CPSP
CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM

Neonatal hyperbilirubinemia – Severe (2011-2013)

Infants 60 days or less

PROTOCOLS

Principal investigator

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Background

Severe neonatal hyperbilirubinemia is very rare and can be associated with significant morbidity, including bilirubin encephalopathy and death. During the acute phase of bilirubin encephalopathy, severely jaundiced neonates are noted to be lethargic and hypotonic with a poor sucking reflex. If the hyperbilirubinemia is not treated, the neonate can become hypertonic, develop a fever and a high-pitched cry. The hypertonia is manifested by backward arching of the neck (retrocollis) and trunk (opisthotonus). This condition may lead to neonatal death. On postmortem examination, deposition of bilirubin is noted in the basal ganglia and various brainstem nuclei and is termed "kernicterus" (yellow staining of the brain). Furthermore, if neonates survive the acute phase, they are at a risk of developing chronic encephalopathy which presents later in life with athetoid cerebral palsy, sensorineural hearing loss, dental dysplasia, and paralysis of upward gaze. They less often will develop intellectual and other handicaps. Several recent studies have found severe hyperbilirubinemia to be associated with other developmental delays, such as autism, speech delay, and global developmental delay, without the co-occurrence of chorioathetotic cerebral palsy.

Based on epidemiological studies, a number of risk factors have been found to be associated with severe hyperbilirubinemia in the newborn. These include: jaundice presenting in the first 24 hours, jaundice visible before discharge from hospital, previous sibling with jaundice, Asian race, gestational age between 35-37 weeks, exclusive breast feeding, male gender and infant bruising/cephalohematoma. Additional risk factors identified by laboratory investigations include Rh and ABO incompatibility and glucose-6-phosphate dehydrogenase (G6PD) deficiency. Rh disease is now rare and the blood type and Rh sensitization status of the mother is usually known at the time of a delivery. Many hospitals are no longer performing routine blood typing in infants of group O mothers so that the ABO status of the infant is often unknown. ABO incompatibility has been associated with cases of kernicterus in the United States. In Canada, there was very little documentation regarding

incidence of severe neonatal hyperbilirubinemia until the Canadian Paediatric Surveillance Program (CPSP) study from 2002 to 2004 estimated an incidence of one in 2,480 live births. Subsequently, a CPSP kernicterus study from 2007 to 2009 estimated an incidence of approximately 1 in 43,000 live births which was significantly higher than previous estimates (unpublished data).

These and other studies influenced the 2007 Canadian Paediatric Society's position statement "Guidelines for detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants (35 or more weeks' gestation)". Some of the key recommendations were to:

- measure a total serum bilirubin (TSB) or transcutaneous bilirubin (TcB) on all infants in the first 72 hrs of life and plot on the developed nomograms;
- use TSB/TcB, gestational age and direct antiglobulin test (DAT) status to determine need for intervention and timing of follow-up;
- arrange follow-up within 24 hours, if discharged prior to 24 hours of age;
- support breastfeeding;
- perform systematic risk assessment prior to discharge;
- treat with phototherapy and/or exchange transfusion as per guidelines.

Similar guidelines had been introduced by the American Academy of Pediatrics in 2004. There have been a number of studies since then looking at the effects of screening guidelines, which have found increased rates of phototherapy usage and decreased readmission rates for neonates. Given the limitations of these studies, results have not been able to adequately assess the effect of screening guidelines on rates of severe hyperbilirubinemia or kernicterus.

Theoretically, the issue of severe neonatal hyperbilirubinemia and kernicterus is an "avoidable phenomenon" if recognized early and managed appropriately. This study will lead to increased awareness regarding the effectiveness of the new CPS guidelines on the management of infants with neonatal jaundice and their role in improving patient safety, quality of care and ultimately reducing the cost to the public health care system.

The goal of this surveillance study is to compare rates of severe hyperbilirubinemia/ kernicterus pre- and post-introduction of the Canadian guidelines and comment on their effectiveness.

Methods

Through the established methodology of the CPSP, over 2,500 paediatricians and paediatric subspecialists will be actively surveyed on a monthly basis to report cases of severe hyperbilirubinemia. A detailed clinical questionnaire will be completed for reported cases**.**

Objectives

1) To obtain epidemiological data about the incidence of severe neonatal hyperbilirubinemia, post-introduction of the 2007 CPS position statement "Guidelines for detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants".
2) To compare results (2011-2013) to the initial study results (2002-2004).
3) To identify the timing of presentation, etiology and associated triggers or risk factors for the hyperbilirubinemia.

Neonatal hyperbilirubinemia – Severe (continued)

Case definition

Report any infants 60 days of age or less with unconjugated hyperbilirubinemia and who have had:

1) peak serum total bilirubin > 425 μmol/L

or

2) neonatal exchange transfusion.

Exclusion criteria

Infants who have had exchange transfusion for well-documented Rh isoimmunization disease or who were born at less than 35 weeks gestational age.

Duration

March 2011 to February 2013

Expected number of cases

The CPSP study, prior to the 2007 revised guidelines, identified 258 cases. If the guidelines are effective and widely used, fewer cases are expected. The expected number of cases is approximately 150 new cases per year.

Ethical approval

St. Michael's Hospital, University of Toronto

Analysis and publication

The investigators will analyze data, and annual results will be distributed to CPSP participants. Interim data will be presented at various paediatric meetings. Peer-review publication will be pursued.

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