British Inherited Metabolic Disease Group

Contact Details Name:
Hospital
Telephone:

This protocol has 4 pages

MAPLE SYRUP URINE DISEASE –ACUTE DECOMPENSATION

(MSUD, Maple syrup disease)

(standard version)

- **Please read carefully. Meticulous treatment is very important as there is a high risk of neurological complications including cerebral oedema.**

- **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

MSUD is disorder affecting the breakdown of branched chain amino acids (BCAA = Leucine, Isoleucine & Valine). In classical (severe) MSUD the only significant pathway for the removal of BCAA is via protein synthesis as there is very little renal excretion of the branched chain amminoacids. The encephalopathy is the result of accumulation of the BCAA (particularly leucine), which are toxic at high concentrations. There may be no hypoglycaemia, hyperammonaemia or acidosis. Plasma amino acids can seldom be measured urgently, so management has to be based on the clinical state.
Decompensation is often triggered by metabolic stress such as febrile illness, particularly gastro-enteritis or fasting but an obvious cause is not always apparent. The early signs of decompensation may be subtle, lethargy or ataxia. Vomiting is common and should always be taken seriously. However the signs may be difficult to assess such as irritability or just 'not right'. Always take illness seriously as there is a risk of death or permanent neurological damage. Listen to parents carefully as they probably know much more than you do.

Treatment aims to:
(a) Inhibit protein catabolism and promoting anabolism by providing high calorie intake combined with the child's usual MSUD amino acid formula.
(b) Lower BCAA levels by stopping or restricting 'natural protein' ('exchanges'). If this is insufficient, BCAA can be removed by haemodialysis
(c) Ensure a balance is maintained between leucine, isoleucine and valine during decompensation giving supplements of individual aminoacids.

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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. Consider early transfer to specialist metabolic unit for intensive management including haemodialysis/haemofiltration.

⇨ 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 is very important as the major complication of MSUD is cerebral oedema presenting with progressive encephalopathy. Should the child deteriorate, particularly around the time of a change of shifts.

The following tests should be done:

pH and blood gases
U & E
Full blood count
Aminoacids (quantitative) – *Ask the laboratory to measure these as soon as possible*
Blood culture
Urine ketones

4. Management

Immediate 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.

- Factors that will influence the decision include, how ill is the child and have they deteriorated suddenly in the past?
- 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

- **In MSUD enteral feeds should be used wherever possible to promote anabolism and protein synthesis. It is easier to give more energy as well as the aminoacid mixture. If the peripheral circulation is compromised give intravenous fluids, but it may still be possible to give the aminoacid mixture and some energy orally.**

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A. ORAL/ENTERAL.

If the child is not vomiting, enteral feeds should be tried first. This has the advantage that the MSUD aminoacid mixture can be given.

If the patient is vomiting, treat with intravenous fluids.

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.

Click here for detailed guidance on the emergency regimen for a child with maple syrup urine disease

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

The branch chain aminoacid free aminoacid mixture should be added starting with a low dose 0.5 g /kg/d. This should be increased as quickly possible to 2 g/kg/d.

Note: This refers to the quantity of pure aminoacids. To make the solutions either use accurate scales (check on the container for the % aminoacids in the preparation) or the manufacturer's scoops according to their instructions.

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.

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If possible, a concentrated amino acid preparation should still be run whilst the child is receiving intravenous fluids.

Click here for information about the enteral amino acid regimen for a child with maple syrup urine disease receiving intravenous fluids.

- 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.**

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

- Intra-lipid may be added 2g/kg/d (0.4ml/kg/hour of 20% solution).

- 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
Urea & electrolytes,
Aminoacids (quantitative)

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

If deteriorating (clinical state, fluid overload), seek specialist help. Haemofiltration (haemodialysis) may need to be considered urgently. Note peritoneal dialysis is less efficient. Exchange transfusion is dangerous and should not be used.

6. Re-introduction of enteral feeds: As many more calories can be given enterally safely enteral 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. The BCAA free aminoacid mixture should be given as tolerated and natural protein introduced adjusted according to the plasma BCAA concentrations. 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

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