NOVO NORDISK BEST PRACTICES IN DIABETES MANAGEMENT:

Strategies To Prevent and Manage Hypoglycemia

Middle Eastern Endocrinologists Share Their Approaches to Treating Hypoglycemia

While hypoglycemia is a condition that diabetics around the world can experience, there are culturally determined differences in how endocrinologists treat the condition. We recently spoke with two Middle Eastern endocrinologists on their successful approaches to dealing with hypoglycemia in their diabetes patients.

> "I try to get diabetes patients to eat frequent small meals rather than one or two meals per day."
> –Faisal Hashim, MBVS, PhD

The approach to treating hypoglycemia taken by Faisal Hashim, MBVS, PhD, a consultant at Almana General Hospital in Jubail, Kingdom of Saudi Arabia, begins with one simple step: "I decrease the insulin dose. I also try to get diabetes patients to eat frequent small meals rather than one or two meals per day. Big meals can lead to a patient first experiencing hyperglycemia and then a few hours later hypoglycemia. I advise them to divide each meal into two shares, with an injection and one share taken together and then the second share taken three or four hours following the insulin injection. Diabetes patients are much less likely to experience hyperglycemia by taking a smaller meal followed by a snack three to four hours later. This approach works with most patients."

Dr. Hashim estimates that 10% of his patients report experiencing hypoglycemia. "The majority of events are at night. Sometimes it will occur in patients who have missed a meal due to unexpected demands at their jobs.

"Because we don't have continuous glucose monitoring systems readily available here, we have patients do more frequent testing. For adolescents, we advise their families to try to do the testing without waking up the child unless they have to." Dr. Hashim notes a happy coincidence: "Many people here are in the habit of waking up around 4 a.m. to recite some morning prayers, which happens to be right about the time hypoglycemia commonly appears. That is a big help when you want people to test right around that time."

Hypoglycemic Unawareness: "A Nightmare"

Hypoglycemia unawareness, as well as symptoms masquerading as hypoglycemia, are conditions Ali Sultan, MD, endocrinologist at International Medical Center Hospital in Jeddah, Kingdom of Saudi Arabia, has routinely encountered in his practice. "Fortunately, the percentage of my patients who experience hypoglycemia is not significant. And luckily, none of them has been where they needed emergency measures taken."

Still, he says, hypoglycemic unawareness can be "a nightmare for us and for patients. Patients come to us with their blood sugar level very uncontrolled and asking for help in controlling their diabetes and improving their blood sugar levels." Dr. Sultan educates patients to know what the signs of hypoglycemia are. "I tell them what they might experience. Knowing in advance what can happen helps them not be afraid if and when they have an actual hypoglycemic episode."

There is one drawback: Patients can often mistake some symptoms as indicative of hypoglycemia. "I tell them to protect themselves from over-reacting to the symptoms by immediately measuring their blood sugar level. Just thinking and feeling that they are having a hypoglycemic episode is not a good reason to take inappropriate actions. I have patients who think they are feeling hypoglycemic at 150 mg/dL or 170 mg/dL because they are used to having blood sugar levels of 250 mg/dL.

"Once they start checking their blood sugar level frequently and they see that they are not really hypoglycemic, I still understand that what they are feeling is not good. I don't want them to have it, so I advise them to eat something not sugary that will raise their blood sugar level. Yogurt, which is very common in our culture, is good for that. It has some, but not a lot, of sugar, it's nutritious, and generally low-fat. It's usually enough to increase patients' blood sugar level to the point that their hypoglycemic symptoms fade away."

Other steps Dr. Sultan takes may include allowing diabetes patients to have a higher A1c level, such as 8% rather than 7%, for patients who struggle with hypoglycemia. "For younger and more cooperative patients who do frequent blood testing, I do push for 7%. Also, I involve the patient's family, which at this stage of management is almost mandatory. I equip them with Glucotabs and glucagon."

> "Fifty years ago, diabetes was not that frequent in the Middle East. Since then, we've seen increased obesity, followed by a big increase in type 2 diabetes. –Faisal Hashim, MBVS, PhD

Patient Information Sharing?

In some countries, diabetes patients who are strangers to one another often informally share information in person, or visit websites that can help them locate local groups that get together to discuss their diabetes and how it has personally affected them. In the Middle East, the situation is different.

"My colleagues who have been trained in North America say that group sessions and information sharing are helpful," says Dr. Sultan, "but I don't find it happening much in our part of the world. Patients here don't want anyone else besides close family members knowing that they are diabetic." He says that putting people together to relate their experiences to one another would be a good thing. "It would be very helpful but we have to deal with patients' beliefs and customs and not try to force them to do something that may work in other areas but would be very distressing for them to do."

