

New drugs for diabetes could treat host of other issues

Newer drugs within a class originally developed to treat diabetes are now gaining attention as potential treatments for a host of other medical problems, aside from their effects such as significant weight loss.

The most potent among the newer drugs are semaglutide and tirzepatide, both of which can lead to weight loss of about 20 per cent. Semaglutide, developed by Danish pharmaceutical company Novo Nordisk, is sold as Ozempic for the treatment of diabetes and at a higher dosage as Wegovy for obesity. US rival Eli Lilly markets tirzepatide as Mounjaro for diabetes and Zepbound for weight loss.

Early research, however, suggests that these glucagon-like peptide 1 (GLP-1) drugs may be able to do much more, such as treating dementia, addictions and mental conditions.

In March, Wegovy was approved by the US Food and Drug Administration for use to reduce the risk of cardiovascular death, heart attack and stroke in adults with cardiovascular disease who are either obese or overweight.

In the same month, Novo Nordisk announced the early termination of its clinical trial for Ozempic – conducted in 28 countries with more than 3,500 participants – because of the very good early outcomes. It said the trial showed a significant 24 per cent reduction in the progression of chronic kidney disease and in cardiovascular and kidney-related deaths for people treated with 1mg of semaglutide compared with those receiving a placebo.

Such a big reduction in the progression of the disease could have a significant impact on the number of people getting kidney failure and requiring a transplant or lifelong dialysis.

“I can now tell my patients it will protect your kidneys,” said Dr Tham Kwang Wei, a senior endocrinologist at Woodlands Health.

Singapore has one of the highest diabetes-induced kidney failure rates in the world, with six new cases diagnosed every day. The National Kidney Foundation, the biggest dialysis provider here, estimates that the country spends \$300 million a year on dialysis



Semaglutide is sold as Ozempic for the treatment of diabetes. Early research suggests such GLP-1 drugs may be able to do much more, such as treating dementia, addictions and mental conditions. PHOTO: REUTERS



A BIG DIFFERENCE

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DR THAM KWANG WEI, a senior endocrinologist at Woodlands Health.

treatment.

The trial also showed that there was a 20 per cent reduction in deaths from any cause in the

group on semaglutide compared with those on placebo.

Several other studies are now exploring the effect of the GLP-1 drugs on neurodegenerative diseases, addictions and mental conditions such as depression and anxiety. Secondary outcomes from previous trials appeared to indicate possible benefits.

Dr Tham said: “The main reason we are seeing such dramatic health impact... from the newer generation of treatments is that these medications result in greater amount of weight loss of 18 to 22.5 per cent at their respective highest doses in clinical trials than the other obesity medications, which can result in maximum of 10 per cent weight loss.”

She said another benefit is that the drugs can reduce inflammation and oxidation in the blood vessels and tissues.

This, she said, “further enhances insulin sensitivity and glucose metabolism, improves tissue function of the heart, blood vessels and brain cells, which, in turn, results in reduction in heart attacks and strokes, improves cognitive function, and reduces Alzheimer’s disease and chronic kidney disease”.

Associate Professor Lita Chew, SingHealth’s group chief pharmacist, noted that while the two blockbuster drugs – semaglutide and tirzepatide – belong to the

same class of medication, there are some slight differences which can result in different effects on medical problems.

“A drug works like a key that fits into a receptor (lock), which can be found across different cells. Depending on how well it binds and which receptors are targeted, a drug can give rise to various effects. For this reason, even drugs that belong to the same class can have different effects and potency,” she explained.

An article in the Nature journal on Sept 26 postulated that these drugs might work along different pathways. It said the body has two GLP-1 systems – one in the brain and the other in the gut. While stating that the mechanism of GLP-1 drugs is not fully understood, the article said they likely work on receptors in the brain that control tastes and rewards.

It stated: “They are thought to dampen the brain’s reward system so that an individual might not feel the urge to drink another glass of wine, smoke another cigarette or eat another slice of pizza to get that extra rush of pleasure.”

Added Prof Chew: “When selecting a medication, doctors and patients work together, considering the primary condition, whether there are any other health issues, and preferences such as cost and the choice between pills or injections.”

The newer drugs are significantly more expensive and there is no subsidy for them. For example, prices for the Ozempic pen – which is used for four weekly injections – range from \$250 to more than \$400 in Singapore.

There is, however, the Medication Assistance Fund – a special subsidy for expensive drugs that some people require – for an older GLP-1 drug, dulaglutide, which is marketed by Eli Lilly as Trulicity. It costs about \$130 for a month’s supply. People who qualify through means testing can get a subsidy for the medication ranging from 40 per cent to 75 per cent. But there are possible serious side effects, such as pancreatitis, gallbladder problems, thyroid cancer and kidney injury.

The doctors say that while the newer drugs, which seem to have milder side effects, appear to be the magic bullet that cures many ills, people should not take these drugs unless their medical conditions require them to do so.

Said Professor Tai E Shyong, a senior endocrinologist at the National University Hospital: “We do not yet know what the long-term effects of these drugs are.”

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