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STANDARD GUIDELINE SUBJECT:

Hyperbilirubinemia Assessment

PURPOSE:

The purpose of this guideline is to:

- Assist in the prompt detection of hyperbilirubinemia.
- Identify neonates at risk of severe hyperbilirubinemia and decrease the risk of bilirubin induced neurological dysfunction (BIND) and the need for exchange transfusions by identifying and treating hyperbilirubinemia sooner.

DEFINITIONS:

Acute Bilirubin Encephalopathy (ACE) – the acute phase of BIND. May be reversible or cause permanent damage.

Autoimmune Hemolytic Anemia – formerly known as the COOMBS test; this test identifies autoimmune hemolytic anemia which is associated with severe hyperbilirubinemia.

Bilirubin – a by-product of the hemolysis of hemoglobin from red blood cells. Bilirubin is direct (conjugated) when it conjoins with glucuronic acid making it water soluble and excretable. Bilirubin is a neurotoxin and when it is indirect (unconjugated); it can pass through the blood-brain barrier and cause permanent disabilities. Indirect bilirubin levels rise when bilirubin levels exceed the amount of glucuronic acid available to conjugate.

Glucose-6-Phosphate Dehydrogenase (G6PD) – is an enzyme that assists in the neonate’s ability to conjugate, and therefore excrete, bilirubin. A deficiency in this enzyme puts the neonate at a much increased risk for severe hyperbilirubinemia. Newborns of Asian/African/Mediterranean and Middle Eastern descent are at risk for this deficiency.

Kernicterus – permanent sequelae of BIND.

Neonatal Hyperbilirubinemia – Increased levels of bilirubin above the 95th percentile for age on the Bhutani nomogram is associated with bilirubin induced neurological dysfunction which has permanent sequelae called kernicterus.

Severe Neonatal Hyperbilirubinemia – defined when levels are above 428 micromol/L.

Neonatal Jaundice – the yellow discoloration of the skin/sclerae caused by bilirubin deposition. Is not a reliable indication of hyperbilirubinemia.

Total Serum (TSB) – total serum or plasma bilirubin level including both direct (conjugated) and indirect (unconjugated) bilirubin.

Transcutaneous Bilirubin (TcB) – a measurement taken by a hand held device that uses multi-wavelength spectral reflectance from the skin surface to estimate total serum or plasma (TSB) bilirubin. Helps eliminate the need for invasive blood sampling.

IMPORTANT POINTS TO CONSIDER:

66% of normal neonates will become clinically jaundiced in the first week of life. The majority of these will have physiological jaundice. Physiological jaundice usually self resolves but will be treated with phototherapy if the levels reach a certain threshold (according to Bhutani nomogram).

There are two types of hyperbilirubinemia:

- **Physiological jaundice** is the “normal” jaundice neonates get due to the relative polycythemia, shortened erythrocyte life span of neonatal RBC’s, immature liver and the increased enterohepatic circulation of neonates. These bilirubin levels usually peak by 3-4 days post birth and usually self resolves within 1-2 weeks post birth. Physiological jaundice may also occur if the neonate does not receive enough breastmilk (breastfeeding failure jaundice) which is resolved by increasing the breastmilk intake of the neonate. Breastmilk jaundice is the persistent jaundice beyond the first week of life in neonates that are exclusively breastfed. It peaks later than normal jaundice, at about 3-5 days of life and can last up to 12 weeks.
- **Pathological hyperbilirubinemia** is not “normal” and bilirubin levels can rise to dangerous levels and cause permanent disability. This is often marked by an increased level of direct (conjugated) bilirubin. Underlying causes may be sepsis, rubella, toxoplasmosis or any disorder which blocks the clearance pathways of bilirubin (i.e. ileus, cholestasis, liver disease, biliary tract disease, Crigler-Najjar syndrome, Gilbert’s syndrome).
 - Pathological jaundice is suspected if:
 - Jaundice occurs within the first 24 hours of life
 - Total Serum Bilirubin (TSB) level is higher than the 95th percentile for age
 - The TSB level rises by more than 3.42 micromol/L per hour or 86 micromol/L per day
 - Direct bilirubin concentration is more than 17 micromol/L if the total bilirubin is less than 86 micromol/L
 - If the direct bilirubin is more than 20% of the total bilirubin if the total bilirubin is greater than 86 micromol/L
 - Treatment is required.