Dr. Hashim agrees with Dr. Sultan's observations. "There are no such groups in my country. It's very difficult to form them. Patients don't want to discuss their problems with other patients. They only want to talk to doctors or professional people." Instead, he relies on direct education delivered in his clinic by professional healthcare workers—diabetes nurses, social workers, and psychologists.

"The younger a patient is, the more we involve the family. Even adolescents tend to come with their parents. Sometimes the parents themselves have type 2 diabetes, which is very prevalent in Saudi Arabia, affecting 20% of the adult population (age-adjusted).[1] So parents who already know about diabetes precautions and routines get involved in helping their children improve their diet and other parts of diabetes management, such as reminding a child or adolescent on dosing insulin, and preparing nutritious foods for him."

Patients Who Live Alone

A more difficult group of people to treat for hypoglycemia is diabetics who live alone, though Dr. Hashim notes, most live with their families. "We have one physician colleague who lives alone. He injected himself with short-acting insulin and then went to prepare his meal. But he fell in the kitchen and went into hypoglycemia. This has happened twice. Because of his experience we advise people who live alone to place their meals in front of them before injecting insulin." The idea is that the person can immediately consume something that his bolus insulin can work on as opposed to the insulin dramatically lowering his blood sugar because the meal it is intended to cover has been delayed.

Westernized Diet

Both Drs. Sultan and Hashim note extensive changes in Middle Eastern dietary habits that have been influenced by the popularity of American convenience foods and diets. "Beginning in the 1990s and into the 2000s, we have been on exactly the same road the West has traveled in terms of dietary changes," says Dr. Sultan. This dietary shift has fueled the increase in prevalence of obesity and diabetes.

Dr. Hashim adds: "Fifty years ago, diabetes was not that frequent in the Middle East. Since then, we've seen increased obesity, followed by a big increase in type 2 diabetes. I think that obesity is the main forerunner of diabetes—the care for diabetes and obesity overlap."

"Our patients are like other patients around the world but maybe more so because our diet has so many carbohydrates such as sweets and rice," says Dr. Sultan. "We eat too much bread here and that is a big concern."

> "The presence of diabetes educators in diabetes treatment centers has made a significant difference in the care provided." – Ali Sultan, MD

Diabetes Educators

One source of help that Dr. Sultan especially appreciates is the care provided by diabetes educators. "We are lucky at this hospital to have three. They get along well with patients and use modern technology to stay in touch with our patients. They are there to help 24/7," an availability that is very reassuring to both endocrinologists and patients. The availability of diabetes educators for Dr. Sultan reaches back to 1995. "Their presence in diabetes treatment centers has made a significant difference in the care provided."

Welcome Sign: Unused Glucagon

Middle Eastern endocrinologists look for signs, direct or indirect, that their treatment and education of diabetes patients is working. When asked if his glucagon-equipped patients may have to resort to using it two or three times a year, Dr. Sultan says he is pleased to respond "No. I'm pretty happy that my patients who have glucagon on hand rarely use it. Instead, they'll come in and say, 'My glucagon has expired. Can you give me a new one?' That tells me that they are not having severe hypoglycemia because they've never had to use glucagon. I'm very happy to give them replacement glucagon."

Dr. Sultan says he has to keep in mind one concern about glucagon. "We have to import it, so that by the time it arrives here, glucagon designed to be effective for one year may already be six or even nine months old. If we give it to patients, we make sure to tell them how long they have before the glucagon expires and they need a replacement."

Dr. Hashim says that getting patients to understand the use of glucagon can be difficult. "People here tend not to go for it because there is a lot of resistance for using any kind of injection. So we are not using actually glucagon that frequently. Rather we advise patients to eat some sugar or dates in case of hypoglycemia. That is something they can understand, use, and apply better."

Treating the Elderly

As lifespans have increased world-wide, diabetics also are living longer, and so there are more older people at risk for hypoglycemia. Notes Dr. Hashim, "hypoglycemia in the elderly is more dangerous than it is in the young. The elderly may already have ischemic heart disease or other cardiac ailments. Hypoglycemia tends to create arrhythmia in the heart that can lead to sudden death. With hypoglycemia you get a gush of hormones like adrenaline, noradrenaline, and cortisol. These hormones increase the heart rate and can put the patient's heart into arrhythmia.

"Because hypoglycemia is more dangerous in the elderly, we tend to relax their blood glucose control. We try not to aim for a very low glycosylated hemoglobin A1c, opting for 8%, for example. It makes patients slightly hyperglycemic but it helps them avoid hypoglycemia."

