NEONATAL JAUNDICE – UNCONJUGATED HYPERBILIRUBINEMIA MANAGEMENT

1. BACKGROUND
   • 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 first week of life, and about 10% of breastfed babies are still jaundiced at 1 month of age.
   • While the cause of jaundice in most cases is physiological, co-existing pathological causes need to be identified because they often have serious consequences if left untreated.
   • The following are guidelines adopted from the recently published UK NICE (National Institute for Health & Clinical Excellence) Guidelines (May 2010) and American Academy of Pediatrics guidelines (2004).
   • Bilirubin encephalopathy is an uncommon but serious problem and can occur at different levels in different infants. For example, preterm and sick infants are more vulnerable to brain toxicity from high levels of bilirubin.

2. THE SCOPE
   These guidelines cover the management of unconjugated hyperbilirubinaemia and do not address:
   o Jaundice that requires surgical treatment to correct the underlying cause (e.g. biliary atresia etc)
   o Conjugated hyperbilirubinaemia (I.e. conjugated fraction greater than 25 micromol/litre)

3. CLINICAL PRACTICE

Screening for jaundice

In all babies
   • Medical or nursing staff should examine the baby for jaundice at every opportunity especially in the first 72 hours.
   • Check whether there are factors associated with an increased likelihood of developing significant jaundice soon after birth. These include:
     1. Gestational age less than 38 weeks
     2. Previous sibling with neonatal jaundice requiring phototherapy
     3. Visible Jaundice within the first 24 hours of life.
     4. Rhesus negative babies (Setting for Rhesus isoimmunisation)
     5. O blood group mothers (setting for ABO incompatibility)
   • When looking for jaundice (visual inspection):
     1. Check the naked baby in bright and preferably natural light
     2. Use TcB if any concern/doubt

Urgent additional care for babies with visible jaundice in the first 24 hours
   • Measure and record serum bilirubin level urgently (within 2 hours).
   • Urgent medical review and investigations to exclude pathological cause of jaundice. These must include review of mother’s blood group and Rhesus status and infant’s blood group and typing and direct antiglobulin test (DAT or coombs’ test), G6PD and ?FBC to rule out Blood group incompatibility and haemoglobinopathies.
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- Interpret bilirubin levels according to the baby’s postnatal age in hours and manage hyperbilirubinemia according to threshold table and treatment threshold graphs below.
- Continue to measure the serum bilirubin level every 6-12 hours (depending on the rate of rise of bilirubin) until the level is both:
  1. Below the treatment threshold
  2. Stable and/or falling

How to measure the bilirubin level

- Transcutaneous bilirubinometer (TcB) – for babies with a gestational age ≥35 weeks and more than 24 hours old.

- Serum bilirubin – (1) babies less than 24 hours old, (2) baby is 24-48 hours old and TcB>250 μmol/babies, (3) baby is >48 hrs old and TcB > 280μmol/L, (4) babies less than 35 weeks gestation at testing, and (5) babies under phototherapy

Use of Transcutaneous Bilirubinometer (TcB)

- Calibrate the device daily and sign in the TcB Book. Both the values for the long and short optical paths should read within ± 1.0 of the reference value in TcB manual.
- Clean the tip of the TcB with an alcohol wipe.
- Place the tip of the TcB on the neonatal forehead flush with the baby’s skin below the hairline.
- Avoid any bruised or discoloured areas of skin.
- Take three single TcB readings, removing the device from forehead in between each reading and awaiting for green light to appear before reapplying. The TcB will then display a result.
- Take three single TcB readings, the TcB will then display a result.

How to manage hyperbilirubinemia

- Use the bilirubin level to determine the management of hyperbilirubinemia in all babies. See the following treatment threshold graphs.
- Do not subtract conjugated bilirubin from total serum bilirubin when making decisions about the management of hyperbilirubinemia.

Phototherapy Management

Starting Phototherapy

- Use the following phototherapy threshold graphs to decide on phototherapy.

- In babies with gestational age of 35 weeks or more:
  1. Look for any risk factors such as isoimmune haemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis or albumin <3.0g/dl.
  2. There is an option to provide phototherapy at TSB levels 35-50 μmol/L below those shown the graphs in any infant with risk factors.

- In babies with gestational age ≤34 weeks
  1. Look for any risk factors such as isoimmune haemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis or albumin <3.0g/dl.
  2. There is an option to provide phototherapy at TSB levels 20 μmol/L below those shown on the graphs in any infant with risk factors.

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During Phototherapy
- If serum bilirubin prior to starting phototherapy is within 50 micromol/litre of exchange transfusion threshold, repeat serum bilirubin 4-6 hours after initiating phototherapy. Otherwise, repeat serum bilirubin every 12-24 hours to make sure serum bilirubin level is stable or falling.

Stopping phototherapy
- Stop phototherapy once serum bilirubin has fallen to a level at least 50 micromol/litre below the phototherapy threshold.
- Measure bilirubin using TcB 12-24 hours after ceasing PT to rule out rebound of significant hyperbilirubinaemia. If TcB is >250, serum bilirubin is required.

