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An AOM Clinical Practice Guideline Summary

HYPERBILIRUBINEMIA

This summary provides easy access to some of the most essential content of **AOM CPG No. 18 – Management of Hyperbilirubinemia in Healthy Term and Late Preterm Neonates**, and is intended for use in conjunction with the full-length Clinical Practice Guideline (CPG). For a complete analysis of the research relevant to the management of hyperbilirubinemia, along with citations, refer to the full CPG.

DEFINITIONS

Hyperbilirubinemia: A condition in which there is an excess of bilirubin in the blood and tissues of the body. (1)*

Jaundice: The yellowing of the skin and the whites of the eyes as a result of the buildup of bilirubin in the blood and tissues of the body. (1)*

Severe hyperbilirubinemia: A total serum bilirubin (TSB) concentration greater than 340 µmol/L at any time during the first 28 days of life. (7)

Critical hyperbilirubinemia: A TSB concentration greater than 425 µmol/L at any time during the first 28 days of life. (7)

Acute bilirubin encephalopathy: The clinical manifestation of bilirubin toxicity; clinical presentation can progress from lethargy, hypotonia and poor suck, to hypertonia of extensor muscles (with opisthotonus, rigidity and retrocollis), high-pitched cry, fever and irritability and eventually to seizures and coma. (7,46)

Chronic bilirubin encephalopathy: The clinical sequelae of acute bilirubin encephalopathy including athetoid cerebral palsy, hearing deficits, developmental delay, oculomotor disturbances and dental dysplasia. (4,7)

Kernicterus: A pathological finding of deep-yellow staining of the brain by bilirubin and evidence of neuronal injury. (4,7)

TYPES OF JAUNDICE

Physiologic jaundice: The most common form of jaundice; typically becomes apparent between 24 to 72 hours of life. There are no underlying pathological causes of physiologic jaundice. (7)

Pathologic jaundice: Jaundice that manifests as a symptom of an existing underlying condition. Is characterized by rapidly rising bilirubin concentrations that exceed 85.5 µmol/L on the first day, 171 µmol/L on the second day, or 205.2 to 222.3 µmol/L on the third day. (47)

Prolonged jaundice: Any jaundice lasting more than 14 days in term infants and more than 21 days in preterm infants. (15)

*The terms **hyperbilirubinemia** and **jaundice** are used interchangeably throughout this document.

RISK FACTORS

SEVERE HYPERBILIRUBINEMIA

What are the factors associated with the development of severe hyperbilirubinemia?

According to the National Institute for Health and Clinical Excellence (NICE), the most significant risk factors for severe hyperbilirubinemia are as follows (1):

- Gestational age under 38 weeks (OR 0.6 to 20.70)
- Previous sibling with neonatal jaundice requiring phototherapy (OR 2.3 to 6.0)
- Visible jaundice in the first 24 hours of life (OR 2.9 to 10.1)
- Suboptimal feeding (OR 0.4 to 10.75)

Good Practice Statements:

1. Identification of risk factors for severe hyperbilirubinemia typically occurs in an ongoing manner throughout the course of the prenatal and postpartum period in the context of Ontario midwifery care

   Regardless of risk factors, review the following as part of an informed choice discussion with clients:
   - that jaundice is common, short-lived and usually harmless; however, a small number of babies will develop severe hyperbilirubinemia, which can be harmful if not treated;
   - how to detect visible jaundice, particularly within the first 24 hours (visibly yellow in lighter-skinned infants and/or yellow sclera or with blanched skin in darker-skinned infants and/or yellow sclera) and signs of hyperbilirubinemia, including poor suck, lethargy and reduced feeding, dark urine and pale, chalky stools; and
   - how to contact the midwife if jaundice is suspected in the newborn.
2. Share with clients how risk factors, if present, may impact considerations for screening and management of severe hyperbilirubinemia.

   These good practice statements recognize the client as the primary decision-maker, the midwife's ability to identify emerging risk factors for severe hyperbilirubinemia and the need for timely decision-making.

PROLONGED JAUNDICE

What are the factors associated with prolonged jaundice?