Flexible Dosing

Another approach to defending against hypoglycemia is flexible insulin dosing, where patients don't inject insulin at set times during the day. Instead, they inject insulin just before they are eating a meal, adjusting the dose to the meal's carbohydrate content. It's a strategy that Dr. Hashim has used often. "We do it especially for adolescents or younger people who, as we know, like to eat and exercise whenever they want. They don't have a regular timetable like adults or elderly patients who are more likely to eat at a certain time and work at a certain time. Younger patients tend to be very flexible in their approach. Flexible dosing helps quite a lot, as well as using basal insulin with a long half-life, which can cover for them if they sometimes miss injections."

However, says Dr. Hashim, it takes practice to get used to and good at flexible dosing. "Because we don't have continuous monitoring devices we have patients use blood glucose meters and test strips as frequently as possible so that we can see after a week or 10 days how we need to adjust the dosage and timing of their insulin injections. From the start we emphasize that they need to know how to manage their condition because diabetes is with them 24 hours but we are not. They have to know what to do at any stage of a problem."

Hypoglycemia Remains a Concern for US and UK Doctors and Patients

For a majority of people with diabetes and the health-care experts who help them, hypoglycemia is the leading cause for concern. Left untreated—or even undetected—it is a condition that not only threatens diabetics' health but in some cases can pose mortal danger to a diabetes patient.

Who is most likely to experience hypoglycemia and what are the best approaches to treating it? Three diabetes experts from the United States and the United Kingdom spoke with us recently to answer those questions.

> "About 30% to 40% of people with type 1 diabetes suffer from one to three episodes of severe hypoglycemia in a given year."
> – Philip Cryer, MD

Who Suffers From Hypoglycemia?

"About 30% to 40% of people with type I diabetes suffer from one to three episodes of severe hypoglycemia in a given year," says Philip E. Cryer, MD, Irene E. and Michael M. Karl Professor of Endocrinology and Metabolism in Medicine, Washington University in St. Louis, Missouri. "However, there are a lot more people with type 2 diabetes so the majority of episodes of severe hypoglycemia occur in people with type 2. It's at a lower percentage than type 1 diabetes but from a much larger population.

"There is a subset type 2s, what I call advanced type 2, who are at risk for severe hypoglycemia. Although less common, it is associated with increased mortality."

Dr. Cryer defines severe hypoglycemia as an episode that requires the assistance of another person. The most serious risk it poses is death. How much of a mortal threat? Citing a pivotal study on blood glucose control and mortality rates, he notes: "Eight percent of the people who participated in the Diabetes Control and Complications Trial and died during follow up were thought to have died from hypoglycemia. That's a pretty worrisome number." [2]

Who Is Most Likely to Experience Hypoglycemia?

Aaron Leong, MD, research fellow at Massachusetts General Hospital in Boston, thinks nocturnal hypoglycemia is common to particular sets of patients. "Four groups of diabetic patients are the most susceptible: 1) patients who are on insulin at some point in their lives, especially type 1s; 2) long-standing diabetes patients who are very insulinized; 3) labile diabetes patients; 4) and the elderly.

Dr. Cryer adds that the severity of hypoglycemic episodes not only varies from person to person but can vary in the same person at different points in time. Repeated episodes create greater susceptibility. "If a person has hypoglycemia today, then a lower glucose concentration will produce symptoms of hypoglycemia tomorrow."

John Wilding, DM, professor of Medicine and honorary consultant physician, Obesity and Endocrinology Research, Institute of Ageing and Chronic Disease, University Hospital Aintree in Liverpool, United Kingdom, thinks that duration rather than age is a big contributing factor in hypoglycemia. "For both type 1 and type 2 diabetes, the incidence of hypoglycemia increases with duration of diabetes. In type 1, it has to do with the amount of residual insulin secretion." A patient who still has the ability to produce some insulin will inject some analog insulin on top of it, producing too much insulin for the amount of blood sugar it is covering. "Even though the remnant insulin is a very small amount, reducing the injected volume of insulin to compensate can often protect to a small extent against hypoglycemia. The other factor is patients' ability to produce glucagon, which opposes insulin and raises blood glucose levels.

"Over time, especially if their diabetes has been poorly controlled, patients lose the ability to secrete glucagon. That means the longer you have diabetes, the less likely you are to respond quickly to hypoglycemia by secreting glucagon. Another important factor is hypoglycemia unawareness, which means that if you experience many episodes of hypoglycemia, the brain gets used to it. Diabetics don't recognize that they are becoming hypoglycemic," notes Dr. Wilding.

Hypoglycemic Unawareness

Another problem in dealing with hypoglycemia, especially nocturnal hypoglycemia, is the reluctance of some patients to report episodes to their doctor. "Reporting of nocturnal hypoglycemia isn't automatic to patients," says Dr. Leong. " Many of them deal with nocturnal hypoglycemia on their own." They also may report hypoglycemic episodes indirectly without knowing what they were experiencing. "Some patients might tell

me that they have poor sleep or are waking up in the middle of the night not exactly sure why they're waking up and feeling very hungry and having to snack at 3 a.m. Things like that tell me that perhaps they're having nocturnal hypoglycemia."

