

Case Study: Lessons Learned in the Care of a 63-Year-Old Woman with Type 2 Diabetes

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Control of type 2 diabetes mellitus (DM) has deteriorated rather than improved during the last decade in the United States, despite a greater understanding of the disease and the availability of various therapeutic options. Achieving recommended glycemic targets in patients with type 2 DM requires overcoming several barriers, including the fear of hypoglycemia and its associated consequences. Insulin analogues offer new options in diabetes management and may help patients achieve better glycemic control while limiting the incidence of hypoglycemic episodes. Greater awareness of the symptoms of hypoglycemia, intensified blood glucose self-monitoring, and new diabetes treatment options allow for achievement of glycemic targets without increased risk of hypoglycemic episodes. A case study of a 63-year-old woman with type 2 DM offers important lessons learned in diabetes management. (*Clinical Cornerstone*. 2005;7[Suppl 3]:S18–S24) Copyright © 2005 Excerpta Medica, Inc.

INTRODUCTION

Despite a greater understanding of diabetes and several new treatment options, control of type 2 diabetes mellitus (DM) in the United States has deteriorated rather than improved during the last decade.¹ Fear of hypoglycemia and its associated consequences is often an obstacle to intensive management of patients with type 2 DM and introduction of insulin to their therapeutic regimen. Although careful monitoring for any signs of hyper- and hypoglycemia is part of diabetes management, fear of hypoglycemia should not prevent physicians and their patients from aggressively pursuing optimal glucose control. Following a brief discussion of relevant issues relating to diabetes management and hypoglycemia, a case study of a 63-year-old woman with type 2 DM is presented to communicate important considerations in clinical practice.

ESTABLISHING TARGETS FOR GLYCEMIC CONTROL

Treatment goals and guidelines for diabetes management have been developed by several leading clinical organizations, including the American Diabetes Association

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(ADA), the American Association of Clinical Endocrinologists (AACE), the International Diabetes Federation, and the Council for the Advancement of Diabetes Research and Education (Table I in the article by Dr. Lawrence Blonde in this publication). For example, AACE has set aggressive glycemic targets: glycosylated hemoglobin (A1C) $\leq 6.5\%$, fasting and preprandial glucose < 110 mg/dL, and 2-hour postprandial glucose < 140 mg/dL.² ADA recommends glycemic targets of A1C $< 7.0\%$, fasting and preprandial glucose of 90 to 130 mg/dL, and 2-hour postprandial glucose < 180 mg/dL.³ Both AACE and ADA have taken a leadership role in communicating the key message: to aggressively help patients with DM reach recommended A1C levels and glycemic control. Clinicians are encour-

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aged to help patients with DM reach A1C levels as low as possible without unacceptable side effects.⁴

Despite the availability of these guidelines, which are based on evidence from clinical trials, and our understanding of the complex nature of diabetes, many people with type 2 DM in the United States are not achieving target goals for glucose control. For example, in a comparison of 2 National Health and Nutrition Examination Surveys (NHANES), 44.5% of individuals with type 2 DM in NHANES III (1988–1994) had A1C levels $<$ 7.0% compared with only 35.8% of individuals in NHANES (1999–2000).¹ A report by AACE indicates that 2 out of 3 Americans with type 2 DM failed to meet the A1C target of \leq 6.5%, based on an analysis of data collected during 2003 and 2004.⁵

Furthermore, a prospective cohort study by Grant et al⁶ of 598 adults with type 2 DM found that, owing to concerns relating to hypoglycemia, treatment regimens of only 51% of patients with elevated A1C levels were intensified.

CONSEQUENCES OF POOR GLYCEMIC CONTROL

Failure to achieve glycemic control increases the risk of diabetes-related complications. The microvascular complications (eg, retinopathy, nephropathy, and neuropathy) and macrovascular complications (eg, myocardial infarction, stroke, and peripheral vascular disease) of diabetes are of serious concern,⁷ and cardiovascular (CV) events are among the most costly of the complications.⁸ Elevated A1C levels are strongly correlated with higher levels of retinopathy, nephropathy, neuropathy, CV events, and amputations.^{9–13} Data from the Norfolk cohort of the European Prospective Investigation of Cancer and Nutrition study showed that a patient's A1C level predicts all-cause, CV, and ischemic heart disease mortality for people with and without DM; in fact, every 1.0% increase in A1C was associated with a 28% increase in risk of

death, independent of age, blood pressure, serum cholesterol, body mass index (BMI), or cigarette smoking habit.^{14,15} Given the increase in risk of complications and mortality associated with uncontrolled type 2 DM, intensive management of patients to achieve target A1C levels is critical.

