Nurse Practitioner Perspective

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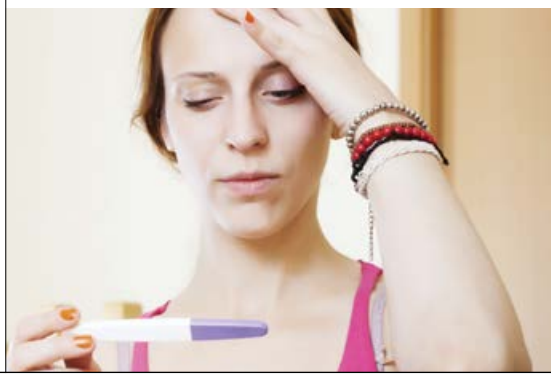

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Innovation Over Insulin Resistance

How technology can increase adherence

By Cheryl Haas Winter, MS RD, MS APRN, CDE, BC-ADM, FNP-BC

DIABETES MELLITUS (DM) now affects 29.1 million people in this country, with 90% to 95% of these cases attributable to type 2 DM (T2DM).[1] This number is projected to increase by 165% between 2000 and 2050,[2] especially among younger people who will live longer with the disease and consequently develop severe insulin deficiency.[3] The standard glycemic marker is hemoglobin $A1_c$.[4] The glycemic goal recommendations by the American Diabetes Association is promotion of an $A1_c$ level less than 7%,[5] while the American Association of Clinical Endocrinologists recommends an $A1_c$ of 6.5% or lower.[4]

Conventional Therapy

Conventional therapy for T2DM involves the use of oral antidiabetes (OAD) agents. Although conventional therapy can initially promote and maintain an $A1_c$ in the acceptable range, monotherapy (e.g., with metformin) is unlikely to achieve or maintain control for long.[5] Earlier use of combination therapy may facilitate relieving glucose toxicity and reaching $A1_c$ goal.[5]

When $A1_c$ is initially greater than 8%, no single oral therapy will reduce it by more than 1.5% to 2%. Therefore, combination therapy is necessary.[5, 6] However, even with dual combination therapy (addition of a sulfonylurea or a thiazolidinedione) that permits a goal $A1_c$ to be reached, secondary failure occurs in approximately 4 goal $A1_c$ years.[7] It is tempting to add a third oral agent or a noninsulin injectable, but the cost and side effects of triple antihyperglycemic therapy must also be considered.[3,5]

General understanding of dose response and time to maximal effect of some OAD treatment regimens is often lacking, and many patients therefore continue taking OADs longer than they should, rather than progressing to more optimum treatment.[6] Research shows that the average patient can accumulate 5 $A1_c$ years of glycemic burden of greater than 8% from diagnosis until starting insulin, and about 10 $A1_c$ years of burden greater than 7%.[8]

Early Introduction of Insulin

Major consequences of uncontrolled DM include microvascular and macrovascular sequelae that worsen as the disease progresses.[9] However, a 40% reduction in the risk of microvascular complications and a 14% reduction in macrovascular complications can occur with every one percentage drop in $A1_c$.[1,4,10] Early introduction of insulin provides potential for even greater macrovascular reduction, since insulin can reduce the level of proinflammatory cytokines, thus providing a protective quality against endothelial damage. The early introduction of insulin also can lower insulin resistance, reverse glucose toxicity and prolong beta-cell function.[11] In addition, lower levels of glycemia *at the time of initial therapy* are associated with lower $A1_c$ over time and decreased long-term complications.[6] Despite the advantages to adequate and early glycemic control, 1 in 5 people in the U.S. has $A1_c$ levels higher than 9.0%.[12]

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Psychological Insulin Resistance

Overwhelming evidence suggests that insulin therapy is the most effective treatment for T2DM, that early use can reduce long-term complications, and that all patients with T2DM will eventually require insulin for glycemic control.[3,12] However, patient- and provider-specific barriers to insulin use propel continued treatment with less optimum measures.[13]

A "psychological insulin resistance" (PIR) has developed, and its main feature is patient and provider misconceptions about insulin use as a treatment for T2DM.[12,14] Most primary care providers delay insulin therapy until absolutely necessary, but specialists are less likely to do so.[15] With the number of endocrinologists decreasing and the number of T2DM cases increasing, primary care providers will screen, diagnose and treat DM.[16] Therefore, overcoming provider-specific barriers to prescribing an early insulin regimen can reduce fears and improve acceptance of this treatment.

Some of the provider-specific barriers to using insulin as a treatment for T2DM are fear of increased hypoglycemic events, weight gain, suboptimal insulin initiation, and lack of time for dose titration.[12,17] Patient-specific barriers include embarrassment about injections in public and fear of injections.[18]

Insulin Analogs

The simplicity and efficacy of the insulin analogs can help facilitate a patient's transition to insulin therapy and reduce PIR.[11] With the availability of long-acting insulin analogs such as insulin glargine and detemir versus older human insulin, such as neutral protamine hagedorn, the risks associated with insulin use have declined. These long-acting insulin analogs are slowly absorbed and distributed and last up to 24 hours.[11] They are considered "basal" insulin, and they suppress excessive liver glucose production, the primary reason for the elevated fasting glucose concentrations in patients with T2DM.[5] The pharmacokinetic profile of rapid-acting insulin analogs such as aspart, lispro and glulisine mirror endogenous insulin more closely than regular human insulin, thus allowing injection to be given immediately before or just after a meal.[11] This flexibility is appreciated by patients.