Dr. Leong considers two possibilities as he works to determine if a patient has experienced hypoglycemia. "One is a really high blood sugar level in the morning—reactive hypoglycemia—where they might have had a hypoglycemic event during the night but don't realize it. The other is probing to see if they have been snacking at midnight, either because they went hyperglycemic with really high blood sugar or were dealing with blood sugar level at around 4 millimoles per liter or below. In general, if a patient is a very well controlled, especially a type I, and his A1c levels are below 7%, I just ask him straight out if he experienced any hypoglycemia overnight. For patients with A1c levels in the 10% range, it's most likely hyperglycemia."

Dr. Leong says a common problem among patients is their unawareness of whether they have had a hypoglycemic episode. "Patients who sense they are having a hypoglycemic episode usually wake up but may fall back asleep and not remember. So sometimes you need help from a partner who sleeps in the same room and is aware when a patient wakes up in the middle of the night." Dr. Leong builds on that late-night wakefulness by advising his patients, whether aware or unaware, to check their blood sugar level at 3 a.m. or 4 a.m.

"Nocturnal hypoglycemia can happen at any time from midnight to 6 a.m. To avoid it, I may decrease a patient's nighttime insulin dose or advise them to have a late-night snack before going to bed. Typically snacking with some protein will prevent a hypoglycemic episode overnight."

Is there a workable treatment for hypoglycemia unawareness? Dr. Cryer says that one approach has succeeded in many cases. "It's now known that hypoglycemia unawareness is reversible. It's not a permanent feature of diabetes. So for the patient who doesn't know and doesn't recognize their hypoglycemic episodes, that phenomenon can be reversed by a rather short period of time—two or three weeks of scrupulous avoidance of hypoglycemic episodes. The idea is that episodes of hypoglycemia cause unawareness. So if you can avoid those episodes, the awareness will come back."

Clinical Inertia: A Doctor-Patient Conspiracy?

Clinical inertia is defined as the failure to intensify therapy of any sort when it's clinically necessary. It's very common in diabetes. Dr. Wilding says it often is the result of a relationship between patient and doctor where both parties look the other way when it comes to changes in the patient's numbers. "I think of it as a conspiracy between the doctor and the patient," says Dr. Wilding. "The typical consultation would go something like this:

Doctor: "Well, your A1c is rather high today, isn't it?"

Patient: "Yes, it's at 8%. Well, doc, there was that recent holiday, and then I had a vacation, and I really haven't been doing much exercise lately. I'm going to really try hard and I'm sure at my next visit, my numbers will be better."

Doctor: "Okay. Let's set up your next appointment."

"This goes on for years sometimes, and nobody changes anything. It's a kind of conspiracy, very common, where the agreement is that neither the patient nor the doctor is willing to address the real issues."

What Is the Threshold for Hypoglycemia?

Is there a blood glucose level at which a physician can say definitively that a patient is suffering from hypoglycemia? Dr. Cryer says it is difficult to say whether even a single patient is experiencing hypoglycemia let alone assigning a number to patients in general. "Blood glucose thresholds for hypoglycemic symptoms can change in people with diabetes, so that the glucose level that causes symptoms at one point in time for a type 1 patient can be quite different from the glucose level that would cause symptoms at another point in time. So you can't really put a number on it. The closest one can come to a number is the plasma glucose concentration at which glucose counter-regulatory responses, such as increases in epinephrine and glucagon that occur as glucose levels fall in non-diabetic individuals—say in the range of 65 to 70 milligrams per deciliter. That's a marker for biological hypoglycemia in non-diabetic individuals."

Treating hypoglycemia: One date contains 15 grams of carbohydrate and will raise blood glucose levels by 50 mg/dL

Dr. Wilding acknowledges that symptoms alone won't tell you if you are observing a real case of hypoglycemia. "The only way you can actually tell is to measure the blood glucose level. Hypoglycemia would be below 3.5 mmol per liter or 65 mg/dL to 70 mg/dL."

> "The idea that everybody with diabetes needs to have an A1c of less than 7% just isn't logical. Some people will do fine at less than 7%. Others may require 7.5% or 8%." – Philip Cryer, MD

Dangers Posed by Sulfonylureas

Dr. Cryer says there are three components to a successful treatment of hypoglycemia: first, acknowledge the problem, then identify risk factors, and finally, apply the relevant principles of intensive glycemic control. "Control falls into the two categories of drug selection and technology. With respect to drug selection, hypoglycemia is caused by insulin, sulfonylurea, and glinide. Other medication used to treat type 2 diabetes don't cause hypoglycemia. So the first consideration in drug selection is to avoid sulfonylureas and glinides.

