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LANCET REPORT

Hormone drug combination therapy gives new hope to tackle diabetes

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New findings from clinical studies on thousands of type-2 diabetics in the US and Canada may open up a new treatment to counter the world's most prevalent disease.

The systematic review and meta-analysis study, led by a doctor of Indian origin and published in the latest edition of *The Lancet*, finds that a combined treatment with a drug that mimics the action of a gut hormone and basal insulin is much more effective in improving blood sugar control than all existing anti-diabetic treatments. The new approach also reduces the risk of hypoglycemia, or low blood sugar, and weight gain associated with the existing treatment regime.

Gut hormones or gastrointestinal hormones control various functions of the digestive organs. They are secreted by enteroendocrine cells in the stomach, pancreas and small intestines.

Basal insulin typically keeps blood glucose at consistent levels during periods of fasting.

"Achieving normal blood sugar levels in people with type 2 diabetes is compromised by the adverse side effects plaguing currently available treatments. Some anti-diabetic treatments increase risk of hypoglycemia and weight gain, which put patients at increased risk of heart attack and stroke, as well as reducing their quality of life," said Ravi Retnakaran, lead author of *The Lancet* report and an endocrinologist at Mount Sinai Hospital, Toronto, who led the clinical studies.

The hormone-based therapy was recently introduced as a new treatment for patients with type 2 diabetes because of its ability to regulate blood sugar levels and to generate weight loss as opposed to weight gain. Moreover, these hormones—GLP-1 agonists—only stimulate insulin secretion when blood glucose levels are high, without increasing risk of hypoglycemia.

The hormone-based therapy was recently introduced as a new treatment for patients with type 2 diabetes because of ability to regulate blood sugar levels

However, their optimal role in the management of type 2 diabetes has yet to be established, Retnakaran said in a *Lancet* note reviewed by *Mint*.

Retnakaran and colleagues identified 2,905 studies over 64 years involving basal insulin and GLP-1 agonists in adults with type 2 diabetes. The analysis of 15 randomized trials involving more than 4,300 participants showed that the combination of basal insulin with GLP-1 agonists resulted in a 92% greater likelihood of achieving target blood sugar control, with similar rates of hypoglycemia and an average weight loss of more than 3kg compared with other anti-diabetic treatments. Compared with full basal insulin-based treatments, the combined treatment generated modestly better blood sugar control, but had a 33% lower risk of hypoglycemia and weight loss of almost 6kg more. According to Retnakaran, combining a GLP-1 agonist with basal insulin is a treatment strategy that can achieve the ideal triumvirate of short-term outcomes in diabetes management. "Optimal glucose control alongside weight loss and a low risk of hypoglycemic episodes. As such, this combination treatment could improve the management of people with type 2 diabetes," he said.

"Perhaps the most practical and immediate issue is whether the fixed-dose combinations of a GLP-1 agonist and basal insulin in development will supersede other approaches. This is an unsettled question, but it seems likely that fixed-dose combinations will be welcomed in view of their convenience and efficacy," said John Buse, chief of the division of endocrinology at the University of North Carolina School of Medicine and a co-author of the report.

However, the cost of this hormone-based therapy is expected to be high, at least in the initial period of introduction. "The major barrier to widespread adoption of these treatments is cost—both GLP-1 agonists and insulin analogues are among the most expensive in diabetes care. One can hope that some incremental cost savings will come with combined products. It has been a 20-year journey, but the combination of GLP-1 agonist and basal insulin has finally arrived as a more powerful and safer alternative to insulin in the management of type 2 diabetes," said Buse.

China and India, the two most populous countries, have the widest prevalence of diabetes disease.

The latest and one of the most comprehensive nationwide surveys for diabetes in China, published in the *Journal of the American Medical Association* in the first week of September, shows the country has 114 million diabetics. India has 67 million patients and it is growing at least 10% a year, according to Indian Dietetic Association.

The International Diabetes Federation (IDF) estimates that at least 285 million people are diagnosed with diabetes worldwide. This number is expected to touch as high as 438 million by the year 2030, according to IDF.

New drugs