Congenital Hyperin

Congenital hyperinsulinism (also called hyperinsulinemic hypoglycemia) is a disorder of abnormally high insulin levels and the most frequent cause of severe, persistent hypoglycemia-low blood sugar levels-in newborn babies and children. Normally, insulin is secreted by the pancreas in response to high blood sugar levels after eating food. Insulin can then reduce blood sugar to keep it within a normal range, and it also helps to store glucose in the liver as energy reserves. With hyperinsulinism, the pancreas is deregulated and secretes too much insulin all the time, independent of the body's blood sugar levels. This excess insulin starts of chain of reactions that can cause dangerously low blood sugar and a lack of glucose stores, especially when the patient has not eaten recently.

More than half of babies with hyperinsulinism will develop abnormally low blood sugar levels during the first month of life, and almost all children born with this disorder have hypoglycemia within one year. Common symptoms of low blood sugar in babies are often difficult to identify because they are similar to some normal baby activities: irritability, sleepiness, lethargy, hunger, and rapid heart rate. With early treatment and aggressive prevention of hypoglycemia, serious problems such as brain damage can be prevented. If a child's condition is not recognized or if treatment is ineffective in preventing hypoglycemia, prolonged or severe low blood sugar can cause inactivation or death of brain cells because they are not getting enough sugars to use as "fuel." This loss of function can result in permanent brain damage manifesting as seizures, learning disabilities, cerebral palsy, blindness, coma, or even death.

Risk Factors

There are a number of causes of congenital hyperinsulinism. Some forms are temporary and will resolve within days to months, while others are persistent due to genetic defects and do not go away, though in some cases they may become easier to treat as the child gets older. Prognosis correlates strongly to which type of hyperinsulinism each patient has.

The most common genetic defect to cause hyperinsulinism is KATP HI, considered the classic form of the disease. A defect in the genes that make up the potassium channel (called KATP channel) in pancreatic cells allows inappropriate insulin secretion and causes hypoglycemia. This mutation can affect the entire pancreas (diffuse KATP HI) or just one part (focal KATP HI).

A less common form of congenital hyperinsulinism is GDH HI, caused by a mutation in the enzyme glutamate dehydrogenase (GDH). GDH regulates insulin secretion in response to protein intake, so patients with a defective enzyme can develop hypoglycemia after eating a high protein meal without accompanying carbohydrates. Patients do not typically present with symptoms until three or four months of age when they wean from low-protein breast milk to infant formula.

Diagnosis and Management

The diagnosis of hyperinsulinemia is based on history, physical exam, and lab testing. Insulin levels in the blood fluctuate widely over time in patients with hyperinsulinism, so it is more reliable to test for low free fatty acids and ketones at the time of hypoglycemia. Diagnosis can also be made by the glucagon stimulation test, which shows a rise in blood glucose after an injection of glucagon. A fasting study is sometimes required to provoke hypoglycemia and confirm the diagnosis.

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Identifying a genetic defect can help determine the patient's specific type of hyperinsulinism. The DNA from a blood sample can be analyzed for the most common mutations, but this process can take two weeks or longer. For more immediate decisions, acute insulin response studies (AIRs) are performed by injecting glucose and insulin-stimulating drugs over a short period of time. The specific pattern of insulin responses to these agents can help narrow down the genetic mutation affecting the patient's pancreatic cells.

Prompt treatment of hypoglycemia due to hyperinsulinism is essential to prevent brain damage. Short-term, hypoglycemia can be treated by drinking juice or another carbohydrate-containing drink, or if severe, by injecting intravenous glucose. Glucagon infusions may also be given to temporarily stimulate the release of glucose from the liver and stabilize blood sugar levels. Longer-term, a pattern of regular feeding ensures there are no fasting periods during which a child could become hypoglycemic. Breast milk, formula, cereals or other starches, or sugar water via a feeding tube through the nose are all options to ensure that the baby has enough carbohydrates at all times.

Strategies to manage this disease depend on the type of hyperinsulinism. Medications include diazoxide (closes the KATP channel), octreotide (inhibits insulin secretion), and nifedipine (blocks calcium entry into cells). Children with diffuse KATP-HI often require surgical removal of 95-99% of the pancreas. Focal KATP HI may be cured if the affected area is removed, because the remainder of the pancreas is normal. Localization of the lesion helps to get the correct diagnosis and allows the surgeon to remove only a small part of the pancreas if possible.

Education of the patient and family and long-term follow-up are essential to lifelong treatment of hyperinsulinism. Patients should be taught how to check their own blood sugar and manage their diet and medications. Family members should understand the signs and symptoms of hypoglycemia and be instructed to call the local emergency medical service if they are unable to treat a hypoglycemic episode or if the patient does not respond to treatment promptly.

Congenital Hyperinsulinism in Arab Populations

Because congenital hyperinsulinism is so variable, it is hard to accurately measure the incidence in a given population. It has been estimated that in Oman and Kuwait, about 5 babies per 100,000 live births have hypoinsulinemia. The number is far higher in Saudi Arabia, where about 37 per 100,000 births are affected. In comparison, in the United States congenital hypoinsulinemia occurs in approximately 2-4 patients per 100,000 live births. Particularly in Saudi Arabia, genetic counseling about the risk of recurrence in subsequent children may be appropriate. Techniques for prenatal diagnosis are available at some medical centers.