THERAPEUTIC OPTIONS

In addition to educating patients with type 2 DM about the nonpharmacologic approaches of diet modification, weight control, and regular exercise, physicians can consider a host of pharmacologic approaches based on each patient's characteristics and level of glucose control. Oral agents for type 2 DM include 4 major classes: secretagogues (sulfonylureas, repaglinide, nateglinide); biguanides (metformin); α -glucosidase inhibitors (acarbose and miglitol); and glitazones, which are also known as thiazolidinediones or TZDs (pioglitazone and rosiglitazone). All of these agents differ in their mechanisms of action, efficacy, and potential for adverse effects. Sulfonylureas, repaglinide, metformin, and glitazones help reduce fasting and preprandial glucose, with lesser effects on postprandial increments.¹⁶ α -Glucosidase inhibitors and nateglinide help reduce postprandial glucose elevations.¹⁶ Although reductions in A1C levels are similar with sulfonylureas, metformin, and glitazones, secondary failure to monotherapy usually occurs regardless of the oral agent used; therefore, combinations of the different oral agents may be useful for achieving better glycemic control.¹⁶

Given the progressive nature of diabetes, most people with type 2 DM eventually require insulin. Earlier initiation of insulin therapy to help avoid the consequences of poor glycemic control is often the preferred course of action. Unfortunately, a number of barriers exist, including fear of hypoglycemia, that often prevent or delay the addition of insulin to the therapeutic regimen of patients with type 2 DM.

HYPOGLYCEMIA AND DIABETES

Whereas careful monitoring for signs of hyper- and hypoglycemia is part of diabetes management, the symptoms of hypoglycemia can vary greatly.^{17,18} Compounding the issue, different organizations and clinical trials use different measurements to determine hypoglycemia. These measurements vary from 55 to 70 mg/dL; however, most individuals can tolerate a plasma glucose level of 60 to 70 mg/dL without problems.

Consequences of hypoglycemia include confusion, disorientation, loss of consciousness, seizure, and increased risk of accident or injury. Acute consequences include coma, cardiac dysrhythmia, neurologic deficits, and death.

Hypoglycemia can occur in people with diabetes who are being treated with intensive therapy, defined as therapy targeted to specific, stringent blood glucose goals with frequent monitoring and adjustments made on a daily basis; but it can also occur in those who are being treated with conventional therapy, defined as therapy aimed at maintenance of clinical well-being with no specific glucose target. Although clinical trials have shown a higher rate of hypoglycemic episodes in some patients with type 2 DM who are being treated intensively,^{9–11} rates of major hypoglycemic episodes are still low, at about 1% to 2% annually.¹² Studies have shown that patients can achieve glycemic control as measured by A1C levels with intensive therapy and at the same time decrease the risk for severe hypoglycemia.¹⁹

Although it is true that hypoglycemia can be a problem in some people with DM, such concern should be considered on an individual basis. For example, studies show that hypoglycemia in people with DM is most common in people age 65 years and older.²⁰ The risk is greater for people with type 1 DM than for people with type 2 DM. For people with type 2 DM, the risk of severe hypoglycemia is minimal and should not be used as an excuse for failing to achieve glycemic goals.²¹

With the advent of new insulin analogues, physicians can now target for improved postprandial results, lower A1C levels, and help prevent hypoglycemia. Severe hypoglycemia is rare in patients with type 2 DM who are carefully monitored and who follow their prescribed regimen carefully.

BENEFITS OF GLYCEMIC CONTROL USING INSULIN ANALOGUES

Insulin analogues offer new options in diabetes management and may help patients limit hypoglycemic episodes while achieving better glycemic control. Insulin analogues are made by modifying the chemical structure of human insulin. Long-acting (glargine and detemir) and rapid-acting (lispro, aspart, glulisine) insulin analogues are now available. These analogues make it possible to more closely mimic physiologic insulin profiles.²²

