The Dakota Diabetes Coalition is proud to offer a regular column on diabetes and related concerns every other Friday.

	Dr. Eric Johnson is a family practice doctor in Grand Forks with a special interest in diabetes -- and a special knack for writing. As a member of the Dakota Diabetes Coalition, he has generously made himself available to answer questions through our listserv. If you have comments, or questions for Dr. Johnson to address in future columns, please contact gailhand@q.com Visit the Coalition's website! http://www.ndhealth.gov/diabetescoalition/

A1C and glucose variability

Tailoring treatment to the individual

For many years, the hemoglobin A1C test has been the standard for measuring diabetes performance over the preceding 8 to 12 weeks. This test is a good measurement of an average blood sugar level. For example an A1C of 7% may represent an average glucose level of ~150-160, as opposed to an A1C of 9%, which would represent an average daily glucose level of ~250-260.

This can be confusing for patients for different reasons:

1) The A1C represents a **continuous** 24 hours/7 days a week average of blood glucose, which may be different than the average of the finger stick glucose values obtained on a home monitor. For example, if a patient checks 2 blood sugars daily at the same times every day, and we do a 90 average of those values, that average only reflects blood glucose levels at those time periods, not the entire 24 hour day. I

explain it like this-the finger stick glucose is a ‘snapshot photograph’ of blood glucose, the A1C is a ‘movie’ of blood glucose.

2) A1C does not account well for glucose variability. A patient may have a range of blood glucose values between 60 and 200, but still have an average of ~140, which would be an A1C of <7%. However a patient may have a range of 40-440, and still have an average of 140, with the same resultant A1C. At present, variability is best measured by frequent finger sticks, usually pre-meal, 2 hour post-meal, bedtime, an occasional 3 a.m., or with continuous monitor devices, available as clinic or home devices (more on this later).

Why A1C matters

A real benefit of A1C testing is that there is a lot of good data tying A1C levels to the development of diabetes complications. This is more so the case for microvascular complications, such as eye disease, kidney disease and less so for macrovascular disease such as heart attack, stroke and peripheral arterial disease. The original Diabetes and Complications Control Trial (DCCT) published in 1993 established this for persons with type 1 diabetes, and the UKPDS trial, published in 1998, showed similar findings for persons with type 2 diabetes. Basically, these are the studies that lead to the recommendations of A1C targets of 7% or less. Neither of these studies primarily addressed the role of glucose variability in the development of complications, but instead considered the role of average blood glucose level as measured by A1C.

Glucose and heart disease

Recently, the consideration of glucose variability has become more important, particularly its relationship to the development of cardiovascular disease. There are really two components to consider when looking at glucose variability: 1) post-prandial glucose excursions, and 2) overall variation or range of blood glucose values. Most everyone would be aware of the importance of aspiring prophylaxis, cholesterol management, and blood pressure control in decreasing heart disease and stroke in persons with diabetes. Several studies have been published that address blood glucose as a risk factor for cardiovascular disease in both type 1 and type 2 patients, both inpatient and outpatient.

In considering reducing glucose variability in a type 2 patient, a fundamental principle that governs all glucose treatment decisions needs to be considered: the decline of beta-cell function, and thus, insulin production over time. Most type 2 patients with A1C values >9% on two oral agents, or patients diagnosed longer than 5 years will need to be on insulin therapy to achieve an A1C of less than 7%. More modern analog basal insulin products (glargine and detemir) generally make this easier, with less

hypoglycemia and perhaps less weight gain. All of these insulins come in easy-to-use pen devices as well, which have high patient acceptance.

An interesting phenomenon of A1C values is that the closer a value is to 7%, the larger proportion of that A1C value comes from post-prandial blood sugar values. For example, with an A1C of 7.3%, about 70% of that value comes from post-prandial values. With an A1C of 10%, about 50% comes from post-prandial values. This means that at some point, patients on insulin not only need to consider a basal insulin, but a meal-time rapid-acting insulin as well to address their post-prandial needs. Often, this is initiated by adding a rapid-acting insulin with the evening meal, with additional rapid-acting injections added at other meals and snacks over time.

Consider oral agents

In patients diagnosed in the past five years, there are other agents that may address post-prandial blood glucose levels. Exenatide (Byetta), an injectable GLP-1 'gut hormone' analog, can be very effective in controlling post-prandial blood glucose levels, as well as the oral agent sitagliptin (Januvia), which is in the DPP-IV inhibitor family. However, these agents are not a substitute when insulin is indicated, as their functions are still predicated on beta-cells still producing adequate insulin. Furthermore, neither of these products has an FDA indication with insulin. Synthetic Amylin (Symlin) can be used along with insulin for reduction of post-prandial glucose, but often, maximizing an insulin program will 'go a long way' for many patients in reducing post-prandial glucose and overall glucose variability.

One of the simplest strategies for reducing glucose variability in patients on multiple daily injection insulin therapy is to try to balance the basal and total bolus each day to be about 50/50. For example, the basal insulin (long-acting: glargine or detemir) should be 50% of the daily total, and all of the bolus (rapid-acting: glulisine, aspart, lispro) insulin combined should be about 50% of the daily total. Taking the proper dose of rapid-acting with meals and snacks, avoiding excessive correction boluses, will usually reduce variability as well.

Many of these pitfalls are noted when patients are placed on 72-hour continuous monitoring devices by their provider. Under-dosing meals is a common mistake noted on this data. Even basic dosing of rapid-acting per carbohydrate intake can improve the patient's performance. Usually, type 1 patients are started on 0.5-1.0 units/15 gram carbohydrate, and type 2 patients on 2 units/15 gram carbohydrate, with subsequent titration based on 2 hour post-prandial glucose values.

Insulin pumps have the potential to reduce glucose variability significantly, particularly when combined with continuous monitoring.

Not the easy way out

However, if one is considering a pump because it will be 'less work', or that it will be hooked up, turned on, and forgotten about, this won't solve the problem, and can actually cause other problems. Pumps (+/-) continuous sensors are excellent tools if the data is analyzed and changes are made in response to that data. This means people need to check multiple times every day, not occasionally, or just when it's "convenient." Modern pump systems, available over the last 5 years, allow for easier data management.

Patients who do well with these devices typically follow a few simple steps explained by a certified pump trainer. By working with the diabetes care team, people will often reduce their glucose variability, and can easily adapt to changing conditions, such as levels of activity, food intake and to illness or pregnancy. Patients who did a good job of checking blood sugars multiple times daily *and responding to those values* are more likely to do well with pumps.

In summary, A1C and glucose variability are both important in type 1 and type 2 diabetes management. In addition, patients often report a better sense of well-being and exercise performance with less variability. Modern analog insulins, available in pens, are workable for nearly all diabetes patients, and once people are adequately trained, pumps can be very effective.

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