Congenital Hyperinsulinism International
Collaborative Research Network

CHI CRN Advocacy Statement

What is advocacy?

Advocacy means taking action to support people to say what they want, secure their rights, and get the services they need.

This statement is prepared as part of Congenital Hyperinsulinism International's (CHI) Collaborative Research Network initiative to improve the lives of children, young people, and families experiencing a most challenging illness. The need for this statement arises from discussions with hundreds of parents, young people, doctors, nurses and other professionals from around the world. There will be breakthrough developments in the future, and we anticipate that this statement will be updated to account for new treatments, diagnostic modalities and other advances.

Introduction

Congenital Hyperinsulinism (HI) is the most common cause of persistent hypoglycemia (low plasma glucose or low blood sugar) in infants and children. Low plasma glucose due to HI is extremely dangerous. If not treated promptly and appropriately, hypoglycemia can lead to brain damage, developmental delays, and even death. Prompt initiation of treatment with glucose (ideally by intravenous infusion) to restore plasma glucose to the normal range is critical for preserving vital functioning of the child.

What is HI?

HI is a rare disease affecting approximately 1 in every 28,000 babies born each year. HI is complex to manage even under the best of circumstances. Since most children's hospitals encounter less than two cases of HI per year, to prevent severe brain damage, it is important for any infant suspected of having the condition to be transferred to or managed in collaboration with one of the CHI Centers of Excellence (COE) located around the world, where there is an expert level of knowledge combined with significant experience in treating infants and children with the condition. Contact with a COE for guidance on initial and continued management of infant/ child with HI is essential. Link to information on COEs: The CHI Centers of Excellence (COE) Program – Congenital Hyperinsulinism International (congenitalhi.org)

Immediate recognition of hypoglycemia and initial management

Safe and appropriate treatment must be available to prevent long-term neurologic sequelae at the local treating hospital and during transfer to a COE or intermediary hospital.

It is imperative that hypoglycemia be detected as early as possible, even within the first hours of the infant/child's life. Any concern of infant feeding or behavior raised by family, nursery/midwifery staff or other medical care team members must result in a plasma glucose check. A glucometer is essential in all hospital nurseries.

Family concerns must be addressed since caregivers, parents, or other family members, without ability to identify cause, are often the first to notice and verbalize concern that something is amiss in the newborn. Signs of hypoglycemia in the newborn include excessive hunger or feeding disinterest, lethargy, difficulty to rouse, jitteriness, irritability, or convulsions. As infants/neonates do not always display typical signs of hypoglycemia, a parent or other family member or health care provider

concerned that something is not right should lead to an immediate blood glucose check taken from a heel stick. Every baby born with HI must have access to a timely diagnosis to prevent brain damage and death.

Blood tests ***at the time of hypoglycemia*** can diagnose HI by measuring the levels of glucose, ketones, insulin and other substances in the same blood sample. We recommend genetic testing for all children except those likely to have transient or stress-induced HI.

Targeted HI genetic testing may also be necessary to identify specific mutations that aid in the patient's future treatment decisions. The high dextrose concentrations required for safety may only be used in a hospital as lines inserted into central blood vessels are not safe alternatives for home use.

Medication is often a vital component of treatment. Diazoxide, the only oral medication approved for the treatment of HI, is the first line therapy. It is imperative that diazoxide be available for the treatment of HI for all infants around the world. Diazoxide is on the World Health Organization (WHO) List of Essential Medications and should be added to every country's List of Essential Medications. Without diazoxide, lifelong disabilities can result unnecessarily, yet many families report serious difficulties in accessing this medication.

If the infant/ child's form of HI does not respond to diazoxide, a second medication called octreotide is often necessary after the infant/child has reached an appropriate age; octreotide is given via subcutaneous injection. It is critical that octreotide also be available to all children for whom it is prescribed by their physician. Short and long-acting octreotide/lanreotide should also be added to the WHO list of Essential Medications for HI, and they should be added to every country's list.