"The second way is to use physiologic insulin replacements, and the third is the use of insulin analogs. They are advantageous with respect to the frequency of hypoglycemia, particularly nocturnal hypoglycemia, with the use of both long-acting and short-acting insulin analogs. The recognition that hypoglycemia is an important problem for people with diabetes who are treated with insulin or a sulfonylurea or glinide is relatively recent."

Individualized Glycemic Goals

Dr. Cryer cites a fourth step: selecting an individualized glycemic goal. "I wrote about this in an article in *Diabetes*.[3] The appropriate glycemic goal is the lowest A1c that does not cause severe hypoglycemia and that preserves awareness of hypoglycemia because we know that prior hypoglycemia can result in loss of awareness.

"Individualized glycemic goals are needed. The idea that everyone with diabetes needs to have an A1c level of less than 7% just isn't logical. Some people will do fine at less than 7%. But others may require 7.5% or 8% in order to have their diabetes controlled safely," says Dr. Cryer.

"A1c levels are a moving target," says Dr. Leong. "One person's goal may have been set at 7% but in five years things can change. Now, that person's A1c level is 8%. Or maybe the physician thinks another patient should be aiming for 7%, but he has experienced multiple hypoglycemic episodes and is now very vulnerable to hypoglycemia. So now maybe targeting an A1c level of 8% for both patients is the best course."

Working With the Elderly

How should endocrinologists manage older people with diabetes? Can treatment for them be too aggressive? "There's been a lot written lately about overtreatment of diabetes at the US Department of Veterans Affairs (the US agency in charge of healthcare for military veterans)," says Dr. Cryer, "which showed that elderly patients were still being treated very aggressively for hypoglycemia."[4] That treatment was an indication that the VA was giving elderly veterans insulin doses that were too high. "For older people with diabetes, it is pointless to aim for an A1c level of less than 7%." These patients won't live long enough to reap the benefits of tight glucose control, he explains.

Dr. Leong agrees. "If patients are older than age 70, they could develop complications later on but I don't think there's going to be a huge impact on their lives. Physicians need to weigh the risks and benefits, dangers of hypoglycemia, especially with elderly patients who have limited eyesight, limited dexterity, limited social support. There are many things already working against them where over-treatment can cause hypoglycemia.

"So would I target every patient older than age 70 at an A1c level of 8% or 8.5%? Probably not. There's still some patients older than age 70 who could benefit from an A1c target of 6.5%. Again it's looking at comorbidities, their level of function, how mentally prepared and willing they are in terms of wanting to achieve a lower A1c level."

Dr. Wilding agrees there is evidence that if a patient's blood sugar is very high over a long period of time, "bringing it down to low-normal levels around 70 mg/dL or 80 mg/dL might cause some people to experience hypoglycemia at a slightly higher blood glucose level."

His advice is different for younger patients. "There it's a very different story. I tell them that I hope and expect them to live another 30 or 40 years, so let's aim for tight control."

Educating Hypoglycemic Patients

"An important step in preventing hypoglycemia is to provide structured patient education," says Dr. Cryer. "We had a group of patients who were having trouble with hypoglycemia. We performed structured education and they did better." He says that while endocrinologists gather important information from diabetes education programs, randomized clinical trials are needed. "We already know that structured patient education is helpful with respect to hypoglycemia. This is basically teaching the individual patient how their drugs work, when they're likely to produce hypoglycemic episodes and how to minimize those risks."

Another important tool in treating hypoglycemia is simple blood glucose testing. "Testing is a kind of biofeedback," says Dr. Leong. "I start by getting patients to check their blood glucose levels more frequently. Once they see the numbers—whether too low or too high—they have a better understanding. I reinforce those patients' insights by meeting with them more frequently. I won't wait six months to see them again."

He also handles questions from patients via e-mail. "Generally messages from patients ask for advice. They may send me their current blood sugar levels and ask if them being ill all week with a cold is causing their readings to fluctuate. Or are unusual readings the result of something they ate?" Dr. Leong says giving advice helps patients fix their problem.

> "Clinicians need to train patients to develop good pattern recognition."
> – John Wilding, DM

"Clinicians need to train patients to develop good pattern recognition," says Dr. Wilding. "If patients' blood glucose level is always low before lunch, they probably took too much insulin with breakfast. The advice is: decrease the insulin dose before breakfast. If blood glucose levels are always low in the morning, patients probably dosed too much insulin before they went to bed. Decrease the insulin before bedtime. It really is as simple as that. Unfortunately, many patients find it hard to grasp that concept so they snack defensively or if their blood sugar is high, chase their tails by taking extra doses of insulin."