Three V-Go Dosing Options

20 units/24 hours (0.83 units/hr) basal rate
30 units/24 hours (1.25 units/hr) basal rate
40 units/24 hours (1.67 units/her) basal rate

Prescribing Insulin Regimens

When prescribing an insulin regimen, it is necessary to understand the relative contribution of fasting and postprandial glucose to $A1_c$. Postprandial glycemic control accounts for approximately 70% of overall glycemic control when the $A1_c$ is less than 7.3% and for approximately 50% of overall glycemic control when the $A1_c$ is 7.3% to 8.4%. This means the impact of postprandial glycemic control on overall glycemic control increases as $A1_c$ values get closer to the recommended $A1_c$ values.[19] Ideally, an insulin regimen that is both basal and prandial (multiple daily injections, or MDI) would be more effective in achieving $A1_c$ goals. However, insulin-naïve patients are often reluctant to start with this more complicated regimen, and providers are also reluctant to invest the time needed to educate the patient about MDI. Thus, when providers do initiate insulin, they tend to start with basal insulin only and gradually increase it.

However, data from the Glycemia Optimization Treatment Study showed that only a minority of patients reached adequate $A1_c$ control with rigorous titration of insulin glargine toward a target fasting plasma glucose (FPG) concentration of 80 mg/dL to 120 mg/dL.

Additionally, the 80-mg/dL target groups required 20 units more insulin than the 120-mg/dL target group, with the incremental $A1_c$ reduction achieved by only 0.25%. With progressively lower target FPG concentrations, the rates of severe hypoglycemia events increased.[20] Thus, for patients not reaching glycemic goals with OADs, noninsulin inject-

ables and/or intermediate or long-acting insulin, prandial insulin is required.[5] The goals of intensive insulin therapy can be achieved with MDI, and glucose excursions can be covered with premeal doses of a rapid-acting insulin.[21] Still, patient adherence remains a concern with MDI therapy.

Premixed insulin analogs, such as lispro 75/25, lispro 50/50 and aspart 70/30, consist of a rapid-acting analog and a protamine suspension of the analog. These may be a more convenient method of insulin delivery than MDI therapy, since it is administered only twice daily, before morning and evening meals. In addition, premixed insulin analogs tend to have a greater lowering of the $A1_c$ compared to basal insulin alone, but they also may cause slightly more hypoglycemia and weight gain. Unlike MDI, titration from the shorter-acting to the longer-acting component is not possible. This therapy is thus fairly inflexible and patients need to have consistency in meal times to prevent hypoglycemia. However, it may be an appropriate insulin regimen for patients who eat consistent amounts at regular times and who require a more simplified approach beyond basal insulin therapy.[5]

The V-Go device. *photo courtesy Valeritas*

One insulin therapy option that can dramatically aid in achieving the goal of near-normal glycemia while minimizing many of the feared risks of insulin therapy, is use of an insulin pump or continuous subcutaneous insulin infusion (CSII). Unlike MDI, CSII uses only rapid-acting insulin and provides greater flexibility in timing of meals and snacks. It also eliminates three to four injections per day. Programmable basal rates optimize overnight glycemic control, while other features allow the programming of temporary basal settings to lower or raise the amount of insulin provided based on a person's exercise activities or stressful events, including illness or menses. Unlike MDI, CSII offers enhanced insulin pharmacokinetics, thereby requiring less insulin and thus improved insulin sensitivity and absorption and less weight gain.[21]

Innovative Insulin Delivery

CSII is clearly the most effective method of achieving glycemic control.[21] However, CSII using the insulin pump is often cost-prohibitive and requires a high level of user training.[22] An innovative nonelectronic insulin delivery device, the V-Go (see

photo),[23] is making CSII more affordable and is simplifying and facilitating basal-bolus insulin delivery currently achieved with MDI or combination insulins. PIR is minimized or significantly reduced with this type of insulin delivery.[18, 24] For patients already using basal-only, MDI or combination insulin regimens but not well-controlled, the V-Go is an attractive alternative because it allows discreet delivery and eliminates concerns about forgetting insulin supplies away from home. These are common reasons for skipped injections. In addition, metabolic control appears to be maintained or improved with a reduction or maintenance in daily insulin dose.[18, 24]

The V-Go attaches to the skin using a hypoallergenic adhesive. Once applied, a needle-button is pressed to insert a small 4.6-mm, 30-gauge stainless steel needle subcutaneously, which immediately initiates delivery of a continuous preset basal rate of a U-100 rapid-acting insulin. To meet prandial needs, on-demand bolus dosing is administered by the patient in 2-unit increments. A pair of buttons for bolus delivery are positioned at 90° from one another and sequentially pressed to prevent accidental dosing. The V-Go is waterproof. After 24 hours, the needle release button is activated by the patient to retract the needle back into the V-Go (which acts as its own self-contained sharps container), and then removed from the skin to be disposed of. V-Go dosing options are shown in the table.[23]

