

Type 2 diabetes

The role of insulin

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Diabetes mortality rates continue to escalate despite advances in therapy and more aggressive management guidelines promulgated by the American Diabetes Association (ADA) and the American College of Endocrinology (ACE). The Diabetes Control and Complications Trial (DCCT) and United Kingdom Prospective Diabetes Study Groups (UKPDS) trials have clearly demonstrated the benefits of intensive diabetes control, and an increasing body of evidence has been focused on the contribution of postprandial glucose (PPG) levels to elevated levels of glycosylated hemoglobin A1C. Moreover, the results of large, randomized, controlled clinical trials such as these have clearly demonstrated that improved glycemic management is associated with reductions in the microvascular complications, specifically retinopathy, nephropathy, and neuropathy, that are associated with inadequately managed diabetes.¹⁻⁷

Since publication of the DCCT and UKPDS findings, it has become clear that tighter control of blood glucose in type 2 diabetes can significantly reduce the development and progression of microvascular complications. Furthermore, the frequency of macrovascular

Practice recommendations

- Type 2 diabetes is characterized by insulin resistance and a progressive decline in insulin secretion. (SOR: A)
- Forty percent of patients with type 2 diabetes will require insulin therapy at some point in their lives. (SOR: B)
- Improved glycemic control in patients with type 2 diabetes is associated with improved quality of life and more stable employment with less absenteeism and increased productivity. (SOR: B)
- The addition of insulin to oral antidiabetic agents further reduces glycosylated hemoglobin A1C levels, fasting plasma glucose levels, and generally, postprandial glucose levels. (SOR: A)
- When initiating insulin therapy in patients with type 2 diabetes, insulin analog premix or basal insulin is a reasonable and effective choice. (SOR: A)

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TABLE 1

Tips on initiating insulin therapy

- ◆ The natural history of diabetes inevitably leads to the need for insulin therapy in most patients. It is important to educate the patient about this point early in the process of care and remind her/him with some regularity that insulin is not a punishment, it is perhaps the most effective treatment available. In addition, it should be emphasized that insulin is not needed because the patient was "bad." People with type 2 diabetes are living longer, and insulin often is needed to keep diabetes in optimal control.
- ◆ Diabetes education is a necessary preparation for patient self-management.
- ◆ Addressing the patient's fears and concerns about diabetes and insulin therapy is also critical for successful self-management.
- ◆ Referral to a dietitian is essential.
- ◆ Have the patient self-administer the first dose of insulin in the office.
- ◆ The easy start regimen for biphasic insulin aspart 70/30 is 12 units before supper, or alternatively, 5 or 6 units twice daily before breakfast and supper.
- ◆ The initial dosing regimen for insulin glargine is 10 units at a consistent time during the day, generally between dinner and bedtime, with frequent assessment for a dose increase.
- ◆ The prescription for insulin should include the brand name, type (70/30, 75/25, glargine, NPH, regular, etc.), form of administration (pen, cartridge, syringe), and the approximate total daily dose. Always write for a month's supply with enough refills to last until the next scheduled appointment. The prescription should include pen, cartridges, needles or syringes, and glucose strips.

complications may be decreased by near-normalization of blood glucose levels.⁸

Despite these benefits, blood glucose levels continue to be poorly controlled in many patients with type 2 diabetes.⁹ Results from UKPDS showed a gradual decline of glycemic control from the time of randomization in patients receiving conventional treatment, while in the United States, the number of patients in good glycemic control (A1C <7%) has declined from 44.5% during 1988-1994 to 35.8% in 1999-2000.¹⁰ Even with the most effective therapeutic interventions available, control of the rising levels of glycemia associated with type 2 diabetes can be a challenge for the patient and physician alike.

