

- Diseases— Diabetes

WINNING THE FIGHT AGAINST DIABETES

Philippine Daily Inquirer · 14 Jul 2018 · B3 · By Charles E. Buban

WORLDWIDE, diabetes rates have tripled over the past 18 years—from 171 million in 2000 to 451 million this year.

Unfortunately, if the current trend continues, the total number of individuals with diabetes is expected to reach 693 million by 2045, pushing the global cost of the disease to unimaginable levels. The current global cost of the disease is already reaching \$850 billion a year, a reason why science is striving to find a cure to this chronic disease. But how close are we? Essentially, those with diabetes have several issues to contend with:

- how to successfully control their A1C, blood pressure, and cholesterol while dealing with their medicine's rising cost; compliance (the number of times their medicines should be taken every day); and how they should be administered, especially these medicines must be delivered by injection.
- finding and accessing the services of a dietitian or a nutritionist as they need to follow an individualized meal plan to manage their condition.
- how to eat right if the food they need to eat is mostly way beyond their budget or is not readily available.
- squeezing exercise into their busy daily routine.
- how to quit smoking and stay off the nicotine dependence

Failure to address these issues has contributed to diabetes epidemic that is spreading particularly fast in less developed countries as more people there adopt Western diets and urban, more sedentary, lifestyles.

While both Type 1 and Type 2 diabetes are characterized by having higher than normal blood sugar levels, the cause and development of the conditions are different: Type 1 diabetes results from the individual's immune system mistakenly attacking the insulin-producing beta cells in the pancreas (nobody knows yet, why this occurs, or how to stop it).

People with Type 1 diabetes need to inject themselves with insulin to compensate for the death of their beta cells so they are now insulin-dependent.

On the other hand, people with Type 2 diabetes don't have this problem. Instead, those with Type 2 diabetes lose their ability to respond to insulin—known as insulin resistance. As a result, the body compensates for the ineffectiveness of its insulin by producing more. Over time, the strain placed on the beta cells can destroy them, diminishing insulin production.

For years, the biotech industry has been striving to develop new if not improve existing diabetes treatments in order to chase the holy grail, that is, finding a lasting cure for both Type 1 and Type 2 diabetes.

Artificial pancreas

After a long lead-in period, artificial pancreas technology is well on its way to revolutionizing the treatment of diabetes. Artificial pancreas systems are wearable devices that take charge of the crucial process of measuring glucose levels and delivering precise doses of insulin.

This system can keep the disease on a tighter leash than they can, by testing more frequently and delivering more precise insulin doses.

However, an artificial pancreas doesn't replace the actual organ as the device involved are not implanted or surgically attached—they only take over one of the organ's digestive responsibilities: that

is, regulating glucose levels.

The United States Food and Drug is closely monitoring three main categories of Artificial Pancreas Delivery Systems being perfected:

- The threshold suspend device system, which is being designed to help reverse the dangerous drop in blood glucose level (hypoglycemia) or reduce the severity by temporarily suspending insulin delivery when the glucose level falls to or approaches a low glucose threshold.

This type of system serves as a potential back-up when the patient is unable to respond to a low blood sugar (hypoglycemic) event.

- insulin-only system is designed to automatically increase or decrease the amount of insulin infused based on the Continuous Glucose Monitoring (CGM) values. These systems could be hybrid systems that only automatically adjust basal insulin with the user manually delivering bolus insulin to cover meals, or could also be fully closed loop systems, where the system can automatically adjust basal insulin and provide insulin for meals.

- A bi-hormonal control system on the other hand, use two algorithms to instruct an infusion pump to deliver two different hormones: one is the insulin to lower glucose levels and another to increase blood glucose levels. The bi-hormonal system is designed to mimic the glucose-regulating function of a healthy pancreas more closely than an insulin-only system.

Innovative technologies

Aside from developing artificial pancreas, diabetes management is also on the verge of being disrupted by innovative technologies that include noninvasive glucose monitoring sensors, wearables, and apps.

The United Kingdom-based company MediWiSe is currently perfecting GlucoWise, a noninvasive, pain-free device that makes traditional blood sampling a thing of the past.

This unique sensor will allow one to monitor blood glucose levels without the need to pierce the skin. It will allow unlimited testing without the need for costly consumables (like sensoruse sensor strip), so the patient could now test as often as he or she likes without having to worry about the cost or pain.