Infants undergoing phototherapy may no longer look jaundiced due to a bleaching of the skin. Color is not an adequate measurement of bilirubin levels. This must be done by a TSB.

Elevated direct bilirubin levels are never normal and may be indicative of cholestasis, liver and/or biliary tract disease.

Exclusive breastfeeding should be encouraged – assist mothers to feed at least 8 times/day. Supplementation (if needed due to hydration/weight loss) should be done with expressed breastmilk as often as possible. Neonates approaching the threshold for exchange transfusion should be transferred to a tertiary center to receive IV fluid supplementation and treatment.

Limitations to TcB include:

- TcB may not be accurate in levels above 257 micromol/L. Bilirubin levels above this need to be confirmed by a TSB.
- TcB is not accurate in neonate undergoing phototherapy. These neonates require a TSB. TcB may be used again once the phototherapy has been discontinued for 24 hours.
- TcB may be affected by skin pigmentation: overestimation in dark skinned neonates and may underestimate in light skinned neonates.

PROCEDURE:

1. All neonates shall be visually assessed for jaundice every 8-12 hours post birth and at discharge. Jaundice usually appears head to toe. If neonate is jaundice below the umbilicus a TcB or TSB shall be done.
 - Jaundice is assessed by balancing the neonate's skin by pressing a finger over a bony prominence.
 - The neonate's sclera should also be inspected for jaundice.
2. All neonates should receive TcB or TSB testing prior to discharge, as per Canadian Pediatric Society recommendations. TcB testing should be done on the neonate's forehead, unless extensively bruised. The sternum may be used as a secondary site.
3. If TcB results do not appear to be congruent with the physical assessment, obtain a TSB to confirm levels.
4. All results are to be plotted on the Bhutani nomogram. On-line interactive calculators can be accessed at www.bilitool.org or http://www.uptodate.com/contents/calculator-newborn-hyperbilirubinemia-assessment?source=see_link&utm_popup=true.
5. Next steps are determined on the zone, as follows (see Supporting Documents):
 - High risk zone: notify primary care provider. Do TSB immediately (if result was from a TcB) and repeat TSB in 24 hours.
 - High intermediate risk zone: term infants – repeat TcB in 24 hours or immediately prior to discharge. If less than 28 weeks, obtain a TSB.
 - Low intermediate risk zone – ongoing clinical assessment. Repeat TcB/TSB not required post discharge.
 - Low risk zone – no follow up required post discharge.
6. If the bilirubin is above the 95% on the Bhutani nomogram for age, further testing shall include:
 - Blood type and direct antiglobulin test (AGT)
 - Complete blood count and smear
 - Reticulocyte count
 - G6PD measurement if clinically appropriate
 - Direct (conjugated) bilirubin
7. Neonates with levels above normal for their age shall be established on phototherapy. Phototherapy may be given via a bili blanket, an isolette, a bili pad or any combination of these.
8. Neonates receiving phototherapy shall have their vital signs (except blood pressure) taken every 4 hours and a TSB taken at least every 24 hours.
9. If any neonate is jaundice prior to 24 hours of age, a TSB and an AGT shall be performed.
10. Consider a consult to a tertiary centre if the neonate:
 - Fails to respond to standard phototherapy (bilirubin continues to rise or does not decrease)
 - Approaches the exchange transfusion levels (see Supporting Documents)
 - Had a documented bilirubin greater than 400 micromol/L
11. If a bilirubin is not routinely done on discharge (as is the standard), the newborn shall be visually assessed and if risk factors or signs and symptoms exist (jaundice, lethargy, inadequate feeding), a bilirubin shall be ordered prior to discharge home. Signs and symptoms of hyperbilirubinemia include:
 - Jaundice within 24 hours of life
 - Rapid rise in TSB levels
 - TSB not responding to phototherapy
 - Excessive weight loss
 - Pallor
 - Vomiting
 - Lethargy

- Poor feeding
 - Apnea
 - Temperature instability
 - Tachypnea
12. Document elevated bilirubin levels, treatment and plan for follow-up by hospital or primary care provider on the postpartum referral form.
 13. Adequate follow-up plans need to be in place prior to discharge of the neonate.

SUPPORTING DOCUMENTS:

- [CLI.5810.SG.012.SD.01](#) Bhutani Nomogram
[CLI.5810.SG.012.SD.02](#) Guidelines for Exchange Transfusions

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