BIMDG
British Inherited Metabolic Disease Group

MANAGEMENT OF NEWBORN BABIES WITH A FAMILY HISTORY OF A FATTY ACID OXIDATION DISORDER (EVEN IF ONLY SUSPECTED)

- **Please read these guidelines carefully to avoid death and major complications**

Background
It is essential to have a careful plan for the management of babies who are at risk of having fatty acid oxidation disorder (FAOD). These include:

- Trifunctional protein deficiency
- Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency
- Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency
- Carnitine palmitoyl transferase (CPT) I deficiency
- Carnitine palmitoyl transferase (CPT) II deficiency
- Carnitine acylcarnitine translocase (CACT) deficiency
- Multiple acyl-CoA dehydrogenase (MAD) deficiency (also called glutaric aciduria type II).

NOTE: It can be difficult to diagnose individual disorders clinically. Do not guess! Discuss with a specialist.

These guidelines **do not apply** to patients with:

- Severe multiple acyl CoA dehydrogenase deficiency with multiple congenital malformations as the disorder is lethal.
- Carnitine transporter deficiency (also called primary systemic carnitine deficiency) is treated with carnitine supplements & the measures outlined below are not usually needed.
- Medium Chain acyl CoA dehydrogenase (MCAD) deficiency: a separate, simpler sheet of guidelines is available (click here)

Patients with fatty acid oxidation disorders can present with:

a) encephalopathy (drowsiness, seizures etc) with hypoglycaemia, brought on by infections, fasting or vomiting.
b) sudden death, probably due to cardiac arrhythmias
c) cardiomyopathy (not MCADD)
d) muscle weakness or rhabdomyolysis (particularly in patients with milder defects).
e) acute fatty liver of pregnancy (AFLP) or HELLP syndrome *in the mother* (most commonly LCHAD & trifunctional protein deficiencies but now known to be associated with almost all FAOD).

Treatment usually involves a low-fat diet, frequent feeding and, providing ample glucose during acute illness, either orally or intravenously. Medium chain triglycerides (MCT) are beneficial in LCHAD & VLCAD deficiencies but are strictly contraindicated in MCAD and severe forms of MAD deficiency.

Problems are common in the newborn period and appropriate management at this time is essential. Obviously, it is helpful to establish promptly whether the baby is affected since, if they are not, it allows everyone to relax.

General Guidelines

1. The management should be discussed with the specialist metabolic team in advance. Topics should include the feeding plan and the quickest reliable way to establish whether the baby is affected. Urine organic acids cannot and must not be relied on. For most patients this will be blood spot acylcarnitine analysis by tandem mass spectrometry. There are few data to indicate how soon after birth acylcarnitines can be relied on to show abnormalities and we know that special feeds can reduce the diagnostic changes. Thus, we recommend sending blood spots/plasma at birth and regularly thereafter. However cord blood samples are not recommended because of the possibility of maternal contamination. In some patients with partial deficiencies or in those in whom the diagnosis is unknown (but strongly suspected), it may only be possible to exclude the diagnosis by measurement of fatty acid oxidation flux in fibroblasts or a diagnostic fast. In these patients it will be necessary to assume they are affected until the results of the tests are known.

2. At a suitable time in advance discuss mother's preference for feeding, breast or bottle as this will affect management (see below).

3. When the mother is admitted in labour (or, failing this, when the baby is born) inform the responsible consultant / specialist.

4. If there has been Acute Fatty Liver of Pregnancy (AFLP) or HELLP syndrome, presume the baby is affected & admit to the neonatal unit for observation. Also admit babies if the affected sibling presented within the first 2 months. Otherwise, the baby may go to the post-natal ward but should still be observed very closely.

5. The recommended feed depends on the precise defect and may need to be altered for individual patients. Breast feeding presents a problem in two ways. Firstly it contains long chain fat that is contra-indicated in some disorders of long chain fatty acid oxidation. Secondly the milk may not come in for several days so that the child may, in effect, be fasted and become symptomatic. Those that die in the neonatal period as a result of one of these disorders do so usually on day 2 or 3 and are almost always breast fed.

Breast feeding is contra-indicated in Trifunctional protein, LCHAD, CACT & Infantile Onset VLCAD/CPTII deficiencies as well as some patients with infantile onset MADD. Long chain fat should be restricted. If the mother wants to breast feed, give appropriate bottle feeds (see below) until it is known whether the baby is affected and encourage the mother to express in the meantime.

Breast feeding may be permitted in some patients with CPT I and late-onset VLCAD, MAD or CPT II deficiencies**.** Allow the mother to suckle and then offer an appropriate bottle after each feed (see below) until the diagnosis is known.

Note: Monitoring blood glucose concentrations is **not** a reliable method of predicting potential problems.

Bottle feeding

a) Trifunctional protein, LCHAD, CACT & Infantile Onset VLCAD/CPTII deficiencies
Long chain fat should be restricted. Feed the baby with an infant formula in which most long-chain fat is replaced by MCT (such as Monogen® or Lipistart®)

b) Infantile Onset MADD
Give the new baby a very low fat modular feed (usually a high energy infant formula + glucose polymer to 10% CHO but without MCT). If the index case presented *after the first 2 months*, it is probably safe to give the new baby standard infant formula or expressed breast milk for a short period of time (e.g. overnight and possibly until the diagnostic test is available) – discuss with the specialist.

c) CPT I and Late-onset VLCAD, MAD or CPT II deficiencies
The baby can be given normal infant formula or breast fed with top-ups. A few CPT I deficient patients develop marked hepatomegaly or hyperlipidaemia or renal tubular acidosis, in which case an MCT-based feed (such as Monogen® or Lipistart®) may help.

d) Diagnosis unknown. If the diagnosis is unknown, treat as in (a) above.

Management

6. **Ensure the baby maintains a good milk intake.** Feed the baby every **TWO** hours & give top-ups by naso-gastric tube if good volumes are not taken. Target volumes of feed should be:

80ml/kg/day on Day 1
120ml/kg/day on Day 2
150ml/kg/day on Day 3 and onwards

Note: Monitoring blood glucose concentrations is **not** a reliable method of predicting potential problems.

7. If the baby seems lethargic, floppy, drowsy or unwell in any way or vomits, transfer to the neonatal unit urgently and start an IV infusion of 10% dextrose at 100 ml/kg/day. Monitor blood glucose but treatment should be based on the clinical state (since hypoglycaemia *only occurs at a late stage*).If the intravenous infusion needs to continue and there is no oral intake the volume should be increased to 150ml/kg/d over 3 days.

8. Arrange echocardiography if possible (but a normal result does not exclude the diagnosis). If a previous sibling died suddenly at 2-3 days of age, consider cardiac monitoring for the first 4 days or until normal feeds are established and the baby is gaining weight. Always ensure a good energy intake.

Investigations

9. Take 4 blood spots on a Guthrie card, and ideally a plasma sample, shortly after birth and then at 12 hrs of age. Send to the relevant metabolic laboratory for acylcarnitine analysis (after discussion with the biochemist to get a rapid and early answer). Repeat the specimens at 24 - 36 hrs of age & subsequently according to specialist advice. Also send urine for organic acid analysis at approximately 24 hours of age & subsequently if advised by a specialist. If the molecular diagnosis is known in the Index case, an early sample for DNA extraction is advised.

Note: If metabolites are being used to make the diagnosis, the treatment proposed may mask the biochemical changes of disease. Careful follow-up is essential and DNA-based testing may be required if there is doubt.

10. If in doubt at all, discuss with specialist

Date last reviewed February 2020