The progression of diabetes is associated with declining insulin secretion, increased insulin resistance, and eventual β -cell failure. Deterioration of glycemic control is directly related to the progressive loss of β -cell function.¹¹ On average, patients have lost approximately half of their

β -cell function by the time the diagnosis of diabetes is made.¹¹⁻¹⁴ Insulin resistance and progression of insulin secretory dysfunction are major confounders of effective long-term glycemic management,^{12,13} directly contributing to the diminished efficacy of oral antidiabetic agents (OADs), even when used in combination. Although β -cell function is temporarily increased with the use of sulfonylureas, there is no concomitant increase in the longevity of β cells, and the rate of failure remains the same as with other therapeutic strategies.^{12,13}

Diet, exercise, weight loss, and a healthy lifestyle remain essential in the initial and ongoing management of type 2 diabetes. The addition of 1 or more OADs is appropriate when glycemic control can no longer be achieved through the use of the initial nonpharmacologic measures. Similarly, insulin should be added when the combined use of OADs and nonpharmacologic measures are no longer able to achieve glycemic control.¹⁵ The addition of insulin to sulfonylurea therapy improves glycemic control, as shown by a subset analysis of the UKPDS, without promoting weight gain or increased risk of hypoglycemia.¹⁶ Subsequent clinical trials have further corroborated the benefits of insulin in patients with type 2 diabetes. Benefits associated with early initiation of insulin therapy include prevention of glucose toxicity, preservation of existing β -cell function, and prevention or delay of microvascular and macrovascular complications.¹⁷

The initiation of insulin administration is often delayed in patients with type 2 diabetes for several reasons, including a perception that insulin therapy is complex, lacks resources in an office-based practice, fear of hypoglycemia,¹⁸ and provider and patient resistance to its use (TABLE 1). Even when insulin is prescribed early in treatment, low doses are often employed due to the fear of hypoglycemia.^{19,20} Appropriate patient education early in treatment can do much to alleviate fears and misconceptions (TABLE 2).²¹

The safety of insulins has been closely evaluated, particularly with respect to the incidence and severity of hypoglycemia. Although severe hypoglycemia can be life-threatening, most hypoglycemic episodes are mild in patients with type 2 diabetes, involving symptoms that can be readily recognized and effectively self-treated. The variety of options and resources available for diabetic patients who are new to insulin is another area where comprehensive education can be helpful. Many of these options, such as insulin analog premixes, less painful needles, and pen devices, can help simplify aspects of insulin therapy, thereby making it easier to teach and initiate in an office-based setting and increasing its acceptability among patients. The remainder of this review focuses on the role of insulin in patients with type 2 diabetes and provides a comparison of the advantages and disadvantages of selected types of insulin.

OVERVIEW OF SELECTED INSULINS

Along with recognition of the benefits associated with intensive glycemic management, the need for insulin formulations that more closely approximate the physiologic insulin secretion profile has become apparent. The ideal insulin preparation should produce the same biphasic physiologic pattern as that of endogenous insulin in a healthy person, evidencing a rapid rise from a baseline between 5 $\mu\text{U}/\text{mL}$ and 12 $\mu\text{U}/\text{mL}$, reaching a peak concentration of 80 $\mu\text{U}/\text{mL}$ to 120 $\mu\text{U}/\text{mL}$ within 30 to 60 minutes after a meal, and followed by a rapid return to baseline before the next meal (FIGURE 1).²² This physiologic serum insulin profile reflects both the basal-level secretion of insulin, and the stimulated release of insulin following meals. The rapid initial rise in insulin level affords postprandial glycemic control, while the rapid decline reduces the potential for hypoglycemia and secondary weight gain.

Although none of the currently available insulin preparations exactly mimic the endogenous biphasic insulin pattern, the rapid- and short-acting insulins are best suited for coverage of mealtime glycemia, while the intermediate- and long-acting insulins serve to control basal levels of plasma glucose. Various insulin combinations are often used, typically a rapid- or short-acting insulin with an intermediate- or long-acting insulin, to more closely simulate the physiologic insulin profile (FIGURE 2).

