

Hormone infusion improves pancreatic insulin production in cystic fibrosis patients with or at risk for diabetes

July 21 2022



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Cystic fibrosis is well-known for attacking the lungs through thick blockages of mucus, but those with the condition often also develop

diabetes because of the way cystic fibrosis can affect the pancreas. Since diabetes has been linked to worse lung function, this creates a vicious cycle, with diabetes acting as a multiplier on the patient's already damaged lungs. However, new research shows that infusing a hormone called glucagon-like peptide-1 (GLP-1) into patients with cystic fibrosis who have diabetes or are at risk for it can improve function of impaired islet cells in the pancreas, which help keep blood sugar in check. This research was published in *Diabetes*.

"This finding supports the likelihood that GLP-1 agonist medications could have [therapeutic benefit](#) in the treatment and possible prevention of cystic [fibrosis](#)-related diabetes," said the study's co-senior author, Michael Rickels, MD, the Willard and Rhoda Ware Professor in Diabetes and Metabolic Diseases in the Perelman School of Medicine at the University of Pennsylvania. "Better treatment of cystic fibrosis-related diabetes is critical for preserving pulmonary function, and we are now testing longer-term effects of a GLP-1 agonist on metabolism in a separate clinical trial."

Almost 9 out of 10 people with cystic fibrosis also experience pancreatic insufficiency, a condition in which the pancreas is unable to produce enough of the enzymes needed for proper digestion. An estimated one in five people with cystic fibrosis currently have diabetes. A significant complicating factor is that these patients often don't respond to [insulin injections](#) in the same way as people who have diabetes but not cystic fibrosis.

GLP-1 is an intriguing target because it is a hormone involved in digestion. In the pancreas, it helps control insulin production, contributing to the body's natural blood sugar balance. As such, this hormone is heavily tied to the functioning of pancreatic islet cells.

Searching for a more [effective treatment](#) for cystic fibrosis patients who

are pancreatic-insufficient, Rickels and co-senior author Andrea Kelly, MD, a professor of Pediatrics at the Children's Hospital of Philadelphia (CHOP), tested two different types of hormone infusions. These hormones are known to improve the function of [islet cells](#) in the pancreas. While the study's subjects received 90-minute continuous infusions of one hormone or the other, the thought is that medications called agonists that are longer-acting versions of these hormones in the body could be quickly injected just once a week, a contrast to daily multiple insulin injections.

The study was conducted among 36 patients. They received either the GLP-1 hormone or an infusion of the glucose-dependent insulinotropic polypeptide (GIP) hormone. Then, they also each received a placebo infusion on another occasion to serve as a comparison to the hormone infusion.

Natural insulin production in patients who received the GLP-1 hormone rose significantly compared to when they received placebo infusion. Equally important, the researchers saw no change in the body's insulin production among those who were infused with GIP. This likely means that loss of function tied to the [hormone](#) GIP is more complex than what was discovered about GLP-1.

"Identifying the mechanisms underlying diabetes in cystic fibrosis offers the possibility of developing interventions to prevent or delay diabetes development and ease the treatment burden for people with established cystic fibrosis-related diabetes," Kelly said. "This work may also provide additional insight into islet function that may be relevant for other forms of [diabetes](#)."

Rickels and Kelly are conducting a new clinical trial of a currently available GLP-1 agonist as a proof-of-concept of the therapeutic value for this patient population to see whether weekly administrations of the

agonist for six weeks has the same effect as the continuous infusions the team already studied.

If the weekly agonist doses prove effective, it could be an alternative to daily insulin injections, which can be inconvenient and inconsistent.

"Our hope is to delay or significantly reduce the need for complex insulin management through preserving islet function and [insulin secretion](#) in individuals with [cystic fibrosis](#), potentially via a once-weekly GLP-1 agonist injection therapy," Rickels said.

More information: Sarah C. Nyirjesy et al, Effects of GLP-1 and GIP on Islet Function in Glucose Intolerant, Pancreatic Insufficient Cystic Fibrosis, *Diabetes* (2022). [DOI: 10.2337/db22-0399](https://doi.org/10.2337/db22-0399)

Provided by Perelman School of Medicine at the University of Pennsylvania

Citation: Hormone infusion improves pancreatic insulin production in cystic fibrosis patients with or at risk for diabetes (2022, July 21) retrieved 28 January 2023 from <https://medicalxpress.com/news/2022-07-hormone-infusion-pancreatic-insulin-production.html>

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