GlucoWise device is also being paired to an App and will employ Smart Cloud technology that promise to deliver personalized advice and alerts, helping one to fully manage his or her condition.

Similarly, the US FDA already cleared Abbot's FreeStyle Libre Flash Glucose Monitoring System, a device that uses a small sensor wire inserted under the skin to determine glucose levels in adult with diabetes.

The individual, however, will need a wand-like device that must be waved over the sensor to measure and give a readout of the user's glucose levels.

Inhaled insulin

The most promising alternative route of insulin administration may be pulmonary delivery by inhalation. While inhaled insulin has been under development for years, it is only recently that an oral inhaler became available to the market.

At the moment, the only approved inhaled insulin is MannKind's ultra-rapid-acting inhaled insulin Afrezza, which is applicable to both adult patients with Type 1 and Type 2 diabetes who need additional control beyond oral drugs but are not fully comfortable with injections.

However, patients who are considering this option are strongly advised to work closely with their doctor especially if they have a lung condition such as asthma, chronic obstructive pulmonary disease (COPD), a history of lung cancer, liver or kidney disease, an electrolyte imbalance, and heart disease or heart failure.

This is because Afrezza has been found, in some cases, to cause serious side effects, including sudden lung problems like bronchospasms.

New class of drugs

There is no such thing as a one size fits all approach to diabetes management so pharmaceutical companies are continuously developing new kinds of drugs, formulated to assist a patient's body in its ability to metabolize glucose and to successfully reduce the necessity for treatment with more aggressive diabetes management drugs like insulin.

Among these drugs recently introduced include exenatide extended-release Bydureon, a once weekly injectable drug for people with Type 2 diabetes. Bydureon is similar to drug Byetta but is designed to be released to the body much slower thus, requiring just one injection a week (Byetta is injected twice a day).

Bydureon works by responding to the presence of carbohydrates in the small intestine, stimulating release of insulin and at the same time, inhibiting the release of glucagon (a type of hormone released in response to low blood glucose levels and to events whereby the body needs additional glucose).

Bydureon has also been shown in studies to be beneficial for weight loss.

In April 2018, the US FDA approved Bydureon as an add-on to basal insulin in adults who need extra blood sugar control. However, because of its price, doctors only recommend this drug to those who really need of better blood glucose control.

Empagliflozin (Jardiance) is another once-daily diabetes drug that is used to control blood glucose levels in people with type 2 diabetes. In 2016 the US FDA approved a new indication for this drug as studies found it to be able to lower the risk of cardiovascular death in adult patients with Type 2 diabetes and heart disease.

This is significant because death from heart disease is 70 percent higher in people with diabetes compared to those without the disease.

Another interesting development is the introduction of insulin glargine Toujeo, a longacting insulin injection designed to help patients with diabetes control their blood sugar levels over a 24hour period.

In the clinical trials evaluating Toujeo, all of the primary study endpoints were met by demonstrating similar blood sugar control with Toujeo as compared to similar insulin product. Toujeo's onset is within six hours, and it has a duration of up to 36 hours, reaching a steady blood level by about day five.

To help lower the number of injections per day as well as the number of pens used for those who need higher insulin doses, the Toujeo comes in SoloStar pen that can make life easier for patients with Type 2 diabetes.

Commonly known as glucagon-like peptide 1 (GLP-1) receptor agonists, these drugs are normally prescribed for patients who have not been able to control their condition with just metformin and/or other oral drugs. They can be taken alone, or alongside metformin and/or other diabetes drugs.

The GLP-1 receptor agonists work by mimicking the functions of the natural incretin hormones in the body that help lower post-meal blood sugar levels.

These drugs stimulate the release of insulin by the pancreas after eating, even before blood sugars start to rise. They could also inhibit the release of glucagon, a type hormone secreted by the pancreas and causes the liver to release its stored sugar into the bloodstream.

Also, these drugs could slow glucose absorption into the bloodstream by reducing the speed at which the stomach empties after eating, thus making a person feels more satisfied after a meal.

Overall, most experts see GLP1 receptor agonists as effective and innovative agents for patients with Type 2 diabetes and other chronic conditions, who are either uncontrolled or intolerant to firstline metformin therapy.