Basal insulin formulations suppress hepatic glucose production between meals and overnight, and reflect 40% to 50% of daily needs for an individual. Therefore, approximately half of the insulin (or combination of insulins) dose should cover glycemia associated with the basal need, reserving the remaining half for mealtime needs (FIGURE 1). Low basal concentrations of insulin reduce hepatic glucose production while allowing sufficient glucose levels for brain energy production. The stimulated insulin release that occurs with food intake is primarily responsible for limiting postprandial hyperglycemia. Characterized by an immediate rise and sharp peak at approximately 1 hour following each meal, postprandial insulin (reflecting 10% to 20% of total daily insulin requirements for each meal) concentrations return to basal levels in 2 to 4 hours. Regimens of rapid-acting insulin attempt to mimic this stimulated insulin secretory pattern.

The principal goal of intensive glycemic management is to achieve the lowest possible glycosylated hemoglobin A1C without inducing hypoglycemia. With exogenous insulin therapy, this can be accomplished through the use of insulin analogs, which are designed to approximate the effects of physiologic insulin secretion. Various insulin analog formulations allow for improved basal or postprandial coverage, while premixed formulations provide control for both.

TABLE 2

Addressing attitudinal barriers to insulin therapy

Barrier	Suggested discussion points
The injection hurts.	May hurt less than SMBG. Advantages of insulin pens and thinner, smaller needles.
My life will be more complicated.	Specific 'complication' that concerns the patient. Taking insulin may be less complicated than multidrug regimens.
It means my diabetes is getting worse.	Diabetes is a progressive disease. Insulin can help control blood glucose levels and keep the disease from getting worse.
It means I have failed to follow my treatment regimen.	No matter how closely the treatment regimen is followed, insulin might be needed since diabetes is a progressive disease.
I will have low blood sugar reactions.	How to avoid hypoglycemia. How to manage hypoglycemia.
It will decrease my quality of life.	Benefits observed quickly. Increased energy, better sleep, feeling better.
I will develop complications.	Insulin may reduce the risk of complications.
People will treat me differently.	Strategies for coping with specific people or situations.
Insulin will not help my diabetes.	Effectiveness of insulin in controlling blood glucose and associated benefits.

CONVENTIONAL (HUMAN) INSULIN

Conventional insulins are ultimately limited by time-action profiles that do not closely match physiologic insulin secretion. As a result, there is a higher incidence of hypoglycemia, and the dosing schedules of conventional insulins do not enhance compliance. Weight gain, which exacerbates diabetes, frequently accompanies treatment with conventional insulins. Regular human insulin has a relatively slow onset of action, and must be administered at least 15 to 30 minutes before meals for greatest effectiveness. Furthermore, peak effect and duration of action are longer than those of the rapid-acting insulin analogs.

RAPID-ACTING INSULIN ANALOGS

In recent years, analogs of human insulin have been designed to better reflect the physiologic insulin secretion profile. The ideal rapid-acting insulin analog should have the following characteristics: onset of less than 1 hour, duration of fewer than 4 hours, and similar effects in all patients. Rapid-acting insulin analogs (aspart, glulisine, and lispro) are associated with a more rapid onset and shorter duration compared with regular