He's aware that diabetics can be tempted to eat what they want and rely on big bolus injections to cover the glucose. "That's always a bit of a risk. We try to teach patients who are willing to learn about carbohydrates so that for short-acting insulin they can make a decision about how much insulin to take based on how much carbohydrate there is in the food. But even that's inexact because it depends on the glycemic index where some carbohydrates are absorbed faster than others."

Waiting for the Great Breakthrough

How close are research and medical communities to be able to confidently say, "We now know how to cure diabetes?" "We understand the condition a lot more these days," says Dr. Wilding. "We understand that the two main forms of diabetes, type 1 and type 2, are very different. For type 1, we have made advances in immune therapy over the last decade.

"Immune therapy could be able to preserve what beta cells are left, or maybe even allow regeneration to occur if type 1 diabetes is diagnosed early enough. A convergence of immune therapy with technology—continuous glucose monitors and insulin infusion joined with computers—would combine to create an artificial pancreas. Although it would take direct control away from the patient, it wouldn't be because the patient isn't intelligent enough to manage his diabetes, but simply because the kind of control called for is so very hard to do."

10 Current Global Research StudiesAnd Theories About Hypoglycemia

Hypoglycemia is an often unavoidable part of the experience of having diabetes. The studies summarized below, all published during 2015 or 2016, represent a cross section of current research on hypoglycemia.

Neonatal Hypoglycemia Studies

Neonatal hypoglycemia studies— Is there a sweet story of success yet?

Endocrinologists have known about neonatal hypoglycemia for years. The condition is a normal one for newborns. But the question is, what is a normal blood sugar reading for a newborn? This study reports on some possible answers.[5]

Neonatal hypoglycemia: is 60 the new 40? The questions remain the same

This study reports on an "enhanced" understanding of blood sugar values that newborns experience compared with higher levels only a few days later. The concern here is how doctors can quickly identify neonates who have normal/expected blood sugar levels versus neonates who may have levels that are problematic.[6]

Type 2 Risk Factors for Hypoglycemia

Risk factors for hypoglycemia in patients with type 2 diabetes, hospitalized in internal medicine wards

Type 2 patients in hospital internal medicine units are subject to hypoglycemia in the presence of certain risk factors, including age, neuropathy, and cognitive dysfunction. Patient education may offer a way to lower the number of hypoglycemic episodes among such patients.[7]

Anti-Hypoglycemia Drug Combinations

Which oral antidiabetic drug to combine with metformin to minimize the risk of hypoglycemia when initiating basal insulin?

This trial compared rates of hypoglycemia between one group of type 2s taking metformin and an insulin secretagogue and another group taking metformin and a DPP-4 inhibitor. The metformin-DPP-4 combination worked better.[8]

Reversing Insulin-induced Hypoglycemia

Inhaled formoterol diminishes insulin-induced hypoglycemia in type 1 diabetes

In type 1s, tight glycemic control can invite increased—and dangerous—episodes of hypoglycemia. This study, conducted with 14 type 1 patients, set out to determine whether inhaled formoterol, a highly-specific β2 AR agonist, could be used to antagonize the effect of insulin doses leading to hypoglycemic episodes. The conclusion: maybe.[9]

Different Rates of Hypoglycemia Rates

Hypoglycemia event rates: a comparison between real-world data and randomized controlled trial populations in insulin-treated diabetes

This meta-study is a look at the differences between hypoglycemic episodes in "real-world" settings versus clinical settings. While its conclusion is not much of a surprise—hypoglycemia occurs more often in real-world settings—it does call into question the accuracy of clinical studies that researchers try to structure to closely match the frequency of out-of-clinic hypoglycemic episodes.[10]

Stressing Over Hypoglycemia

Emotional distress in the partners of type 1 diabetes adults

Stress has a big effect on the lives of type 1 diabetics, but what about their spouses or close family? This exploratory study list four types of stress experienced by people close to a diabetes patient: hypoglycemia distress, emotional distress, management distress, and role distress.[11]

Identifying the worries and concerns about hypoglycemia in adults with type 2 diabetes

This is a related study to the study cited above, carried out by the same research team, and focused on insulin-using and non-insulin using type 2s. The researchers concluded that the three factors that most affect these patients are hypoglycemia distress, avoidance, and confidence.[12]

Hypoglycemia Can Cause Neuropathy

Treatment induced diabetic neuropathy—a reversible painful autonomic neuropathy

This study seeks to answer the question of which factor is more likely to induce neuropathy: low blood sugar or insulin. It concludes that low blood sugar is the responsible factor and suggests pre-treatment for neuropathic pain using the nutritional supplement coenzyme Q10.[13]

Tresiba Users Less Likely to Experience Hypoglycemia

Tresiba SWITCH 2 study meets primary endpoint

Novo Nordisk says that users of its new basal insulin, Tresiba® (insulin degludec) experience fewer hypoglycemic episodes than users of other basal insulins. Novo Nordisk's Tresiba trial, SWITCH 2, observed hypoglycemia rates among 721 type 2 patients. One patient group used metformin and Tresiba in combination, while a second group used metformin and another basal insulin.[14]

Can CGM Play a Decisive Role in Control?