Prolonged jaundice that is accompanied by a conjugated bilirubin level greater than 18 µmol/L or greater than 20% of the TSB concentration warrants further investigation, as jaundice may be due to pathological causes. These causes may include (7,8):

- Haemolysis
- Infection
- Congenital hypothyroidism
- Inherited metabolic conditions

Most cases of prolonged jaundice are caused by breast milk jaundice, a condition whereby infants who are exclusively fed with human milk experience elevated bilirubin levels, despite being otherwise healthy. (6)

Good Practice Statement:

3. In the otherwise well, human milk-fed infant with prolonged jaundice (jaundice lasting > 14 days), midwives may consider drawing TSB including the conjugated bilirubin to screen for the need for further investigation.

   If conjugated bilirubin level is > 18 µmol/L or greater than 20% of the TSB concentration, consult with a physician for further investigation of potential underlying causes of prolonged jaundice.

   This good practice statement recognizes continuity of care and the ability of the midwife to assess the need for interprofessional collaboration as the neonate's clinical picture requires.

ACUTE AND/OR CHRONIC BILIRUBIN ENCEPHALOPATHY

What are the factors associated with the development of acute and/or chronic bilirubin encephalopathy?

Based on limited observational data, guideline groups suggest that infants with the following risk factors are at greater risk of developing acute and/or chronic bilirubin encephalopathy at lower bilirubin levels (7,9):

- Isoimmune hemolytic disease
- G6PD deficiency
- Asphyxia
- Respiratory distress
- Significant lethargy
- Temperature instability
- Sepsis
- Acidosis

Midwives who suspect the presence of hemolytic disease (HDN) can order a direct anti-globulin test (DAT). A direct anti-globulin test (DAT or direct Coombs) can be done on an infant's cord blood to identify isoimmunisation, thereby facilitating risk assessment for hemolysis. (10)

Good Practice Statement:

4. For O blood group birthing parents, midwives should consider drawing cord blood and storing it for processing in the event that jaundice presents in the first 24 hours or that a TSB is later drawn for that infant. Although community standards may vary, midwives can consider bringing (i) stored cord blood for DAT processing and (ii) the TSB sample from the infant's heel prick to the laboratory for processing at the same time. If cord blood has not previously been drawn and stored at birth, midwives may consider drawing a tube of blood for DAT and blood type in addition to the TSB by infant heel prick.

   - If the newborn's TSB level is normal and no further testing or treatment is required, cord blood does not need to be tested for isoimmunization.
   - If TSB level is high, have cord blood processed to aid in the identification of the cause of hyperbilirubinemia.

   This good practice statement recognizes cord blood as an aid in the identification of the cause of hyperbilirubinemia in cases where pathologic jaundice may be possible (e.g. when birthing parent has O blood group).

[1] See Considerations for Cord Blood Storage in the community setting in the full Clinical Practice Guideline.

PREVENTION

INFANT FORMULA SUPPLEMENTATION

Can infant formula supplementation be used to prevent the development of severe hyperbilirubinemia?

One observational study found that formula feeding (either mixed or exclusive) may reduce incidence of severe hyperbilirubinemia, need for phototherapy, and lower bilirubin levels. (11) However, this research may not be applicable to the Canadian health care context as it did not diagnose severe hyperbilirubinemia and initiate treatment in accordance with current Canadian guidance.

The work group balanced the rare risk of an infant developing severe hyperbilirubinemia against substantial benefits of human milk feeding.

Recommendation:

5. Midwives should not recommend the use of formula supplementation to prevent severe hyperbilirubinemia in the otherwise well, healthy, human milk-feeding neonate.

   Strong recommendation: very low certainty of evidence

   This recommendation recognizes midwifery support of human milk as the optimal physiological nutrition for infants.

TIMING OF CORD CLAMPING

Can the timing of cord clamping prevent the development of severe hyperbilirubinemia?

Delayed cord clamping likely increases the risk of hyperbilirubinemia and the need for phototherapy among healthy term neonates and late pre-term and term infants with ABO isoimmunisation. (12,13) However, delayed cord clamping poses no increased risk of chronic or permanent harms and has a number of benefits (such as improved long-term iron stores, haematocrit values, and hemoglobin concentrations). (12)

Recommendation:

6. Midwives may offer delayed cord clamping to all clients, taking into consideration hyperbilirubinemia risk factors.

   Informed choice discussions should include:

   - the risks and benefits of delayed cord clamping compared with early cord clamping;
   - how risk factors for hyperbilirubinemia, if present, increase the infant's risk of jaundice; and
   - the client's values and preferences.

   Weak recommendation: moderate certainty of evidence

   This recommendation recognizes the preference for and health benefits of delayed cord clamping while balancing the client's values and preferences.