FIGURE 1

Endogenous insulin secretion: A guide to exogenous needs

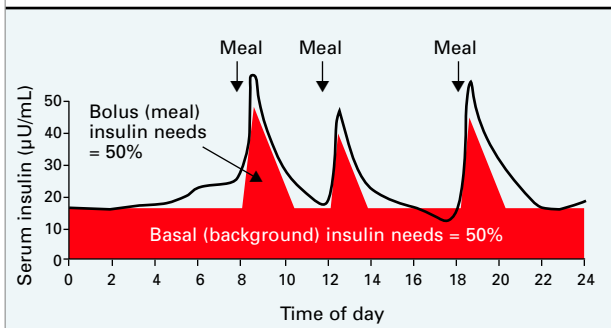
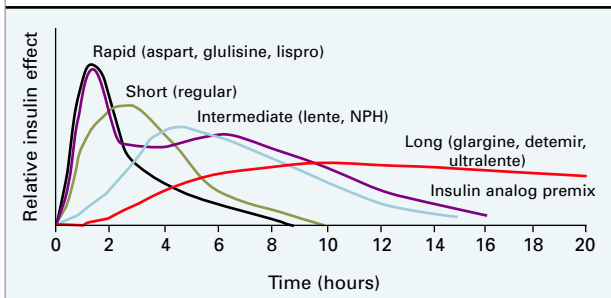


FIGURE 2

Temporal action of selected exogenous insulins



human insulin, thereby simulating the effects of physiologic, postprandial insulin secretion more closely. Rapid-acting insulin analogs are designed to provide a short, rapid burst of insulin to minimize the postprandial rise in glucose. This effect lowers postprandial blood sugars much better than regular human insulin and confers less risk of hypoglycemia between meals. Patients do not have to inject themselves 30 minutes before the meal, but can take their insulin at the time of the meal, which tends to be more convenient. Less variability within individuals has also been documented for insulin aspart than for human regular insulin.²³ The rapid-acting analogs require concomitant basal insulin.

■ BASAL INSULIN ANALOGS

Long- or intermediate-acting insulins have been available for several years, but have been associated with the risk of hypoglycemia, a side effect dreaded by both patients and physicians. Ultralente, the long-acting insulin that has been available for many years, is very difficult to control, particularly because of its variable duration. It also may be difficult to titrate because of the time needed for equilibration after a dose change.

Neutral Protamine Hagedorn (NPH) insulin has also been used for many years. It is a twice-a-day, intermediate-acting insulin with a significant peak, rendering patients prone to hypoglycemia, in particular nocturnal hypoglycemia. The onset, peak, and duration of action of NPH fall between those of the rapid-/short-acting and long-acting insulins.¹⁷

The basal insulin analogs (insulin detemir and insulin glargine) have taken longer to develop than the rapid-acting analogs but are evolving as new choices for the treatment of diabetes. Desirable features for basal insulins are solubility at neutral pH (avoiding problems associated with resuspension) and a long, flat pharmacokinetic profile. The time-action profile of a long-acting basal insulin also should be predictable and reproducible from injection to injection and from patient to patient. While insulin glargine does not possess all of these desirable attributes, its introduction broadened options for therapy by providing relatively peakless coverage lasting for nearly 24 hours. Glargine and ultralente insulin are similar in that neither has a peak effect, but the duration of action for glargine is longer than for ultralente. Insulin detemir is a long-acting insulin analog currently under clinical investigation. It has shown a consistent pharmacokinetic profile across age groups²⁴ and less within-subject variability than either NPH or glargine.²⁵ Detemir has proven superior to NPH in patients with type 1 diabetes.²⁶⁻²⁸ The low variability and more physiologic profile of detemir have been associated with improved glycemic control and tolerability.

■ INSULIN ANALOG PREMIXES

In addition to multiple daily injection regimens and insulin pump therapy, the use of an insulin analog premix can provide coverage of both prandial and basal glucose needs. Insulin lispro premix 75/25 contains insulin lispro protamine suspension as the long-acting component, mixed at a 75/25 ratio with rapid-acting insulin lispro. Insulin aspart premix 70/30 contains rapid-acting insulin aspart, of which 70% has been protaminated to extend the duration of action to provide for a basal insulin component. Insulin aspart premix 70/30 has been shown to lower PPG excursions compared with both human insulin premix 70/30,^{29,30} and insulin lispro premix 75/25.²⁹ In patients with type 1 and type 2 diabetes, insulin aspart premix 70/30 significantly improved postprandial glycemic control without increasing the risk of hypoglycemia when compared with human insulin premix 70/30.³¹