For patients who are on a basal-bolus regime, the question about continuous glucose monitors seems almost inevitable: Do CGMs offer a decisive improvement in blood glucose control? The answers are mixed.

"There is debate about how much of an advantage CGM offers, but I think it's clearly established that there is an advantage," says Dr. Cryer, of Washington University in St. Louis, Missouri. "The downside, of course, is that CGMs are relatively expensive."

For Dr. Leong, of Massachusetts General Hospital in Boston, CGM can't be used for every patient. "The diabetes patients I would consider qualify for CGM, especially for overnight monitoring, would be long-standing patients whose blood glucose levels go up and down all the time—what I call 'yo-yo.'" But before prescribing CGMs, Dr. Leong advises patients to learn how to detect hypoglycemic episodes without such assistance.

Infusion Technology

"Continuous glucose monitoring is very interesting but by itself has not had a big impact in my view," says Dr. Cryer. "The place where CGM is of value is when it is combined with continuous subcutaneous insulin infusion(CSII)—basically the first step in closed-loop insulin replacement. There is some relatively widespread enthusiasm for CSII technology. In theory, it should be better than a basal-bolus regimen because one can vary the rate of insulin infusion throughout a 24-hour period. Nonetheless, evidence that CSII is better than basal-bolus therapy is at best mixed."

Complexities of Labile Diabetes

Some of the most challenging diabetes patients that endocrinologists treat are diabetics who suffer from labile—often called "brittle"—diabetes. Such patients experience seemingly wild and uncontrollable fluctuations in their blood sugar levels. Standard courses of treatment don't work for them. Patients with labile diabetes are a tiny percentage of most endocrinologists' caseloads. Even so, they are a fascinating topic because of the challenges they pose in finding an effective treatment —almost like solving a complex puzzle.

> "Every patient with labile diabetes is unique." – Faisal Hashim, MBVS, PhD

Every Case Is Different

"Every patient with labile diabetes is unique," says Dr. Hashim of Almana General Hospital in Jubail, Saudi Arabia. "There are different reasons for that. In some cases, children who entering adolescence might be brittle. Others come less well-educated backgrounds, some have psychological problems, and some have had diabetes long enough to cause problems like gastroparesis."

Psychological Versus Physical Origins

In some cases, psychological factors may account even more than physical for labile diabetes. Dr. Sultan of International Medical Center Hospital in Jeddah, Kingdom of Saudi Arabia, who estimates that 5% of his patients are labile, says that many of his adolescent labile diabetes patients have psychological problems. "During adolescence they may become resistant to following a routine, which can create some physical issues, but generally their brittleness is from psychological issues. Their mood swings, along with fluctuations in their diet, make things difficult for us and for themselves as well."

Resistance to Psychological Treatment

Another difficulty, says Dr. Sultan, is getting patients with labile diabetics to seek psychological help. "In the Middle East people are very reluctant to accept being psychologically supported. But for the ones we persuade to see a psychologist, things get much, much better for them. They really improve."

"Here in Saudi Arabia," says Dr. Hashim, "programs like patient support groups are not available. So how we approach brittle diabetics really depends on patient education at the clinic provided by our diabetic nurse."

Bad Experiences Can Change Minds

Fortunately, many brittle diabetics can be persuaded to address their condition—although the means of persuasion sometimes isn't pleasant. "After they have seen somebody with complications of diabetes and how they suffer," says Dr. Hashim, "or somebody who has had an amputation or gone blind, such cases tend to make them more keen in handling their problem. They become much better and more compliant at following a program that is intended to give them much better control—the frequency of injections, not missing injections, coming frequently to the clinic, etc. That sort of program tends to be very helpful."

Saved by the Pump?

Because patients with labile diabetes have very changeable needs for insulin, pre-mixed insulin is unsuitable for them, says Dr. Sultan. "With these patients, we try to convince them to use an insulin pump, which is a great help in addressing lots of problems, especially hypoglycemia. Unfortunately, it takes a long time to convince them about a pump. But when we show them how effective pumps are in limiting the dramatic swings between high and low blood sugar levels, they become more accepting of the idea.

"Insurance issues make it quite difficult for us to get pumps for patients," notes Dr. Sultan, but pumps can also be cost-effective while improving patients' quality of life. "We had a brittle patient who was admitted to the hospital almost every two months for diabetic complications. After she went on a pump, things changed—dramatically. It's now almost a year later and she hasn't been admitted even once."