V-Go has the potential to reduce the cost of basal-bolus insulin therapy. Only one type of insulin is required with the V-Go (vs. MDI, which requires two types), and the system uses only vials (vs. the often more costly pen devices).[23] The need for pen needles or syringes is eliminated, and insulin needs are 25% less than with MDI.[21] V-Go is an innovative, safe method of potentially increasing adherence, increasing glycemic control and improving prognosis for people with T2DM.[18, 23,24] ■

References

1. Centers for Disease Control and Prevention. National Diabetes Statistics Report. http://www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf
2. Narayan KM, et al. Lifetime risk for diabetes mellitus in the United States. *JAMA.* 2003;290(14):1884-1890.
3. Hirsch IB, et al. A real-world approach to insulin therapy in primary care practice. *Clin Diabetes.* 2005;23(2):78-86.
4. Lebowitz HE, et al. ACE/AACE consensus conference on the implementation of outpatient management of diabetes mellitus: consensus conference recommendations. *Endocr Pract.* 2006;12(Suppl 1):6-12.
5. Inzucchi SE, et al. Management of hyperglycemia in type 2 diabetes: a patient-centered approach; position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care.* 2012;35(6):1364-1379.
6. Dailey GE. Early insulin: an important therapeutic strategy. *Diabetes Care.* 2005;28(1):220-221.
7. Riedel AA, et al. Secondary failure of glycemic control for patients adding thiazolidinedione or sulfonylurea therapy to a metformin regimen. *Am J Manag Care.* 2007;13(8):457-463.
8. Brown JB, et al. The burden of treatment failure in type 2 diabetes. *Diabetes Care.* 2004;27(7):1535-1540.
9. Riddle M, et al. The treat-to-target trial: Randomized addition of glargine or human NPH insulin to oral therapy of type 2 diabetic patients. *Diabetes Care.* 2003;26(11):3080-3086.
10. Stratton IM, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): Prospective observational study. *BMJ.* 2000;321(7258):405-412.
11. Freeman JS. Insulin Analog Therapy: Improving the Match with Physiologic Insulin Secretion. *J Am Osteopath Assoc.* 2009;109(1):26-36.
12. Reid TS. Insulin for type 2 diabetes mellitus: Separating the myths from the facts. *Insulin.* 2007;2(4):182-189.
13. Ligthelm R, Davidson J. Initiating insulin in primary care. The role of modern premixed formulations. *Prim Care Diabetes.* 2008;2(1):9-16.
14. Polonsky WH, Jackson RA. What's so tough about taking insulin? Addressing the problem of psychological insulin resistance in type 2 diabetes. *Clin Diabetes.* 2004;22(3):147-150.
15. Peyrot M, et al. Addressing barriers to initiation of insulin in patients with type 2 diabetes. *Prim Care Diabetes.* 2010;4(Suppl 1):S11-S18.
16. Currie D. Center trains community providers on state-of-the-art diabetes care. *Nation's Health.* 2008;38(4):7.
17. Davies M, et al for the ATLANTUS Study Group. Improvement of glycemic control in subjects with poorly controlled type 2 diabetes: Comparison of two treatment algorithms using insulin glargine. *Diabetes Care.* 2005;28(6):1282-1288.
18. Kapitza C, et al. Basal-prandial insulin delivery in type 2 diabetes mellitus via the V-Go: a novel continuous subcutaneous infusion device. *J Diabetes Sci Technol.* 2008;2(1):40-46.
19. Raskin P, et al. Initiating insulin therapy in type 2 diabetes: a comparison of biphasic and basal insulin analogs. *Diabetes Care.* 2005;28(2):260-265.
20. Tanenberg, R, et al. Glycemia Optimization Treatment (GOT): glycemic control and rate of severe hypoglycemia for 5 different dosing algorithms of insulin glargine in patients with type 2 diabetes. American Diabetes Association 66th Scientific Sessions, June 9-13, 2006, Washington, DC.
21. Bode BW, et al. Diabetes management in the new millennium using insulin pump therapy. *Diabetes Metab Res Rev.* 2002;18(Suppl 1):S14-S20.
22. Aye T, et al. Toward closing the loop: an update on insulin pumps and continuous glucose monitoring systems. *Endocrinol Metab Clin North Am.* 2010;39(3):609-624.
23. V-Go Instructions for Patient Use. Valeritas, Inc. http://www.go-vgo.com/docs/pdf/Instructions-for-Patient-Use.pdf
24. Rosenfeld CR, et al. The V-Go insulin delivery device used in clinical practice: patient perception and retrospective analysis of glycemic control. *Endocr Pract* 2012;18(5):660-667.

Cheryl Winter *is a nurse practitioner at DiabetesAmerica and DiabeteSteps Rx in metro Houston. She has completed a disclosure statement and reports no relationships related to this article.*