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Cystic Fibrosis Research News

Title:

Incretin dysfunction and hyperglycemia in cystic fibrosis: role of acyl-ghrelin

Authors:

Xingshen Sun[a], Yaling Yi[a], Bo Liang[a], Yu Yang[a], Nan He[a], Katie Larson Ode[b,c], Aliye Uc[b,c], Kai Wang[d], Katherine N. Gibson-Corley[b,e], John F. Engelhardt[a,b], Andrew W. Norris[b,c,f]

Affiliations:

[a]Department of Anatomy and Cell Biology, University of Iowa, Iowa City, IA 52242, USA;
[b]Fraternal Order of Eagles Diabetes Research Center, University of Iowa, Iowa City, IA 52242, USA;
[c]Department of Pediatrics, University of Iowa, Iowa City, IA 52242, USA;
[d]Department of Biostatistics, University of Iowa, Iowa City, IA 52242, USA;
[e]Department of Pathology, University of Iowa, Iowa City, IA 52242, USA;
[f]Department of Biochemistry, University of Iowa, Iowa City, IA 52242, USA

What was your research question?

We wondered whether a hormone named acyl-ghrelin contributes to diabetes in CF. Acyl-ghrelin is a hormone produced in the stomach and can reduce insulin secretion from beta-cells. Prior work has found that patients with cystic fibrosis have elevated levels of acyl-ghrelin in their blood.

Why is this important?

Diabetes occurs when blood sugar is too high and, unfortunately, is a common problem facing many persons with CF. This is termed “cystic fibrosis related diabetes” (CFRD). CFRD occurs in large part because the beta-cells of the pancreas become unable to produce sufficient amounts of insulin to control blood sugar levels. What has perplexed researchers, though, is that plenty of beta-cells remain in the pancreas of individuals who have CFRD. This suggests that the beta-cells in CF have defective function preventing proper insulin secretion. Perhaps elevated acyl-ghrelin is part of the reason insulin secretion is insufficient in CF.

What did you do?

We tested CF ferrets for altered acyl-ghrelin levels. We found that CF ferrets, just like humans with CF, have higher than normal acyl-ghrelin levels. The CF ferrets also developed elevated blood sugar levels, much like humans with CFRD. This allowed us to test whether the elevated

levels of acyl-ghrelin might be contributing to the elevated blood sugar levels. We tested this by administering to CF ferrets a drug that blocks acyl-ghrelin's actions.

What did you find?

The results were striking. The acyl-ghrelin blocking drug dramatically lowered blood sugar levels in the CF ferrets. Furthermore, the acyl-ghrelin blocking drug increased the amount of insulin secreted relative to blood sugar.

What does this mean and reasons for caution?

These results indicate that elevated acyl-ghrelin levels in CF contribute to increased blood sugar levels. This appears to occur via reducing insulin secretion. These results, however, do not have immediate clinical utility, as drugs that block acyl-ghrelin are not available for use in humans. Furthermore, drugs that block acyl-ghrelin have potential side effects which could be dangerous in CF patients, such as nausea, vomiting, and weight loss.

What's next?

There have been few studies to date of acyl-ghrelin in humans with CF, other than to show it is generally elevated. Further human studies are needed to help understand why it is elevated and whether its elevation is correlated with human CFRD.

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cfresearchnews@gmail.com