Type of phototherapy to use
- For term infants 37 weeks and more:
  1. Use single phototherapy unit as a standard. Either conventional blue light PT (e.g. Draeger Phototherapy Unit 4000) or fibreoptic phototherapy (e.g. GE Bilisoft and Medela Bilibed) can be used.
  2. Use multiple PT units to get as much skin exposure as possible if:
     - The serum bilirubin is rising rapidly (>8.5 micromol/litre/hour)
     - The serum bilirubin level is within 50 micromol/litre below the threshold for exchange transfusion.
     - The bilirubin level fails to respond to single PT that is, serum bilirubin continues to rise, or doesn’t fall.
- For preterm infants less than 37 weeks:
  1. Single unit phototherapy with either conventional blue light PT (the preferred type in our unit) or fibreoptic PT can be used as first line treatment.
  2. Use multiple PT units to get as much skin exposure as possible if:
     - The serum bilirubin is rising rapidly (>8.5 micromol/litre/hour)
     - The serum bilirubin level is within 50 micromol/litre below the threshold for exchange transfusion.
     - The bilirubin level fails to respond to single PT that is, serum bilirubin continues to rise, or doesn’t fall.

- Phototherapy Dose: It is recommended to use an irradiance of 30 µW/cm²/nm in the spectral wavelength band of 430-490 nm.
- The Draeger Photo-Therapy 4000 lamp in our unit is a conventional overhead phototherapy device. The head contains four 18W folded blue fluorescent tubes in the central section and two 18W folded white fluorescent tubes, one at each end of the central section. The two white tubes may optionally be replaced by two blue tubes for enhanced treatment. Blue tubes provide the therapeutic light and the white tubes provide light to make it easier for the nurses to work with the lamp by balancing the intense blue colour. The white lights do not produce therapeutic light.
- GE Bilisoft is a fibreoptic blue LED phototherapy system. This light delivers phototherapy that meets the recommendations of the American Academy of Pediatrics including the following specifications:
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<table>
<thead>
<tr>
<th>Components of Phototherapy</th>
<th>AAP Guidelines</th>
<th>Bilisoft</th>
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</thead>
<tbody>
<tr>
<td>Light Intensity</td>
<td>Irradiance level at least 30 µW/cm2/nm</td>
<td>35 (large pad)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>55 (small pad)</td>
</tr>
<tr>
<td>Light Spectrum</td>
<td>430-490 nm wavelength</td>
<td>430-490nm</td>
</tr>
<tr>
<td>Surface Area Coverage</td>
<td>Large surface area</td>
<td></td>
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<tr>
<td>Distance</td>
<td>Distance between the infant and the light source is critical to spectral irradiance level</td>
<td></td>
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</tbody>
</table>

- Medela Bilbed: This is used on the postnatal wards. A blue fluorescent tube is fitted into a plastic crib with a stretched plastic cover over the top for the baby to lie on. The baby is dressed in the Bilicombi baby suit and nursed on the soft plastic cover. This system delivers irradiance up to 40 µW/cm2/nm.

**General Care during PT**
- Place the baby in supine position unless other clinical conditions prevent this.
- Ensure PT is applied to the maximum area of skin.
- Monitor the baby’s temperature
- Monitor hydration of the baby by assessing wet nappies.
- Give the baby eye protection and routine eye care during PT.
- Continuous, rather than intermittent PT is recommended. However, using clinical judgement, encourage short breaks of up to 30 minutes for breast feeding, nappy changes and cuddles.
- No need for additional fluids or feeds routinely but IV fluids/additional nasogastric enteral feeds may be needed in babies who are needing multiple PT and
  - The serum bilirubin is rising rapidly (>8.5 micromol/litre/hour)
  - The serum bilirubin level is within 50 micromol/litre below the threshold for exchange transfusion.
  - The bilirubin level fails to respond to single PT that is, serum bilirubin continues to rise, or doesn’t fall.

**Infants at risk of kernicterus**

Identify babies at risk of kernicterus if they have any of the following:
- A serum bilirubin level greater than 340 micromol/litre in infants 37 weeks and more
- A rapidly rising bilirubin of >8.5 micromol/litre/hour
- Clinical features of acute bilirubin encephalopathy

**Intravenous Immunoglobulin (IVIG)**

- Intravenous immunoglobulin (IVIG) acts by blocking antibody site and preventing the destruction of sensitised erythrocytes. IVIG contains pooled IgG immunoglobulins extracted from the plasma of over 1000 blood donors.
- Use IVIG (500 mg/kg over 4 hours) as an adjunct to continuous multiple PT in cases of Rhesus haemolytic disease or ABO haemolytic disease when the serum bilirubin continues to rise by >8.5 micromol/litre/hour.
- IVIG should only be given with the consent of the neonatologist on-call.
- IVIG is a blood product, so written consent should be obtained from parents.

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Explanatory Note

**Phototherapy thresholds for infants of 38 weeks or more gestation**

For babies of 38 or more weeks of gestation and aged 96 hours or older, our guidelines are based on UK NICE Consensus guidelines which are also comparable with the threshold proposed by the American Academy of Pediatrics.