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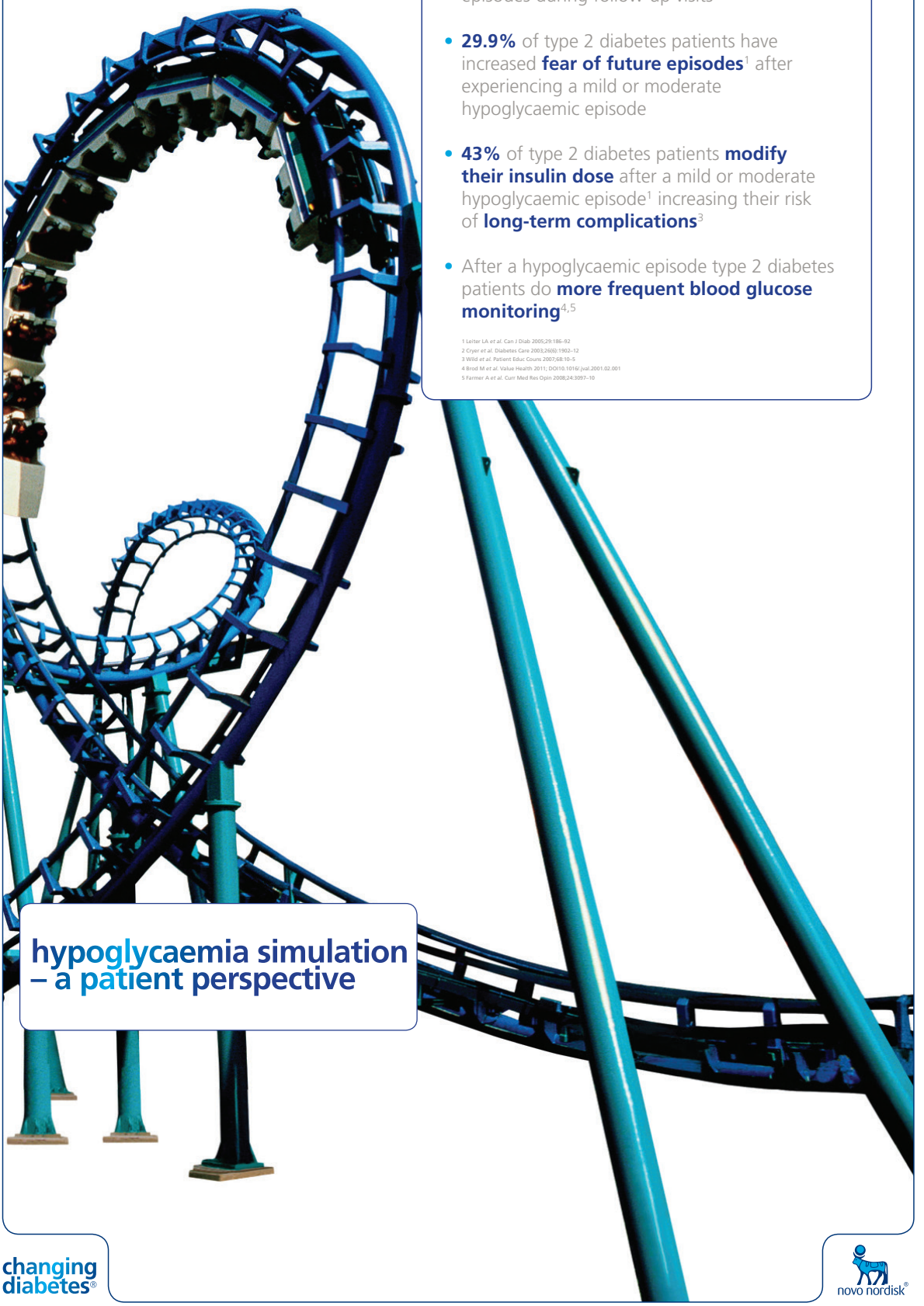

- Hypoglycaemia has a major impact on patient **lifestyle**[1] and is a principal limiting factor to optimal glycaemic control[2]
- **85%** of patients do not talk to their physician about mild-to-moderate hypoglycaemic episodes during follow-up visits[1]
- **29.9%** of type 2 diabetes patients have increased **fear of future episodes**[1] after experiencing a mild or moderate hypoglycaemic episode
- **43%** of type 2 diabetes patients **modify their insulin dose** after a mild or moderate hypoglycaemic episode[1] increasing their risk of **long-term complications**[3]
- After a hypoglycaemic episode type 2 diabetes patients do **more frequent blood glucose monitoring**[4,5]

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