■ CLINICAL TRIALS OF INSULIN

The efficacy of insulin in type 2 diabetes has been extensively investigated in clinical trials. In the majority of these trials, insulin was initiated in patients whose hyperglycemia was not adequately controlled with one or more oral hypoglycemic agents.³²⁻⁴⁰

Long-acting insulin analogs. In a trial comparing various combinations of OADs and bedtime NPH, metformin with bedtime NPH showed the largest decreases in A1C levels. Self-adjustment of NPH doses was based on fasting blood glucose (FBG) assessments, aiming for a level below 108 mg/dL. Despite self-adjustment of the insulin dose, no treatment groups reached a mean A1C value below 7%.⁴¹ In a more recent trial comparing insulin glargine and NPH, both administered at bedtime in combination with oral therapies, an FBG of 100 mg/dL or less was targeted. Systematic titration resulted in approximately 60% of patients in both insulin treatment groups achieving an A1C of 7% or less, with significantly fewer occurrences of nocturnal hypoglycemia observed in the insulin glargine group.⁴²

Short-acting insulin analogs. In a study of sulfonylurea therapy combined with mealtime insulin lispro, bedtime NPH, or twice-daily metformin in patients with type 2 diabetes not maximally controlled with oral sulfonylureas alone, premeal rapid-acting insulin analog lispro with twice-daily glyburide resulted in significantly improved glycemic control.⁴³ Two-hour PPG and A1C levels were significantly lower than the combination of glyburide and metformin or glyburide and bedtime NPH. In a recent trial of rapid-acting insulin aspart, human insulin, and 70/30 premixed human insulin among patients with type 2 diabetes, the most pronounced reductions in A1C and PPG levels corresponded to therapy with mealtime insulin aspart. PPG control correlated with improved A1C values.⁴⁴

Insulin analog premixes. Nearly all studies of insulin analog premixes to date have compared one premix with another (eg, human insulin premix 70/30). One recent study compared twice-daily insulin aspart premix 70/30 to a single shot of long-acting insulin glargine. Each was used with a simple titration schedule in 233 patients with type 2 diabetes who were not achieving glycemic targets on OADs alone. Baseline A1C values were 8% or greater and body mass indices were 40 kg/m² or less. Secretagogues and alpha-glucosidase inhibitors were discontinued during the run-in period, metformin was optimized to 1,500 mg/day or more, and patients receiving pioglitazone were switched to rosiglitazone. Patients were then randomly assigned to either insulin glargine (10 to 12 U) at bedtime or insulin aspart premix 70/30 (5 or 6 U) before breakfast and dinner.⁴⁰

The results confirmed that insulin aspart premix 70/30 provided significantly greater A1C reduction (0.43% more) and better postprandial glycemic control compared with insulin glargine. Of subjects treated with insulin aspart premix 70/30, 66% reached an A1C of less than 7% at 28 weeks compared with 40% of glargine-treated subjects ($P<0.01$). Similarly, an A1C of 6.5% or less was achieved in 42% of patients using insulin aspart premix 70/30 as a starting regi-

men compared with 28% of patients using bedtime glargine ($P<0.05$). No major hypoglycemic episodes were reported.

Furthermore, these data are supported by a separate study by Malone et al that emphasized the importance of addressing PPG in insulin treatment strategies.⁴⁵ An A1C of 7% or less was achieved by 41.4% of patients using twice-daily insulin lispro premix plus metformin and by 22% of those using once-daily glargine plus metformin.

In summary, results of these 2 trials support the use of an insulin analog premix as a reasonable and effective choice when initiating insulin therapy in patients with type 2 diabetes.

