National Patient Safety Agency

RAPID RESPONSE REPORT NPSA/2011/RRR002

Keeping newborn babies with a family history of MCADD safe in the first hours and days of life

October 2011

Supporting information

NHS Evidence
accredited provider
NHS Evidence - provided by NICE
www.evidence.nhs.uk

Contents

1. Background 3

2. National standards and best practice 4

3. Review of evidence of harm 5

4. Advice from clinical staff 6

5. Other Resources 7

6. Cost implications 7

7. Acknowledgements 7

Appendix: Summary of rationale for recommended actions and suggested evidence for compliance 8

References 9

1. Background

Medium chain acyl-CoA dehydrogenase deficiency (MCADD) is a rare inherited disorder where the body cannot metabolise fat properly. Individuals with undiagnosed MCADD commonly present with an episode of encephalopathy (drowsiness, seizures etc) usually accompanied by hypoglycaemia, that can result in coma or sudden death.[i] Fortunately, such catastrophes can be prevented by simple treatment (primarily a regular intake of glucose during illnesses), allowing affected individuals to live a normal healthy life.

Since February 2009, all babies born in England, Scotland and Northern Ireland are offered screening for MCADD.* This is done on blood spots as one of the battery of new born screening tests. Blood spots are collected at 5-8 days of age and abnormal metabolites can be detected in patients with MCADD. The diagnosis is confirmed by mutation analysis and / or urine organic acid analysis. Simple dietary management can then prevent adverse outcomes.

Newborns with MCADD are especially vulnerable to sudden death in the first few days of life, as a regular feeding pattern may not have been established and the breast milk supply may be limited. Therefore babies born to families with a history of the disease need a special feeding regimen and observation from the moment of birth, rather than waiting until they have a positive test result.

The disease affects about one in 10,000 babies born in the UK.[ii] Newborn screening throughout England identifies around 60 cases each year. Around one in 80 healthy people is a carrier of MCADD, but will not have any symptoms. However, if both parents are MCADD carriers, there is a one-in-four chance of their child being born with MCADD.[iii]

Because the national screening programme is detecting cases of MCADD that were previously missed, there will be more families who are aware they could be carriers of MCADD.

A recent publication[iv] reported 5 cases of newborn babies who died from MCADD between 2-4 days of life within an 11 year period and highlighted the risks for babies with MCADD in the first 3 days of life especially if breast fed. The diagnoses were made after death in all cases by acyl-carnitine analysis. In one baby the cause of death had been erroneously attributed to an overwhelming infection. The clinical pictures prior to death showed minimal prodromal signs and the infants generally succumbed rapidly and without warning. During the study period, the Yorkshire region had prevalence for early MCADD death of 1:100,000. This estimate highlights that these deaths are exceptional and underscore the importance of vigilance in babies with a family history in whom such deaths can almost always be avoided.

---

* *In Wales, routine newborn screening for MCADD does not currently take place, although diagnostic testing is carried out where clinically indicated, including babies born to families with a history of MCADD. Preparations are underway for routine screening to be introduced during 2012.*

2. National standards and best practice

Key reference documents for standards of care for newborns with a family history of MCADD are provided by

1. **The British Inherited Metabolic Diseases Group (BIMDG).** This guidance can be accessed via http://www.bimdg.org.uk/guidelines.asp (select emergency protocols, then children). Key components of their guidance *MCAD deficiency: management of newborn babies with a family history*[v] include:

   a. **Diagnosis -** Consultant paediatrician responsible for metabolic diseases should be informed antenatally, urgent testing for MCADD should be discussed, and a clear plan of care for after delivery established.

   b. **Management –** do not wait for test results but ensure baby has a good milk intake, with term baby fed every 4 hours and preterm baby every 3 hours. Particular risks have been reported in breast-fed babies in the first 72 hours due to the quantity and composition of milk from the mother during this period. It is therefore recommended that these babies receive top-ups of formula milk until good milk supply from the mother is established.

   c. **Treatment –** babies not taking adequate volumes orally may be transferred to neonatal units and fed by nasogastric tube. If enteral feed is not tolerated, intravenous infusion is recommended.

   d. **Testing –** Hypoglycaemia only occurs at a relatively late stage so it is not safe to base the management on monitoring of blood glucose.

