3. NEWBORN SCREENING

Principles

- To ensure early detection of children with sickle cell disease through newborn screening.
- To enable the prompt introduction of secondary prevention strategies and parental education for affected infants with sickle cell disease.
- To provide genetic counseling facilities for affected families.

Recommendations

- Health-care providers and policy makers should advocate for the availability of universal newborn screening for SCD throughout Canada. Hemoglobinopathy screening should be integrated within existing newborn screening programs for other inherited disorders.
- Prior to the implementation of universal hemoglobinopathy screening, appropriate procedures need to be developed for documentation, result notification, and clinical follow-up.
- With the implementation of universal hemoglobinopathy screening, there must be a clear policy regarding heterozygous carrier notification. Asymptomatic carriers do not need to be referred to a hematologist.
- A clear protocol should be implemented to enable familial counseling for affected infants and asymptomatic carriers, which will facilitate the discussion of sibling testing, recurrence risk, reproductive options, and prenatal diagnosis.
- Affected newborns should be referred immediately to a comprehensive SCD program and/or to a pediatric hematologist.
- Penicillin prophylaxis should be initiated prior to the age of 2 months.

Background

Newborn screening is an important public-health strategy in the management of sickle cell disease (SCD). Although newborns with SCD are clinically asymptomatic due to the predominance of fetal hemoglobin, early identification of newborns with SCD allows for early introduction of critical interventions that reduce SCD-related morbidity and mortality.

In a report of the first 10 years of a neonatal hemoglobinopathy-screening program in California, Vichinsky *et al* demonstrated an overall mortality rate of 1.8% for infants with neonatally diagnosed SCD compared with an 8% mortality rate among infants who were diagnosed after 3 months of age.[1] Newborn screening allows for the identification of affected families, and provides an opportunity for parental education about the signs and symptoms of infections, splenic sequestration, and other complications of SCD. Newborn screening also provides an entry point for genetic counseling programs.[2,3] Universal screening of all newborns is preferable to selective screening because it has been estimated that as many as 20% of high-risk individuals will be missed with selective screening alone.[4]

In 2006, Ontario was the first province in Canada to implement universal newborn screening for the detection of SCD. The carrier frequency of the sickle gene is cited at 1 in 10 among the African-American population in the United States. The Canadian Task Force on Preventive Health Care (CTFPHC) estimates that this frequency may be higher in Canada.[5] In Canada, the black population is composed largely of individuals of Caribbean and African origin where carrier rates are 10% to 14% and 20% to 25%, respectively. Between 95 and 100 babies with SCD are born in Canada each year, with approximately 60 of these infants in Ontario alone.

Newborn screening can be performed using cord blood or a capillary blood sample from a neonatal heel prick. Initial screening should be performed prior to any blood transfusions. Infants who require emergent transfusions for other clinical indications should have testing done 3 months after the transfusion.

Screening methods include high performance liquid chromatography (HPLC), isoelectric focusing, and hemoglobin electrophoresis. Enzyme-linked immunsorbent assay (ELISA) techniques to detect sickle hemoglobin (HbS) and hemoglobin C (HbC) have also been used.[6] A sickle solubility test is inappropriate in the newborn period,

and should not be performed. With positive newborn screening results, either DNA studies and/or testing of both parents should be done to confirm the results.

Interpretation of newborn screening results

Hemoglobins identified by neonatal screening are generally reported by level of expression or in order of quantity. For instance, a normal infant will show HbFA because, at birth, more fetal hemoglobin (HbF) is present than normal adult hemoglobin (HbA).

Sickle disorder	Neonatal screening result
SS	FS
S beta thal°	FS
S beta thal⁺	FSA / FS
S-HPFH	FS
SC	FSC

Neonatal screening for SCD may also identify non-sickle hemoglobinopathies such as beta thalassemia major, hemoglobin H disease, hemoglobin E disease or hemoglobin C disease. Several other hemoglobin variants may also be detected through newborn screening, such as alpha globin variants; the majority of these are of no clinical consequence.[7]

Carriers of the sickle gene and other hemoglobinopathies are also identified through newborn screening. These patients are usually clinically asymptomatic, but the information may be useful for purposes of genetic counseling. With the implementation of universal hemoglobinopathy screening, there must be a clear policy regarding the notification of asymptomatic carriers.

Carrier state	Neonatal screening result
Sickle cell trait (HbAS)	FAS
Hemoglobin C (HbC) carrier	FAC
Hemoglobin E (HbE) carrier	FAE

References

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