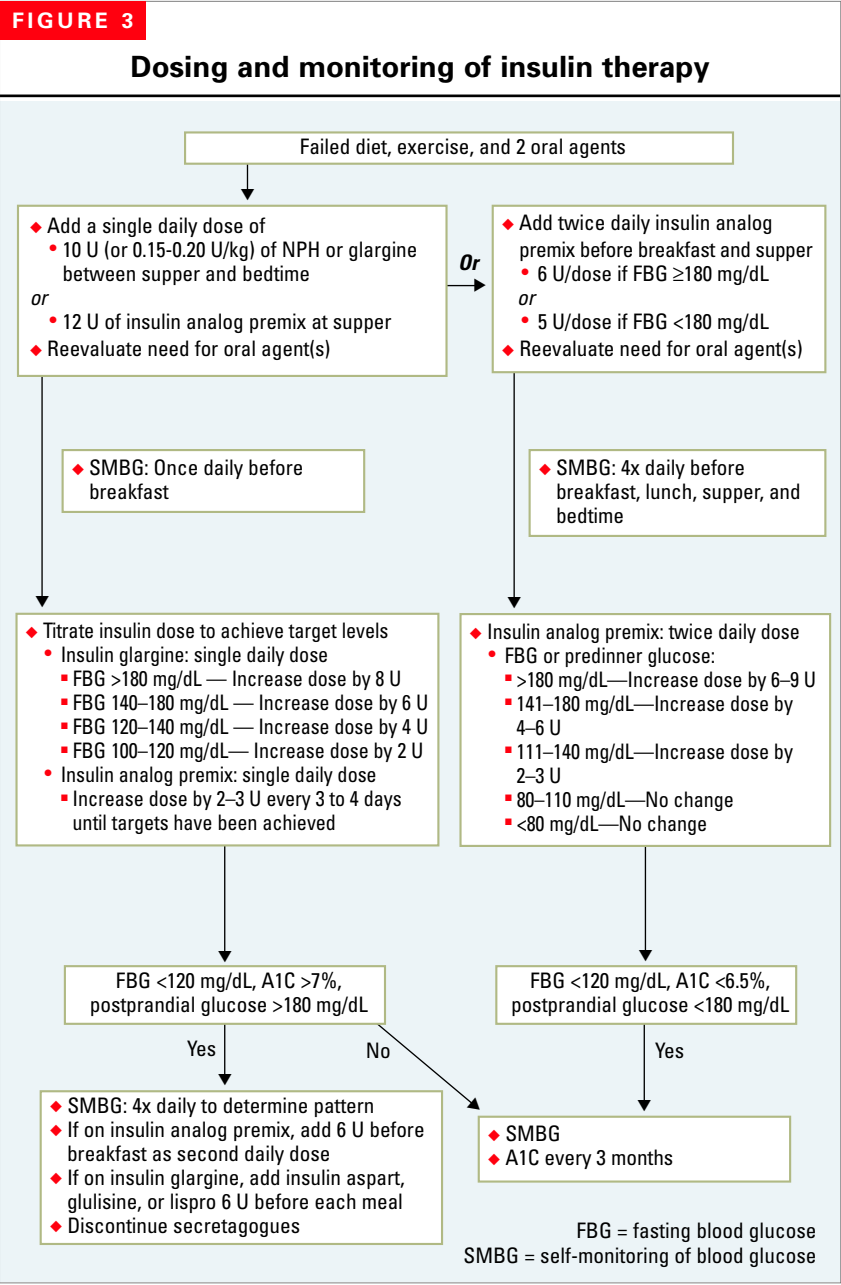
■ INITIATING INSULIN THERAPY

Insulin historically has played a replacement role in type 2 diabetes as it typically has not been initiated until diet, exercise, and a combination of OADs have failed to provide adequate glycemic control. This is unfortunate since it means that the patient's diabetes has been out of control for some time, thereby increasing the risk of long-term microvascular and macrovascular complications. When insulin therapy is initiated early, glycemic control may be improved, thereby achieving clinical benefits that otherwise may have been missed.