When diazoxide or octreotide are not enough to prevent ongoing hypoglycemia, some babies require continuous glucose (dextrose) delivered through a gastrostomy tube (g-tube). These children must have access to glucose (dextrose), gastrostomy tube supplies and medical support, and feeding pumps for home use.

Some infants/children may not respond to existing treatment options; others may have a suboptimal response or adverse side effects. All infants/children with HI who do not respond adequately to existing therapies must have the option of participation in clinical trials for which they are eligible. HI COEs will be able to provide information regarding active clinical trials. To achieve a safe and optimal quality of life, infants/children with HI and their families must be informed of clinical trials for which they are eligible.

When new treatments and imaging techniques are developed and approved by regulatory authorities, they must be added to every country's List of Essential Medications and made available to all who need them.

Genetic testing may indicate diffuse HI (affecting the entire pancreas) or suspicion of focal lesion (affecting one area of the pancreas). Infants/children with focal HI also require specialist imaging to determine where the focal lesion is located, and this expertise is found in Centers of Excellence. Focal HI may be cured by surgical resection; this requires an experienced surgical team. Severe diffuse HI that does not respond to medical therapy may require near total pancreatectomy. This surgery will result in the development of insulin dependent diabetes within a variable timeframe but may be necessary to prevent neurologic sequelae.

The care of infants/children with all types of HI (and those who develop diabetes as a result of near total pancreatectomy) is complicated, necessitating care provided by a knowledgeable multidisciplinary medical team. In addition to medical care, family members of newly diagnosed children will need immediate and ongoing psychological support access to appropriate and high-quality health education, and family care support, to commence during the hospital stay, continuing at home. home.. Infants will require ongoing developmental assessment,
The availability of home glucose monitoring tools is essential to prevent prolonged hypoglycemia over the long-term. Glucometers and test strips must be accessible... Continuous glucose monitoring (CGM) can also be of substantial benefit to families in monitoring unpredictable changes in blood glucose levels.

Infants/children with HI who have been discharged from the hospital to home must also have a prescription for intramuscular glucagon for emergency use, if prescribed by their clinician. Glucagon counteracts the effects of insulin and therefore can be given to quickly reverse severe hypoglycemia at home.

This brief overview of this rare and complex condition outlines the need for available knowledge and resources to prevent the possible long-term neurological sequalae of HI.

We have addressed the immediate needs of infants/children with HI including:

- Timely diagnosis
- Prompt appropriate treatment of hypoglycemia
- Targeted HI genetic testing
- Urgency of transfer to or guidance from an HI COE
- Need for an experienced surgical team when surgery is necessary
- Access to all necessary medications to prevent the ongoing risk of neurologic sequelae; diazoxide, octreotide, glucagon, and dextrose must all be available.
- Access to clinical trials and novel medication lead by clinician decision
- Provision of home glucose testing devices and supplies
- Gastrostomy tube placement and supplies, when necessary
- Feeding pump when necessary

Infants/children with HI require other ongoing services, which may be needed for years at varying levels of intensity including

- Child developmental support (evaluation and therapies)
- Psychological support for parents and children
- Medical care for potential secondary medical issues resulting from HI such as diabetes, seizures, and pancreatic insufficiency
- Home nursing – where available and for the most severe cases.
- Medical day care
- Proper school modifications
- Ongoing involvement of a CHI Center of Excellence
- Transition to adult care

Why is this statement needed?

In CHI's program of engagement with families, detailed analysis of the child and family's journey through the milestones of the illness have been discussed in focused working groups. While the Centers of Excellence provide excellent care, the unfortunate reality is that much needs to be done to raise awareness of illness, its propensity for preventable serious brain damage, and the multidisciplinary needs of the child and family as the child grows and develops -- across health, social care and education services.

Dissemination of the statement

CHI is embarking on a concentrated program of information sharing, ensuring that professional organizations, hospitals and those responsible for commissioning services understand the imperative to improve outcomes.

Further information can be obtained from www.congenitalhi.org.

For additional reading, please see:

International Guidelines for the Diagnosis and Management of Hyperinsulinism | Hormone Research in Paediatrics | Karger Publishers (2023)

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