NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Neonatal jaundice: recognition and treatment of neonatal jaundice

1.1 Short title

Neonatal jaundice

2 Background

a) The National Institute for Health and Clinical Excellence ('NICE' or 'the Institute') has commissioned the National Collaborating Centre for Women's and Children's Health to develop a clinical guideline on the recognition and treatment of newborns with jaundice for use in the NHS in England and Wales. This follows referral of the topic by the Department of Health (see appendix). The guideline will provide recommendations for good practice that are based on the best available evidence of clinical and cost effectiveness.

b) The Institute's clinical guidelines support the implementation of National Service Frameworks (NSFs) in aspects of care for which a Framework has been published. The statements in each NSF reflect the evidence that was used at the time the Framework was prepared. The clinical guidelines and technology appraisals published by the Institute after an NSF has been issued will have the effect of updating the Framework.

c) NICE clinical guidelines support the role of healthcare professionals in providing care in partnership with patients, taking account of their individual needs and preferences, and ensuring that patients (and their carers and families, where appropriate) can make informed decisions about their care and treatment.

3 Clinical need for the guideline

a) Jaundice is one of the most common conditions requiring medical attention in newborn babies. Approximately 60% of term and 80% of preterm babies develop jaundice in the 1st week of life. In most infants with jaundice there is no underlying disease, and the jaundice is termed ‘physiological’.

b) Neonatal jaundice refers to the yellow colouration of the skin and the sclera of newborn babies that results from accumulation of bilirubin in the skin and mucous membranes. This is associated with a raised level of bilirubin in the body, a condition known as hyperbilirubinaemia.

c) Bilirubin is a breakdown product of the red cells in the blood. Red cell breakdown produces unconjugated (or ‘indirect’) bilirubin, which is partly bound to albumin. Normally this is metabolised in the liver to produce conjugated (or ‘direct’) bilirubin, which then circulates through the gut and is excreted in the urine and the stool.

d) Newborn babies have more circulating red cells and a shortened red cell lifespan, so the bilirubin levels are higher than they are later in life. The breakdown and excretion of bilirubin is also slower Thus, a degree of neonatal jaundice is common and is usually benign (harmless).

e) Breast-fed infants are more likely to develop jaundice within the 1st week of life; this is thought to be caused by a lower intake of breast milk and increased circulation of bilirubin between the liver and the bowels (enterohepatic circulation). Prolonged jaundice, persisting beyond the 2nd week, is also seen in breast-fed infants. The mechanism for this later ‘breast milk jaundice syndrome’ is still not completely understood. The condition appears to be generally harmless.

f) Jaundice may also have other, non-physiological, causes, including blood group incompatibility (Rhesus or ABO problems), other causes of haemolysis, sepsis, bruising and metabolic disorders. Gilbert's and Crigler–Najjar syndromes are rare causes of neonatal jaundice. Deficiency of a particular enzyme, glucose-6-phosphate-dehydrogenase, can cause severe neonatal jaundice. G-6-PD deficiency is more common in certain ethnic groups and runs in families. Congenital obstruction and deformities affecting the biliary system, such as in the condition known as biliary atresia, cause an obstructive jaundice associated with conjugated hyperbilirubinaemia. These conditions need surgical treatment.

g) In young babies, unconjugated bilirubin can penetrate across the membrane that lies between the brain and the blood (the blood-brain barrier). Unconjugated bilirubin is potentially toxic to neural tissue (brain and spinal cord) because it acts as a ‘cell poison’ slowing essential processes. Entry of unconjugated bilirubin into the brain can cause both short-term and long-term neurological dysfunction. The acute problems include lethargy, abnormal muscle tone, irritability, temporary cessation of breathing (apnoea) and convulsions. This presentation is known as acute bilirubin encephalopathy. This deposition of bilirubin causes a yellow staining of the deeper neural tissue within the brain; this staining is referred to as ‘kernicterus’. The term kernicterus is also used to denote a group of symptoms typical of chronic bilirubin encephalopathy. These symptoms include athetoid cerebral palsy, hearing loss, visual and dental problems. The exact level of bilirubin that will cause neurotoxicity in any individual baby cannot be predicted.

h) Although neonatal jaundice is very common, kernicterus is very rare. There is a poor correlation between levels of bilirubin in the body and the clinical features of bilirubin encephalopathy. There seems to be tremendous variability in susceptibility towards

bilirubin encephalopathy among newborns for a variety of unexplained reasons. However, there are certain factors that probably influence the passage of bilirubin into the brain and hence increase the risk of acute bilirubin encephalopathy. These include dehydration, prematurity, respiratory distress, sepsis, hypoxia, seizures and hypoalbuminaemia. The rate of rise of the level of bilirubin is probably important, hence the increased risk of kernicterus in babies with haemolytic disease such as G-6-PD deficiency or Rhesus haemolytic disease.