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Insulin analogues are characterized by time-action profiles that allow more flexible treatment regimens with a lower risk of hypoglycemia.²³ Rapid-acting analogues (including insulin aspart and insulin lispro) have a time-action profile with a quicker onset and shorter duration of action than that of regular human insulin; long-acting analogues have a fairly constant, 24-hour time-action profile (**Figure 1**).²³ Together with better tools for monitoring glycemic control and the evidence that near-normal A1C levels reduce the risk of diabetes complications, clinicians are discovering that the proper use of insulin analogues allows patients with DM greater flexibility in the timing of meals, snacks, and exercise, with reduced risk of hypoglycemia and enhanced quality of life.²³

PSYCHOLOGICAL BARRIERS TO ACHIEVING GLYCEMIC CONTROL

In addition to the fear of hypoglycemia, other barriers to initiating insulin therapy, and thereby achieving glycemic control, exist from the perspective of a patient with type 2 DM. These include fear of injection, fear of weight gain, and concern about convenience (**Table**).

These barriers can be addressed in many ways. First, it is useful to point out to people with DM that needle technology for insulin injection has changed dramatically over the past 2 decades. The needles used today are very thin; typically the higher the gauge, the thinner the needle. Second, it is helpful to inform people that not all patients starting insulin will gain weight; studies show that any weight gain can be managed with adjustments in nutrition therapy and the use of newer insulin regimens.²⁴ Therefore, potential weight gain is not a viable reason for avoiding insulin therapy.²⁵ Finally, insulin therapy can be initiated in a simple straightforward manner with the addition of once-daily basal insulin to the existing therapy regimen.

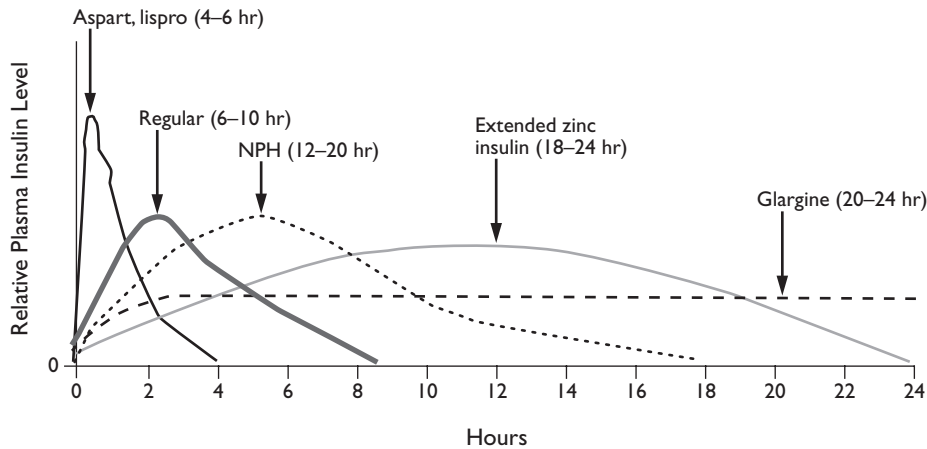


Figure 1. The relative plasma level and relative duration of action of regular human insulin versus insulin analogues. The duration of action will vary widely both between and within persons. NPH = neutral protamine Hagedorn. Reprinted with permission.²³

Health care professionals need to engage patients and their families in a discussion about insulin, as well as the benefits of improved glycemic control, the natural history of type 2 DM, the value of self-monitoring blood glucose and intensive therapy, and the importance of appropriate and timely nutrition intervention to overcome these barriers.²⁶

The following case study illustrates important lessons learned in diabetes management. A careful look at how care was provided to this patient reveals areas for improvement in helping patients with DM achieve optimal outcomes.

CASE STUDY

Presentation

A 63-year-old female with type 2 DM was diagnosed 12 years ago at age 51 during a routine annual gynecologic visit. The patient’s initial symptoms were those of recurrent vaginitis. She was described at that time as

being 5’ 4”, 178 pounds (81 kg), with a BMI of 31 kg/m². She had a history of hypertension, a random plasma glucose level of 248 mg/dL, and a fasting plasma glucose level of 187 mg/dL. She had no classic symptoms of diabetes. No A1C testing was done.

Medical Intervention

This patient was taking a statin, an angiotensin-converting-enzyme inhibitor, and aspirin. She was treated for the recurring vaginitis with vaginal suppositories and pills. However, no diabetes education or instructions on self-monitoring of blood glucose were provided. The patient had been to a dietitian 3 years earlier and was given a 1500-calorie diet plan. She was encouraged to walk 3 to 4 days a week for 30 minutes each day.

Learning Point: The AACE recommendation to “treat to target and be aggressive” was not applied.