For the period from birth to 96 hours, again based on informal consensus, the UK-NICE Guidelines recommended a series of bilirubin levels with 6-hourly stepwise increases at which phototherapy is recommended until the 96-hour threshold of 350 micromol/litre is reached. These recommended levels are presented in table form (see the threshold table).

**Phototherapy thresholds for infants less than 38 weeks of gestation**

With regard to preterm babies, one longstanding and common approach has been to determine the threshold for phototherapy using the simple formula

\[
\text{bilirubin in micromol/litre} = (\text{gestational age} \times 10) - 100
\]

This formula has been proposed for use in paediatric textbooks for many years. UK NICE Guidelines used this formula for babies aged 72 hours or older. For all babies aged less than 72 hours, a lower threshold than the above formula has been chosen because of the evidence that shows that bilirubin levels are rising for the first few days of life.

UK-NICE Guidelines published graphs for each gestational age using the formula for infants of 72 hours of age and older. The threshold levels during the first 72 hours were determined by drawing a straight line from a level of 40 micromol/litre (the upper limit of normal for the umbilical cord blood bilirubin) at birth to the formula-based level at 72 hours.
Exchange transfusion thresholds for babies of 38 weeks or more gestation
Similar considerations were applied to the choice of levels for exchange transfusion. For babies of 38 weeks or more gestation, a threshold of 450 micromol/litre from 42 hours of age onward was recommended in UK-NICE Guidelines. This level was chosen based on the widely accepted view that kernicterus would be very unusual in term babies with serum bilirubin levels lower than this. These levels are also comparable with the American Academy of Paediatrics recommendation of 430 micromol/litre. For babies less than 42 hours age, UK-NICE Guidelines recommended a series of bilirubin levels with 6-hourly stepwise increases at which exchange transfusion is recommended until the 42-hour threshold of 450 micromol/litre is reached. These recommended levels are also presented in table form (see the threshold table).

Exchange transfusion thresholds for babies less than 38 weeks of gestation
For preterm babies, UK-NICE Guidelines used a simple formula (bilirubin in micromol/litre = gestational age × 10) that has been proposed for use in paediatric textbooks for many years. For babies less than 72 hours old, a lower threshold than the above formula was chosen.

Similar to phototherapy, UK-NICE Guidelines published graphs for each gestational age using the formula for infants of 72 hours of age and older. The threshold levels during the first 72 hours were determined by drawing a straight line from a level of 80 micromol/litre at birth to the formula-based level at 72 hours.

Bilirubin Encephalopathy or Kernicterus
Clinically, kernicterus presents as follows:

Stage 1: Poor Moro Reflex, decreased tone, lethargy, poor feeding, vomiting, high-pitched cry
Stage 2: Opisthotonus, seizures, fever, rigidity, oculogyric crises, paralysis of upward gaze.
Stage 3: Spasticity is decreased at about 1 week of age
Stage 4: Late sequelae include spasticity, athetosis, deafness, mild mental retardation, paralysis of upward gaze and dental dysplasia

Other therapies:
Do not use any of the following to treat hyperbilirubinemia:
- Albumin
- Agar
- Barbitalates
- charcoal
- Cholestyramine
- clofibrate
- D-penicillamine
- metalloporphyrins
- Traditional chinese medicine
- Acupuncture
- Homeopathy
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4. SIDE EFFECTS/COMPLICATIONS

5. EDUCATIONAL NOTES

6. RELATED POLICIES/ PROCEDURES/CLINICAL PRACTICE GUIDELINES

7. REFERENCES

1. Neonatal Jaundice. UK NICE Guidelines May 2010. UK National Collaborating Centre for Women’s and Children’s Health. Published by the Royal College of Obstetricians and Gynaecologists, 27 Sussex Place, Regent’s Park, London NW1 4RG.


Jaundice Treatment Thresholds – 23-28 week gestation

*Any risk factors? It is an option to start PT at SBR 35-50 µmol/L below the thresholds in the presence of risk factors including isoimmune haemolytic disease, G6PD deficiency, IUGR, asphyxia, significant lethargy, temperature instability, sepsis, acidosis or albumin <3 g/dl (if measured).
Jaundice Treatment Thresholds – 29-34 week gestation

*Any risk factors? It is an option to start PT at SBR 35-50 µmol/L below the thresholds in the presence of risk factors including isoimmune haemolytic disease, G6PD deficiency, IUGR, asphyxia, significant lethargy, temperature instability, sepsis, acidosis or albumin <3 g/dl (if measured).
Jaundice Treatment Thresholds – 35-37 week gestation

*SAny risk factors? It is an option to start PT at SBR 35-50 µmol/L below the thresholds in the presence of risk factors including isoimmune haemolytic disease, G6PD deficiency, IUGR, asphyxia, significant lethargy, temperature instability, sepsis, acidosis or albumin <3 g/dl (if measured).
Jaundice Treatment Thresholds – >37 week gestation

*Any risk factors? It is an option to start PT at SBR 35-50 µmol/L below the thresholds in the presence of risk factors including isoimmune haemolytic disease, G6PD deficiency, IUGR, asphyxia, significant lethargy, temperature instability, sepsis, acidosis or albumin <3 g/dl (if measured).