgow coma score (for details click here) even if the patient does not appear encephalopathic. This helps other staff to recognise if the child deteriorates, particularly around the time of a change of shift.

The following tests should be done:	Blood	pH and gases
		Glucose (laboratory and bedside strip test)
		Urea & electrolytes
		Full blood count, Blood culture
		Ketones (if available)*
	Urine	ketones

* A bedside ketone meter may be used if a laboratory test is not readily available.

4. Management

Management decisions should be based primarily on the **clinical** status. The first decision about therapy is whether the child can be treated orally or will need intravenous therapy.

- Can the child tolerate oral fluids?

If the child is relatively well - may be treated orally but assess very carefully.
If the child is obviously unwell - must be treated with intravenous fluids

- **If there is any doubt at all, put up an intravenous line.**

- Treat any infection

A. ORAL.

If the child is relatively well, not vomiting and with no respiratory distress, oral feeds may be given. The emergency regimen should be used. This may be given as regular frequent drinks but if the patient is at risk of vomiting or is nauseated fluid should be given either continuously or as small boluses more frequently. For more information about the emergency oral management click here

Age (years)	Glucose polymer concentration (g/100ml)*	Total daily volume**
0-1	10	150-200 ml/kg
1-2	15	100 ml/kg
2-6	20	1200-1500 ml
6-10	20	1500-2000 ml
>10	25	2000 ml

* If necessary, seek help from your local dietitian. In an emergency a heaped 5 ml medicine spoon holds approximately 7g of glucose polymer.

**For each drink the volume will generally be this figure divided by 12 and given 2 hourly but if the patient is nauseated or refuses try frequent smaller drinks or a continuous naso-gastric infusion.

Electrolytes should be added to the drinks using standard rehydration mixtures following manufacturer's instructions but substituting glucose polymer solution for water

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B. INTRAVENOUS.

If the child is unwell

- 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.

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

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

- Sodium bicarbonate is not given routinely but it may be needed if the pH <7.1 or the base deficit is greater than 15 mmol/l or the pH is deteriorating rapidly.

Initially give a half correction [0.15 x weight x base deficit (mmol/l)] mmol sodium bicarbonate over at least 30 minutes. 1 ml of sodium bicarbonate 8.4% contains 1 mmol but this solution should be diluted *at least* 1ml to 5ml of 5% glucose. Then review and check U&E and pH & blood gases. The acidosis normally corrects quickly so that repeat doses of sodium bicarbonate are rarely needed. If further doses of sodium bicarbonate appear to be needed, discuss with the consultant. Before doing so ask why? Is there another explanation such as sepsis? If further doses are given, reduce sodium chloride intake in the other intravenous fluids.

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)
Urea & electrolytes,

⇨ If improving, continue and for intravenous fluids after 6 hours, please refer to the previous section.

⇨If deteriorating, seek specialist help without delay.

6. Re-introduction of oral feeds: Restart oral feeds as soon as possible; once the child is alert and has stopped vomiting. 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