Review of nearly 500 patient cases shows surgery benefits for congenital hyperinsulinism

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A review of nearly 500 cases of infants with severe congenital hyperinsulinism who underwent partial or near-total removal of their pancreas for persistent hypoglycemia at Children's Hospital of Philadelphia (CHOP) showed that surgeons can cure virtually all patients with the focal, or localized, form of the rare genetic disease. Surgery also can prevent complications in patients with the diffuse form, in which defective insulin-producing cells occur throughout the pancreas.

The review, first presented during the 2018 American Pediatric Surgical Association Annual Meeting, represents the world's largest single-center case series of patients with congenital HI.

"Over the course of the past two decades, The Congenital Hyperinsulinism Center at CHOP has taken a multidisciplinary approach that combines pediatric endocrinology, genetics, radiology, pathology, and surgery to diagnose and treat appropriately selected HI patients with pancreatectomy," said N. Scott Adzick, MD, Surgeon-in-Chief at Children's Hospital of Philadelphia and lead author of this paper. "Since most children's hospitals only encounter one or two cases per year, it is important that children with this rare disease receive medical care from an experienced team."

In congenital HI, inherited mutations disrupt the insulin-secreting beta cells, allowing insulin levels to become excessive, essentially making it

the opposite of diabetes. This oversecretion causes persistent hypoglycemia (low blood sugar) and can lead to irreversible brain damage or death if not treated properly.

"Many families experience weeks of stress before they are transferred to CHOP for definite treatment," said Diva De León-Crutchlow, MD, a pediatric endocrinologist and Director of CHOP's Congenital Hyperinsulinism Center and co-author of the paper.

Patients with focal disease can be cured with a selective partial pancreatectomy, which removes only the affected portion of the pancreas and preserves the normal pancreas. Alternatively, patients with diffuse disease often require a near-total pancreatectomy in which surgeons remove at least 95 percent of the pancreas. This surgery helps control the hypoglycemia but increases the patient's long-term risk of developing diabetes. There are also a variety of atypical cases of HI that require special considerations.

According to this review, 47 percent of patients with surgically treated HI between 10 and 20 years old have diabetes, and all patients who developed diabetes had near-total pancreatectomies to treat diffuse HI. The team is studying a variety of aspects of the disease to better treat patients with diffuse HI. In addition to studying the underlying genetic causes of HI, they are also studying how the disease functions at a molecular level with the goal of developing targeted therapies that would reduce the need for surgery.

"We are actively pursuing clinical trials for new therapies that may improve the quality of life for patients with diffuse HI, including an investigational drug called exendin-(9-39) that can increase fasting blood glucose in these patients," De Leon-Crutchlow said. "The therapy has been shown to be effective in older patients and we are currently studying its effects in younger patients."

The study team is also examining the use of modern technology for monitoring and treating hypo- and hyperglycemia in children and adults with hyperinsulinism.

"Our team's approach is able to distinguish focal from diffuse HI, localize focal lesions, and cure almost all focal patients with a partial pancreatectomy, and while we cannot cure diffuse HI, we can help prevent brain damage and severe hypoglycemia commonly associated with the disease," said Adzick. "When all is said and done, the children treated with our approach to focal HI have been able to lead normal lives and not worry about the effects of this rare condition."

More information: N. Scott Adzick, et al, "Surgical Treatment of Congenital Hyperinsulinism: Results from 495 Pancreatectomies in Neonates and Children," American Pediatric Surgical Association Annual Meeting. May 4, 2018; Palm Desert, CA.

Provided by Children's Hospital of Philadelphia