2. **The UK Newborn Screening Programme Centre (UKNSPC)** has responsibility for developing, implementing and maintaining a high quality, uniform screening programme for all newborn babies and their parents. Their guidance and information on MCADD for health professionals and families can be accessed via http://newbornbloodspot.screening.nhs.uk/mcadd.

   Key components of this guidance include:

   a. Documents to support the MCADD screening programme

   b. MCADD information sheets for parents/carers

The UKNSPC guidance emphasises the importance of taking a family history and recommends that:

"*If a mother or her partner has a family history of MCADD you should make a referral to a paediatrician or genetic counsellor for advice. This advice should form the basis of a birth plan (making sure the birth plan is written in the mother's notes). Depending on the risk of the baby having MCADD, the parents may be advised that their baby needs early screening for MCADD. A sample of blood should be collected 24-48 hours after birth on a blood spot card marked 'Family history of MCADD'. The parents will also be given information about any special treatment required after the birth of their baby.*"[vi]

3. Review of evidence of harm

Search strategy

The National Reporting and Learning System was reviewed for reports of incidents occurring between 1st January 2006 and 30th June 2011 using the keywords MCADD, MCAD or dehydrogenase.

Key findings

This search identified two reports of deaths of newborn babies from MCADD who were born to families with a history of the disease. It appeared that although the mothers had mentioned the family history to healthcare staff when they were pregnant, the staff were not aware of the significance of MCADD, and therefore did not arrange any specialist referrals, special feeding regimen or early access to testing.

a. *Baby admitted [from secondary to tertiary care having] collapsed ... died after three hours due to MCADD (metabolic disorder). Two siblings had died of disease too. More awareness of MCADD needed.....*

b. *Family history on both sides of the family of MCADD not noted on antenatal notes, paediatrics not informed. Baby discharged and died day 2.....*

Additional 'no harm' incidents indicated similar omissions, fortunately without any apparent adverse effects. These included three incidents where either there was no plan of care, or the plan of care was unavailable at the time of delivery. One incident related to a lack of communication about family history during pregnancy, which delayed the results of the screening test. One incident was as a result of a plan of care not being carried out. One result was reported incorrectly, although it did not result in any harm. One baby with suspected MCADD was discharged inappropriately.

Some of these incidents suggested that healthcare staff were more focused on early testing for MCADD and testing blood glucose than on the need for a special feeding regimen prior to diagnosis being confirmed or excluded.

Examples of incidents reported to the NRLS

a. *There was some risk for the baby of MCADD deficiency (Metabolic Condition). So clear plan was made by doctor for the baby to have her blood sugars checked in the first 48 hrs* [note this is unlikely to have been an appropriate plan of care: see guidance section above]. *However, it was missed because the plan was not in the right place. The only copy I have seen at 36 hours after birth was in the mother held notes but none in the main maternal or baby notice and there was no sticker in the main maternal notice to indicate paediatric alert.*

b. *Baby delivered [date, time]. Parents concerned that baby must be seen immediately as family history of MCADD. Baby 1st cousin aged 1 year diagnosed at Great Ormond Street and all family newborns to be tested. No paediatric alert and no information from maternal notes.*

c. *At around [time] I was informed by a midwife about the baby condition. Baby was born at around [90 minutes earlier]. Baby was at risk of MCADD, as parents are cousins and they are heterozygous carriers. I looked at the alert folder, reviewed the baby, spoken to parents and plan was made to feed regularly 3 to 4 hourly and pre-feed BM.*

d. *Both parents carriers for MCADD. Last BM was done on baby at 1800 hrs [date]. No BMs done overnight until ward round at 0930 hrs. Repeat BM done before next feed at 1000 hrs [next day] 2.9.* [note reliance on bedside blood glucose testing is unlikely to have been an appropriate plan of care: see guidance section above]. *Baby admitted to SCBU [date time] for low blood sugars. Baby was started on IV fluids.*