SUNLIGHT

Can sunlight be used to prevent the development of severe hyperbilirubinemia?

The quality of the available research on sunlight and hyperbilirubinemia was limited by several serious factors. (14)
The work group considered how sunlight cannot be accurately measured and poses the risk of UV radiation and burns. (15)

Recommendation:
7. There is insufficient evidence to support the use of sunlight as a means of preventing the development of severe hyperbilirubinemia. **No recommendation: very low certainty of evidence**

SCREENING

VISUAL ASSESSMENT

Can visual assessment alone be used to screen for severe hyperbilirubinemia?

Four observational studies identified that the use of visual assessment to determine the severity of jaundice is not accurate and that there is variability among methods and providers. (16–19)

The work group affirmed that visual assessment is an important component of midwives clinical assessment but should not be used in isolation to screen for severe hyperbilirubinemia.

Recommendation:
8. The use of visual assessment ***alone*** is not recommended for screening for severe hyperbilirubinemia. **Weak recommendation: very low certainty of evidence** *This recommendation recognizes that visual assessment for hyperbilirubinemia is an important part of the overall clinical assessment of a newborn but should not be relied on alone to determine a newborn's risk of severe hyperbilirubinemia.*

RISK FACTOR SCORING SYSTEM

Should a risk factor scoring system be used to screen for severe hyperbilirubinemia?

One diagnostic cohort study determined that the majority of infants would be incorrectly classified when screened with a risk factor scoring system which included birth weight, gestational age, oxytoxin use during delivery, vacuum extraction, and feeding method. (20) Incorrect classification has the potential to result in either overtreatment of healthy infants or missed treatment for infants with severe hyperbilirubinemia.

Recommendation:
9. The use of risk factor scoring systems is not recommended for screening for severe hyperbilirubinemia. **Weak recommendation: very low certainty of evidence** *This recommendation recognizes that midwives routinely assess for hyperbilirubinemia risk factors as part of an infant's clinical assessment in the postpartum period but should not use a scoring system.*

TRANSCUTANEOUS BILIMETRE (TCB)

Should a transcutaneous bilimetre be used to screen for severe hyperbilirubinemia?

One systematic review of eleven diagnostic cohort studies demonstrated that TcB measurements obtained from bilimetres cannot provide an exact estimation of an infants' bilirubin level. (21)

Limitations of bilimetres include:

- A tendency to overestimate TSB in babies with a darker skin tones (22–26) and those with higher (more dangerous) bilirubin levels. (27,28)
- A tendency to be inaccurate during or after phototherapy. (29)

Despite these limitations, TcB measurements generally show good correlation with TSB measurements (27) and may be used as an initial screening tool to prompt a follow up TSB test when necessary. (30) Ontario's 2017 *Clinical Pathway Handbook for Hyperbilirubinemia in Term and Late Pre-Term Infants (≥35 weeks)* recommends performing a TSB measurement when a TcB result is within 50 µmol/L of the phototherapy treatment line. (30)

Benefits of bilimetres for midwives include:

- keeping care in the community;
- sparing clients from unnecessary travel and testing; and
- painless and non-invasive nature of the screening tool.

Recommendation:

10. Where screening for hyperbilirubinemia is requested and/or recommended and bilimetres are available to the midwife, TcB screening should be offered.

    Strong recommendation: very low certainty of evidence

    This recommendation recognizes the unequal access to bilimetres across practice groups and the province but affirms the use of bilimetres as an effective screening tool to prompt TSB testing when required and as a promising way to increase community-based care.

UNIVERSAL BILIRUBIN SCREENING

Should all neonates be screened for severe hyperbilirubinemia within 24-72 hours of life regardless of risk factors?

Available research (eight observational studies) on universal bilirubin screening suggested some benefits associated with universal screening including a lower incidence of high bilirubin concentrations and lower rates in readmission to hospital. However, this research has demonstrated that universal screening may have no impact on the need for phototherapy. (31–38)

The work group recognized that there may be limited benefit to performing universal screening in the midwifery context given that midwives perform regular, timely and close follow-up of infants in their care.

Midwives also face several structural and systemic barriers to offering screening universally including:

- no access to bilimetre funding; and
- laboratories may reject blood samples drawn in the community setting.

Universal screening may have consequences for clients including:

- longer hospital stays; and
- travel to clinic or hospital for testing.

Recommendations:

11. The risks and benefits of universal screening should be discussed with all clients as part of an informed choice discussion.

