RESOURCES

Challenge of early discharge – Newborn assessment for jaundice

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Introduction

The purpose of the CPSP study was to obtain epidemiological data about the severity of neonatal hyperbilirubinemia and the related burden of illness (i.e., phototherapy, blood transfusions and exchange transfusions). Severe neonatal hyperbilirubinemia was defined for this study as having a peak bilirubin greater than 425 μmol/L or needing an exchange transfusion. Preterm infants less than 36 weeks of age and infants with Rhesus (Rh) incompatibility were not included. A total of 205 confirmed cases were reported in the first 18 months of the study. ABO incompatibility was the most common etiology, followed by glucose 6-phosphate dehydrogenase (G6PD) deficiency. While 38% of infants did not have a complete workup to determine the cause of their jaundice, 70% had severe hyperbilirubinemia but were discharged and subsequently readmitted within seven days.

Background

Severe neonatal hyperbilirubinemia is rare and can be associated with significant morbidity. In neonates, it can result in encephalopathy and death. During the acute phase of bilirubin encephalopathy, severely jaundiced infants are noted to be lethargic and hypotonic with a poor sucking reflex. If the hyperbilirubinemia is not treated, the infant becomes hypertonic and may develop a fever and a high-pitched cry. The hypertonia is manifested by backward arching of the neck (retrocollis) and trunk (opisthotonus). Eventually, this condition can lead to neonatal death. On postmortem examination, the deposition of bilirubin noted in the basal ganglia and various brainstem nuclei is termed "kernicterus" (yellow staining of the brain). If infants survive the acute phase, they are at risk of developing chronic encephalopathy, which consists of severe sensorineural hearing loss, athetoid cerebral palsy, paralysis of upward gaze, and intellectual handicaps.

RESOURCES

Based on epidemiological studies, the risk factors associated with severe hyperbilirubinemia in the newborn include:

- jaundice presenting in the first 24 hours,
- jaundice noted at discharge from the hospital,
- previous sibling with jaundice,
- gestational age between 35 and 38 weeks,
- breast feeding, and
- infant bruising and cephalhematoma.

(Dennery et al, 2001, Newman et al, 2000)

Additional risk factors identified by laboratory investigations include Rh and ABO incompatibility and G6PD deficiency (Kaplan et al, 2000). Rh disease is now rare, and the blood type and Rh sensitization status of the mother are usually known at the time of a delivery. Many hospitals no longer perform routine blood typing in infants of group O mothers, so the ABO status of the infant is often unknown. Undiagnosed ABO incompatibility in newborns is a concern, as it has been clearly associated with severe hyperbilirubinemia and kernicterus since the 1930s.

The association between neonatal hyperbilirubinemia, kernicterus, and G6PD deficiency was first reported in the 1960s by Doxiadis et al from Greece, and more recently in 2004 by Tan-Dy et al from Toronto. G6PD deficiency is more prevalent in people of Mediterranean, Indian and South East Asian descent, many of whom are immigrating to Canada. G6PD deficiency, an X-linked disorder, results in quantitative reduction in the protective activity of G6PD in the red blood cell, thereby predisposing the cell to destruction. Although G6PD is an X-linked disorder, mutations are frequent and the incidence of consanguinity is high, resulting in effective G6PD deficiency for 10% of homozygous and heterozygous females, due to unequal inactivation of their X chromosomes [Lyon Hypothesis]. Traditionally, older children and adults with this G6PD deficiency develop hemolytic anemia following erythrocyte exposure to oxidizing agents. Neonates can develop hemolytic anemia if they are G6PD deficient, either with or without a typical trigger.

Other rare causes of severe hyperbilirubinemia include sepsis, spherocytosis, pyruvate kinase deficiency, and congenital conjugation defects of the liver. Physiologic jaundice may also lead to severe hyperbilirubinemia and occurs more frequently in near-term infants and breast-fed babies (Seidman et al, 1995). For this latter group of infants, dehydration may be a contributing factor.

Challenge of early discharge – Newborn assessment for jaundice (continued)

Readmission rates for neonatal jaundice have risen over the last ten years as a result of early discharge. In fact, 70% of the infants with severe hyperbilirubinemia, identified through the CPSP study, were readmitted from home within a week of initial discharge from hospital. These results highlight the importance of a careful assessment of risk factors for severe jaundice in neonates prior to discharge from hospital and the importance of early follow-up post discharge.

Early identification of the etiology of hyperbilirubinemia has a tremendous impact on the management of the infant. Identifying the risk factors prior to discharge from hospital will allow for a more thorough monitoring of these babies for hyperbilirubinemia. This would include:

- more frequent monitoring of bilirubin levels,
- earlier institution of phototherapy, and
- closer follow-up by health-care providers post-discharge.

Full investigation of the infants would include:

- assessment of hydration,
- complete blood count and smear,
- reticulocyte count,
- total and direct bilirubin,
- maternal and infant blood group and Coomb's test,
- G6PD screen, and
- consideration for a septic workup (blood and/or urine culture).

A more aggressive treatment for infants with hemolysis is needed, first, because the rate of increased bilirubin is more rapid with hemolysis, leading to more dangerous bilirubin levels (higher peak levels), and second, because infants with conditions associated with hemolysis (i.e., G6PD deficiency and ABO incompatibility) are at greater risk of developing kernicterus. Prompt management of severe hyperbilirubinemia, including phototherapy and/or exchange transfusion, can reduce the risk of damage from the hyperbilirubinemia (i.e., kernicterus).

Jaundice screening of newborns prior to hospital discharge is essential to identify relatively common but treatable conditions and prevent long-term morbidity and mortality. Early identification of pathological hyperbilirubinemia causes allows treating physicians to monitor adequately and treat aggressively in order to prevent hyperbilirubinemia reaching levels associated with kernicterus.

RESOURCES

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Challenge of early discharge – Newborn assessment for jaundice (continued)

Quiz

1. **In the CPSP study, the percentage of term infants with severe hyperbilirubinemia who were readmitted from home is:**
   a) <10%
   b) 15%
   c) 25%
   d) 50%
   e) >50%

2. **Coomb's testing is done in most hospitals on cord blood from which type of infants:**
   a) All infants
   b) Infants born to mothers with type O blood
   c) Infants born to mothers with Rh negative blood
   d) Infants born to mothers with family history of jaundice, glucose-6-phosphate deficiency or spherocytosis

3. **The term 'kernicterus' refers to:**
   a) Any infant with jaundice and an abnormal neurological examination
   b) A jaundiced infant with retrocollis and opisthotonus
   c) Bilirubin deposition in the basal ganglia
   d) All of the above

4. **Neonatal jaundice and G6PD deficiency can be associated with:**
   a) A normal CBC and smear
   b) Male infants only
   c) Families of Mediterranean descent
   d) Positive Coomb's testing
   e) a and c

5. **G6PD deficiency is a common cause of hyperbilirubinemia in which of the following ethnic populations:**
   a) Indian
   b) East African
   c) Eastern European
   d) Native North American

Answers:
1-e, 2-c, 3-c, 4-e, 5-a