e. *Child's older brother has MCADD. [Specialist service treating brother for MCADD] were unaware his mother was pregnant (they need to be informed of all siblings expected antenatally to discuss at their monthly meetings and highlight the need for urgent sample testing). Parents are asked to inform them [but] this doesn't appear to have occurred in this case. Although screening of baby was done at [hospital of birth] on the day of birth this was not sent urgently and although clearly marked the samples were not processed as a sample of a sibling of a child with MCADD. So the parents then had to wait 14 days for the results and actually got them quicker from the Neonatal screening test taken by the midwives on day 6 than from samples taken on the day of birth.*

Coroners' cases

A coroner's inquest was held into the death of a newborn baby with a family history of MCADD. The baby was discharged home to await routine newborn screening testing without any special feeding regimen and died at home when two days old, and the coroner returned a verdict of natural causes to which neglect by the hospital where the baby was delivered contributed. The coroner subsequently addressed a Rule 43 letter to the NPSA and the Department of Health asking for learning from this avoidable death to be shared as widely as possible.

4. Advice from clinical staff

Informal discussions with frontline midwives and doctors suggested many were unaware of the significance of a family history of MCADD and assumed that no action would be required prior to a confirmed diagnosis.

Specialist services for metabolic disorders suggested that they relied on routine outpatient appointments for children with MCADD to alert parents to ask about special testing and feeding regimens in any subsequent pregnancy. However, as many children were on annual review there was no guarantee that a mother's pregnancy would be noticed by the staff. Normal practice where a sibling to a child with MCADD was expected, or where there was a family history in both parents, was to deliver the special feeding regimen, observation and early testing outlined above in BIMDG [v] and UKNSPC guidance [vi] through an approximately three-day post-natal stay in hospital. Families whose babies were diagnosed only at post-mortem may have had no contact with a specialist service.

The Royal College of Psychiatrists commented that awareness also needed to be raised amongst perinatal psychiatrists, and plan to do this via their networks.

5. Other Resources

A clinical briefing sheet that can be locally circulated to increase awareness of the needs of newborns with a family history of MCADD is supplied with this Rapid Response Report at www.nrls.npsa.nhs.uk/alerts.

Patient/parent information can be found at http://newbornbloodspot.screening.nhs.uk/mcadd and on the 'Contact a Family' website http://www.cafamily.org.uk/medicalinformation/conditions/azlistings/m19.html

6. Cost implications

The direct costs of implementing this RRR would be expected to be minor (e.g. revising local guidance). Where providers of obstetric or midwifery care were not previously compliant with BIMDG guidance on *The management of newborn babies with a family history*,[v] complying with the guidance may result in increased duration of stay in hospital for mothers of babies at risk of MCADD, as would any extension of extra precautions beyond newborn siblings of patients with MCADD and cases where both parents have a family history of MCADD to cases where the family history is less strong.

Safer care for newborns with a history of MCADD would be expected to have cost benefits as well as saving lives, since legal and healthcare costs associated with potentially preventable death and disability could be substantial.

7. Acknowledgements

The NPSA is grateful for the comments, advice and support of:

- Dr. Anupam Chakrapani, Consultant in Inherited Metabolic Disorders, Birmingham Children's Hospital
- Rachel Gould Lead Nurse/Lead Newborn Screening Nurse, Inherited Metabolic Disorders Department
- Dr Andrew Morris, Consultant in Paediatric Metabolic Medicine at Central Manchester University Hospitals NHS Foundation Trust
- Dr Graham Shortland, Consultant Paediatrician with a special interest in metabolic disease, University Hospital of Wales and Chair of the MCADD/PKU Screening Advisory Board
- The UK Newborn Screening Programme Centre, especially the members of the MCADD/PKU Screening Advisory Board
- The Royal College of Paediatrics and Child Health
- The Royal College of Midwives.