i) The correlation between actual bilirubin levels and encephalopathy is variable and probably depends on the weight, maturity and state of health of an individual baby as well as the rate of bilirubin rise. The incidence of kernicterus in healthy term babies probably increases once a threshold of 425 micromoles of bilirubin per litre of serum is crossed, and the number of cases of kernicterus rises in fullterm newborns who have levels above 515 micromol/litre in their serum.

j) Levels of bilirubin can be controlled by placing the baby under a lamp emitting light in the blue spectrum. This converts the bilirubin in the skin to a harmless form that can be excreted in the urine. Phototherapy has proved a very efficient safe and effective treatment for jaundice in the newborn, reducing the need to perform an exchange transfusion (the only other means of removing bilirubin from the body).

k) There is uncertainty about when to treat raised bilirubin levels and there are variations in the use of phototherapy, exchange transfusion and other treatments. There is a need for more uniform, evidence-based practice, and for more widespread consensus-based practice in areas lacking evidence.

4 The guideline

a) The guideline development process is described in detail in two publications that are available from the NICE website (see 'Further information'). 'The guideline development process: an overview for stakeholders, the public and the NHS' describes how organisations can become involved in the development of a guideline. 'The guidelines manual' provides advice on the technical aspects of guideline development.

b) This document is the scope. It defines exactly what this guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health (see appendix).

c) The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

a) Newborn infants from birth to 10 days old.

4.1.2 Groups that will not be covered

a) Newborns with conjugated hyperbilirubinaemia.

b) Babies with jaundice that requires surgical treatment to correct the underlying cause.

c) Babies with jaundice that lasts longer than 10 days.

4.2 Healthcare setting

a) The guideline will cover management in primary and secondary care.

4.3 Clinical management

a) Risk factors behind the development of jaundice:

- maternal factors, including age, race, sex and diabetes
- gestational age and prematurity
- family history
- feeding – breast-feeding and role of fluid supplementation
- blood group incompatibility
- cephalohaematoma and bruising
- sepsis, temperature instability, infections
- acidosis, dehydration
- serum albumin
- vitamin K1.

b) Management in primary care:

- role and timing of clinical assessment
- estimating the extent of hyperbilirubinaemia
- referral to secondary care
- home care and advice to parents
- management after discharge.

c) Management in secondary care:

- assessment
- need for sepsis screening
- investigations including:
  - total serum bilirubin and conjugated bilirubin
  - transcutaneous bilirubin
  - glucose-6-phosphate dehydrogenase deficiency
  - Coombs' test and reticulocyte count
  - urine tests
  - albumin, bilirubin-albumin ratio
  - screening for thyroid disorders and galactosaemia

  - end tidal carbon monoxide concentration and comparison with Coombs.
- Timing of lab investigations.

d) Treatment of hyperbilirubinaemia:

- interpretation of bilirubin levels and use of nomograms
- phototherapy
- exchange therapy
- intravenous gammaglobulin
- tin-mesoporphyrin in treatment
- breast feeding during treatment.

e) Hospital management:

- length of stay
- failure of treatment
- nosocomial infections
- effect on family bonding.

f) Major outcomes that need to be considered:

- mortality.
- seizures
- neurological complications – immediate, short-term and long-term, including effects on future performance and IQ
- complications as a result of management.

g) Information that should be given to parents and carers:

- at the time of initial presentation
- after diagnosis
- about long-term effects, including significant morbidities and functional outcome.

h) Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by

evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use the summary of product characteristics to inform their decisions for individual patients.

i) The guideline development group will consider making recommendations on the principal complementary and alternative interventions or approaches to care relevant to neonatal jaundice.

j) The guideline development group will take reasonable steps to identify ineffective interventions and approaches to care. If robust and credible recommendations for re-positioning the intervention for optimal use, or changing the approach to care to make more efficient use of resources, can be made, they will be clearly stated. If the resources released are substantial, consideration will be given to listing such recommendations in the 'Key priorities for implementation' section of the guideline.

4.4 Status

4.4.1 Scope

This is the consultation draft of the scope. The consultation period is 19 December 2007 to 30 January 2008.

Related NICE guidance

- Intrapartum care: care of healthy women and their babies during childbirth. NICE clinical guideline 55. Available from www.nice.org.uk/CG055
- Routine postnatal care of women and their babies. NICE clinical guideline 37. Available from www.nice.org.uk/CG037
- Antenatal care: routine care for the healthy pregnant woman. NICE clinical guideline 6. Available from www.nice.org.uk/CG006

4.4.2 Guideline

The development of the guideline recommendations will begin in April 2008.

5 Further information

Information on the guideline development process is provided in:

- 'The guideline development process: an overview for stakeholders, the public and the NHS'
- 'The guidelines manual'.

These booklets are available as PDF files from the NICE website (www.nice.org.uk/guidelinesmanual). Information on the progress of the guideline will also be available from the website.

Appendix: Referral from the Department of Health

The Department of Health asked the Institute:

‘To prepare a clinical guideline on the recognition and treatment decisions of babies who are jaundiced.’