Treatment and Outcomes

One year later, this patient experienced no improvement in fasting glucose levels, which remained in the low 200s (mg/dL). Her physician prescribed glyburide (a sulfonylurea agent) 5 mg QD in the morning. The patient did not want to receive insulin shots.

Six months later, the patient’s fasting glucose levels had improved to between 150 and 160 mg/dL, and the glyburide dosage was increased to 5 mg BID. The patient’s physician told her that if she did not follow these instructions, the next step would be to prescribe insulin shots.

TABLE. PATIENT BARRIERS TO INSULIN USE.

Barrier	Solution
Fear of injection	—> Syringes, needles, and pens are now vastly improved
Fear of weight gain	—> Glucose control is more important than mild to moderate weight gain (if any)
Fear of hypoglycemia	—> Low rate of severe hypoglycemia reported in people with type 2 diabetes mellitus

Learning Point: Rather than “threatening” the patient with insulin, the physician could have taken the opportunity to educate the patient about the natural history of diabetes (Figures 2A and 2B)^{27–29} and to explain that most people with DM eventually require insulin. The patient also might have been referred to a certified diabetes educator for further education and counseling.

Follow-up

The patient did not return for follow-up for 3 years, and she stopped taking glyburide after the final refill. When she did return to the physician’s office, she complained of fatigue and reported that she was waking up 2 to 3 times nightly to urinate. The patient requested a second opinion from a different physician.

KEY POINT

Physicians should tell their patients about the progressive nature of diabetes, indicating that most people with type 2 DM eventually require insulin.

The new physician prescribed glyburide 5 mg BID plus metformin 500 mg BID, as well as a glucose meter, with instructions to check blood glucose in the morning. The patient’s metformin dosage was later increased to 1500 mg daily and glyburide was increased to 10 mg BID.

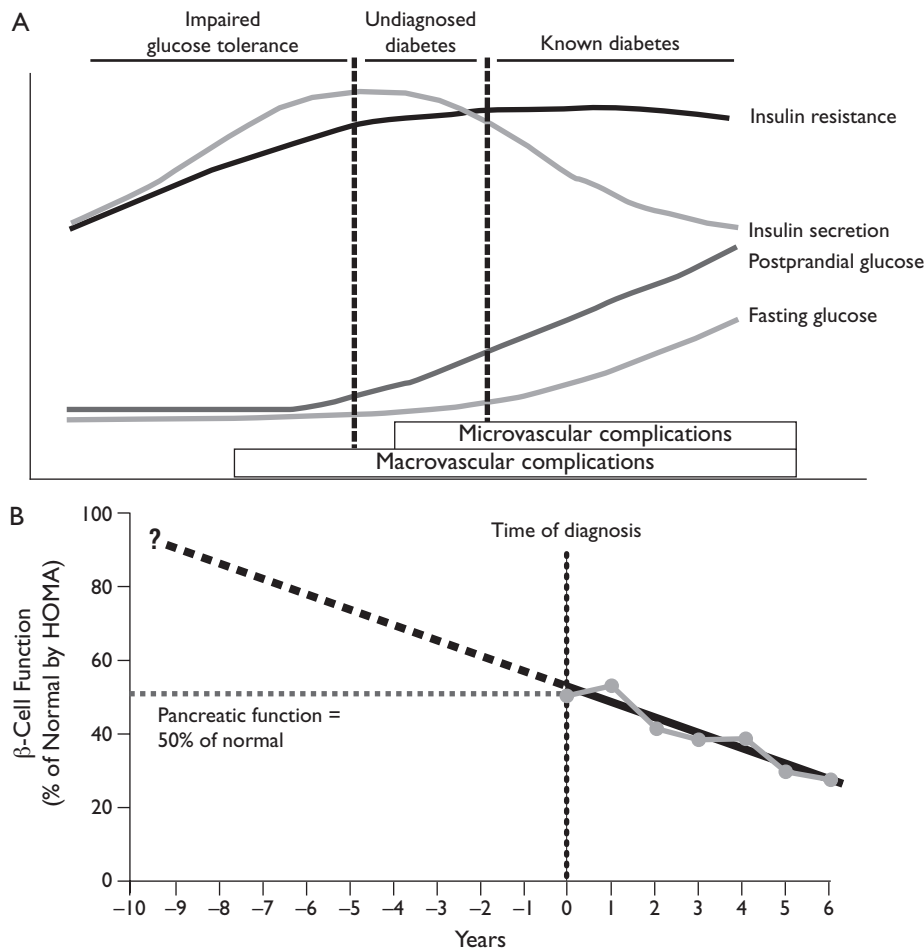


Figure 2. (A) The natural history of type 2 diabetes, from impaired glucose tolerance to undiagnosed diabetes to known diabetes, with the corresponding changes in fasting and postprandial glucose levels and insulin resistance and secretion, and (B) the decline in β-cell function by the time of diagnosis both illustrate the progressive nature of diabetes. HOMA = homeostasis model assessment. Reprinted with permission.^{27–29}