Short-term outcome analysis has shown that improved glycemic control in patients with type 2 diabetes is associated with improved quality of life, higher retained employment, greater productive capacity, and less absenteeism. When these factors are considered, the cost of intensive therapy seems offset by even greater economic benefit, not only to the individual patient but to society as a whole.⁸

A variety of treatment options are available for initiating insulin therapy, allowing the clinician some latitude in tailoring therapy to meet the needs of individual patients. Treatment goals should be established with the patient and be continually revisited to measure success in maintaining these goals. The ideal treatment regimen will mimic physiologic insulin release to control both basal glycemia and mealtime glycemia. One option is to use insulin in combination with oral sulfonylurea agents. For this combination to be effective, significant endogenous insulin secretion must still occur. Since only 50% of normal β -cell function typically remains at the time of diagnosis¹⁴ and insulin therapy is often delayed for several years after diagnosis, this combination is usually effective for only a few years.

Today, many patients start on a single daily injection of basal insulin, whereas others begin with an insulin analog premix injected before meals, starting with the largest meal of the day. Because of the progressive nature of type 2 diabetes, consideration and planning for a subsequent transition to more intensive insulin therapy



insulin can present a challenge. From a single daily injection of basal insulin, the next step towards obtaining adequate postprandial coverage for multiple meals could require 4 or more injections a day.

■ DOSING AND MONITORING
Possible adjustments to OAD dosage and reevaluation of the need for OAD usage are important factors to consider during the transition to insulin therapy. Several methods have been used to calculate the initial insulin dose for patients with type 2 diabetes. Two of the more widely used methods base dosage on either FBG (with adjustment for obesity) or body weight (with adjustment for degree of hyperglycemia). Alternatively, therapy can be initiated as a fixed single daily dose of 10 units (or 0.15-0.20 units/kg) of NPH or insulin glargine, administered subcutaneously at a consistent time between supper and bedtime. Likewise, 12 units of an insulin analog premix can be injected once daily before supper (**FIGURE 3**).

Twice-daily injection of an insulin analog premix, with 5 to 6 units per dose (based on FBG) given before breakfast and supper, is yet another simplified option for the initiation of insulin therapy. Five units should be utilized if the prebreakfast and presupper FBG glucose levels are less than 180 mg/dL or 6 units if they are 180 mg/dL or above. The breakfast dose should be titrated based on the presupper blood glucose level and the suppertime dose based on the pre-breakfast blood glucose level over the previous 3 days. Self-monitoring of

blood glucose (SMBG) before lunch and at bedtime is also helpful to titrate doses.

Although definitive guidelines for SMBG have not been developed, monitoring should be recommended as frequently as is acceptable to the patient, as needed to ensure that glycemic targets are being achieved, and to identify episodes of asymptomatic hypoglycemia. Ideally, patients should monitor 4 times a day (before meals and at bedtime), although less frequent testing often suffices. Since monitoring 4 times a day every day is excessive for most patients on insulin analog premix, an alternative is to test twice a day at differ-

should be considered as early as possible. Initial therapy using an insulin analog premix offers the advantage of allowing progression to more frequent daily injections in a stepwise manner, while using the same product in combination with a rapid-acting insulin analog. Since twice-daily injections of insulin analog premix provide coverage for basal insulin, as well as postprandial coverage for 2 meals, the next step in therapy may involve the addition of one injection of rapid-acting insulin analog to cover an additional meal. The process of adding postprandial coverage, through injections of rapid-acting insulin analog directly to a single daily injection of basal

ent times on 6 days with monitoring 4 times in 1 day only once a week. For example, testing 1 day might be before breakfast and lunch, another day before lunch and dinner, a third day before dinner and bedtime, and so on. For insulin glargine, monitoring before breakfast is appropriate. The insulin dosage should be titrated until glycemic control is achieved based on the prebreakfast FBG level. Regardless of the therapeutic course chosen, once glycemic control has been achieved, SMBG in concert with other monitoring (eg, of A1C value) remains essential as a guide in the adjustments to therapy that will be needed as type 2 diabetes progresses.