    This discussion may address:
    - what is known about risk factors, if present;
    - how visible jaundice, poor feeding, dehydration and weight loss impacts the risk of developing severe hyperbilirubinemia;
    - what is known about the limitations of visual assessment of jaundice;
    - optimal timing of screening: between 24 to 72 hours of age;
    - barriers to and enablers of screening within the client's community context; and
    - the client's values and preferences and risk tolerance.

    Weak recommendation: very low certainty of evidence

    This recommendation recognizes the paucity of high-certainty evidence on the effectiveness of universal screening, the uniqueness of the midwifery context and structural barriers which impact midwives' ability to offer community-based bilirubin screening.

12. If visible jaundice develops, obtaining a bilirubin measurement is recommended.

    For neonates who have previously had a negative TSB screen and in whom visible jaundice subsequently develops, midwives may use their clinical judgement in determining the need to re-screen. Consider presence or absence of other clinical factors associated with severe hyperbilirubinemia (e.g. suboptimal feeding, lethargy, dark urine, pale chalky stools).

    Weak recommendation: very low certainty of evidence

    This recommendation recognizes that the timely, frequent and close follow-up of neonates as a standard of midwifery care limits the benefits associated with universal screening while acknowledging the importance of the clinical manifestation of hyperbilirubinemia.

TREATMENT/MANAGEMENT

FIBREOPTIC PHOTOTHERAPY

Is fibreoptic phototherapy an effective treatment for severe hyperbilirubinemia?

One systematic review showed that fibreoptic phototherapy may increase the duration of phototherapy, and is slightly less effective than conventional phototherapy at lowering bilirubin concentrations within 24 hours of starting treatment. (39)

The workgroup considered the benefits of fibreoptic phototherapy including skin to skin contact and more frequent nursing. Although fibreoptic phototherapy may not be preferred amongst clients that want a shorter duration of treatment, it is the preferred method of treatment in the home and community setting.

Recommendation:

13. Where available, midwives may offer fibreoptic phototherapy using their clinical experience and the clinical context of the client to guide decision-making.

    Weak recommendation: low certainty of evidence

    This recommendation recognizes that fibreoptic phototherapy may increase the duration of treatment and therefore may not be appropriate in all cases, but has benefits such as an increase in skin to skin contact.

Recommendation:

14. Midwives may offer fibreoptic phototherapy in the home as an option for treatment where community-based health infrastructure exists.

    Weak recommendation: low certainty of evidence

    This recommendation recognizes midwives' scope of practice to manage phototherapy, provided midwives have the knowledge, skills, experience and community-based health infrastructure to do so.

FORMULA SUPPLEMENTATION DURING PHOTOTHERAPY

Is the use of formula supplementation during phototherapy an effective method for managing severe hyperbilirubinemia?

One observational study demonstrated that formula supplementation in conjunction with phototherapy may reduce the duration of phototherapy and result in a faster average decrease of bilirubin levels within a 24 hour period. (40)

The work group recognized the various benefits of human milk including improved parent-infant bonding (41,42) and immunologic status (43), and reduced risk for gastrointestinal infection. (42) Therefore, clients should not be deterred from nursing while their infant is undergoing phototherapy treatment and should be provided ongoing lactation support as required.

Recommendation:

15. Midwives should not routinely recommend use of formula supplementation for otherwise healthy infants undergoing phototherapy, discussing the risks and benefits with clients.

    Strong recommendation: very low certainty of evidence

    This recommendation recognizes midwifery support of human milk as the optimal physiological nutrition for infants.

CLIENT EXPERIENCES

What are the experiences of clients who have newborns with severe hyperbilirubinemia and how can they be supported by midwives?

The development of severe hyperbilirubinemia in a newborn is a stressful and often sudden experience that may leave parents feeling unprepared. (44,45) Some parents may be disproportionately impacted by the stress associated with phototherapy including those with limited social support. Midwives can provide ongoing educational and emotional support for clients before, during and following the management of severe hyperbilirubinemia.

Good Practice Statement:

16. Midwifery clients would benefit from discussions with their midwife on:
    - The results of bilirubin testing and their clinical significance, if any.
    - Treatment options and alternatives, including what to expect regarding the impact of treatment on skin to skin and feeding.
    - How to access psychosocial and emotional support during and after their experience of treatment.

    This good practice statement recognizes continuity of care and the skill of midwives in providing health information to clients.

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