Appendix: Summary of rationale for recommended actions and suggested evidence for compliance

This table provides a summary of how the incident reports, local policy review, and literature explored above informed our recommended actions, and gives suggested evidence that organisations may wish to use locally as assurance of compliance with this Rapid Response Report.

	Action	Summary of rationale	Suggested evidence of compliance
1	Local organisations should ensure that midwives, general practitioners, and medical staff working with pregnant women are reminded of the importance of taking an accurate family history at booking and acting on any mention of a family history of MCADD by a pregnant woman (in line with UKNSCP and BIMDG guidance). A clinical briefing sheet is supplied to help inform these staff.	The cases reported to the NRLS together with discussions with frontline staff indicated there was not widespread awareness of the significance of a family history of MCADD, so that even if the pregnant women mentioned it to staff, the appropriate actions may not have been followed.	Electronic or paper record of onwards distribution of the RRR and/or clinical briefing sheet or local alternatives to any staff groups likely to provide healthcare to pregnant women.
2	Obstetric and midwife-led services should review their patient documentation to ensure there are appropriate triggers for asking new patients about family history of inherited diseases.	Revising documentation is a more effective method than simply reminding staff to ask about family history. Whilst the focus of this RRR is MCADD, many other inherited conditions may require pre-birth planning.	Copy of the relevant documentation with a trigger question related to inherited diseases highlighted.
3	Obstetric, midwife-led, neonatal and paediatric services should ensure all relevant local and/or national guidance on MCADD is available to their staff.	National guidance often needs to be made locally applicable with specific content about how to make further referrals or access specialist advice.	Electronic or paper record of national guidance and local protocols (if any) and how they have been made available to relevant staff (e.g. web-based policy collections, hard copy protocol folders).
4	Specialist services for inherited metabolic disorders (adult or paediatric) should ensure that when a baby, child, or adult is diagnosed with MCADD they have reliable systems for routinely informing the family that any future babies will need a special feeding regimen and observation in the first hours and days of life, so that family members are equipped to self-advocate. If informed about any at risk pregnancies, a notification must be sent to the relevant obstetric and neonatal units so that the appropriate guidance is followed after delivery.	Whilst all specialist centres aimed to do this, those consulted during developmental of the RRR indicated there are potential gaps where pregnancies occurred between sibling's visits to the specialist centre or where infants or children had died or been lost to follow-up, and therefore their families had not been in contact with the specialist centre. This action is intended to prompt reflection on whether there are any further ways to strengthen the reliability of their systems. We acknowledge that beyond siblings there may not be consensus on what constitutes a significant family history, and that judgement remains an individual decision within specialist services for inherited metabolic disorders.	Notes of a meeting where any potential strengthening of systems for routinely informing families has been discussed, including an action plan for implementing any agreed changes in practice. Note the role of the family in understanding what should happen in any future pregnancy is intended as a safety net, not as a substitute for efficient systems of communication between healthcare staff.

References

[i] Leonard,J.V.; Dezateux C. Newborn screening for medium chain acyl CoA dehydrogenase deficiency. *Archives of Disease in Childhood* 2009; 94:235-238

[ii] Blakemore AIF; Singleton H; Pollitt RG; Engel PC; Kolvraa S; Gregersen N; et al. Frequency of the G985 MCAD mutation in the general population. *Lancet* 1991; 337:298-299

[iii] NHS Choices. *Medium chain acyl dehydrogenase deficiency (MCADD).* Available online at http://www.nhs.uk/conditions/MCADD/Pages/Introduction.aspx

[iv] Patterson AL; Henderson MJ. Early MCADD death: 5 deaths. *Journal of Inherited Metabolic Disease* 2010; 33:S59

[v] The British Inherited Metabolic Diseases Group. *MCAD Deficiency: the management of newborn babies with a family history* 2008. Available on line at http://www.bimdg.org.uk/guidelines.asp

[vi] UK Newborn Screening Programme Centre (UKNSPC) *The importance of taking a family history* 2010. www.newbornbloodspot.screening.nhs.uk/getdata.php?id=11485