At a follow-up visit, the patient's A1C level was 9.3%, and her self-monitored blood glucose levels remained in the high 100s to low 200s (mg/dL). Treatment options now included increasing the dosage of either glyburide or metformin, or both; adding a third oral agent or initiating insulin therapy; and asking the patient to self-monitor blood glucose more frequently.

Learning Point: Given the elevated A1C level of this patient, the initiation of insulin therapy is indicated to help achieve tight glycemic control, as is more frequent blood glucose monitoring. Diabetes education would be particularly helpful for this patient, to help determine the level of ongoing counseling and support she needs to enhance compliance with an effective diabetes management regimen.

Treatment and Outcomes

With an A1C level of 9.3%, insulin was determined by this physician to be the treatment of choice. The patient initially was prescribed 20 IU of neutral protamine Hagedorn (NPH) insulin, a basal insulin, every morning, and the dose was slowly increased to 60 IU over several months. The patient began to complain of diaphoresis every afternoon, with some tremor; she reported that these symptoms improved if she ate something sweet. The patient recorded a blood glucose level of 68 mg/dL during one of these afternoon episodes. At this point, the treatment options included lowering the NPH insulin dose, changing the time of dosing from morning to bedtime, switching from the basal insulin to insulin glargine, and again recommending more frequent self-monitoring of blood glucose.

Learning Point: Patients must be educated about the potential risk of hypoglycemic events and the symptoms of hypoglycemia. In addition, they must be told that checking their glucose level during an event is of utmost importance.

Medical Intervention

This patient's symptoms are not due to "real" hypoglycemia but are probably secondary to sudden drops in plasma glucose. Nonetheless, she should be instructed to self-monitor and document her blood glucose levels more frequently, but especially when she is experiencing hypoglycemic symptoms, and then provide these data to her physician for follow-up.

Based on what has been presented here, a more intensified treatment regimen is required for this patient. For example, a regimen including a basal-prandial (bolus) insulin may help this patient achieve the A1C target goal of <7.0%.

Learning Point: Basal-prandial treatments offer the option of targeting not only fasting glucose levels but postprandial levels as well. Although the contributions of both fasting and postprandial glucose levels are important at any A1C level, when a patient's A1C level is in the low range, the postprandial glucose level is even more important.

SUMMARY

Physicians must address both the needs and the concerns of patients with DM. Patients' concerns may include fears relating to their inability to follow a complicated insulin regimen, injections, hypoglycemia, or weight gain. The primary objective is to gain glycemic control, which involves aggressively treating diabetes to target A1C levels and using all available tools, including insulin, as needed. Under no circumstances, however, should a physician use insulin as a threat. Indeed, many individuals will not be able to reach glycemic goals without insulin. Although hypoglycemia can be a concern in patients who are aggressively treated, hypoglycemia occurs less frequently with the new insulin analogues as compared with NPH insulin.

Patient education also is important. Physicians should tell their patients about the importance of self-monitoring blood glucose, about the progressive nature of diabetes, and that most people with type 2 DM eventually require insulin. Of special note is the need to communicate the importance of striving for glycemic control as the best course of action to achieve optimal outcomes in diabetes management.

Although glycemic control is directly correlated with the incidence of microvascular and macrovascular complications, glycemic control is less than optimal for most individuals with type 2 DM, despite gains in our understanding of the disease and new treatment options. Greater awareness of the symptoms of hyperglycemia and hypoglycemia, intensified self-monitoring of blood glucose levels, and more intensified treatment regimens with new diabetes treatment options should allow for achievement of glycemic goals without increased risk of hypoglycemic episodes.

CONCLUSION

For people with type 2 DM, the primary focus is to achieve glycemic control. Fear of hypoglycemia should not be a barrier to pursuing optimal diabetes control.

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