If the patient's FBG is within the normal range, but the A1C remains above 7%, 1 or more premeal doses of a rapid-acting insulin analog (insulin aspart, insulin glulisine, or insulin lispro) may be necessary. SMBG is the most effective way to identify the meal(s) for which the extra rapid-acting analog will be helpful. For those patients using once-daily insulin analog premix, a second dose prior to breakfast should be added. The prebreakfast dose should be initiated at 6 units. Also, insulin secretagogues (ie, sulfonylureas, nateglinide, repaglinide) should be discontinued and blood glucose should be monitored before meals and at bedtime.

■ PATIENT EDUCATION

The successful management of type 2 diabetes depends to a large extent on patients' ability and willingness to take control of their disease. It is important to keep in mind that knowing what is best for diabetes is not the same as knowing what is best for a particular person with diabetes.⁴⁶ Consequently, patients first need diabetes self-management education and then to be provided with the ongoing collaboration and support necessary to sustain the level of self-care needed for a lifetime of diabetes. Along with the management of diabetes, the education needs to include information about patients' roles in treating diabetes, costs and benefits of various therapeutic options, costs and benefits of their self-management decisions, behavioral change strategies, and psychosocial issues. Group education is generally more effective than individual education⁴⁷⁻⁴⁹ and is increasingly eligible for reimbursement. Diabetes education that incorporates the behavioral and psychosocial components of diabetes and is culturally specific has been shown to be more effective than knowledge-based programs.⁴⁷⁻⁴⁹

Patients also need ongoing self-management support and collaborative care that links patients with provider contact and resources.⁵⁰ Effective strategies for self-management support include behavioral goal-setting, peer support programs,⁴⁸ nurse care management,⁵¹ and scheduled telephone follow-up systems.⁵²

An important aspect of patient education is addressing patient barriers to the use of insulin therapy.

Psychosocial issues, including the impact of the work and home environments, should be explored with the patient. Although patients with type 1 diabetes readily accept insulin therapy, patients with type 2 diabetes often strongly resist it.

A survey of 1,971 patients with type 2 diabetes not on insulin therapy found that half of the patients expressed significant worry about having to start on insulin therapy (Richard Rubin, PhD, unpublished data). The survey generally found that patient resistance to using insulin was based on beliefs about diabetes and insulin. For example, half of the patients believed that starting insulin would mean that they had not managed their diabetes effectively, and fewer than one-quarter believed taking insulin would help them manage their diabetes. Since patient beliefs and attitudes have a significant impact on self-management behavior, it is essential that these beliefs and attitudes regarding insulin therapy be identified and addressed.

Discussing insulin as a treatment option early in the course of the disease can help remove the fear of the unknown and facilitate acceptance of insulin therapy when it is time to initiate insulin. Additional strategies include addressing the patient's specific fears and concerns, providing a nutrition referral if weight gain is a barrier, and conveying the progressive nature of type 2 diabetes and insulin as one of the steps in the management of type 2 diabetes, rather than as a last resort or a personal failure.⁵³

■ SUMMARY

The ability of nonpharmacologic and oral pharmacologic therapies to maintain glycemic control in type 2 diabetes almost invariably dissipates. Insulin therapy, therefore, is eventually needed in the majority of patients with type 2 diabetes. While many options are available, the newer insulin analogs (insulin glargine, biphasic insulin aspart 70/30, and 75% insulin lispro protamine/25% insulin lispro), which more closely mimic the release and action of endogenous insulin in healthy persons, offer several advantages over conventional human insulins. Comprehensive care for the person with type 2 diabetes includes diabetes education, ongoing adjustments and changes to therapy, and self-management support guided by appropriate monitoring and screening for the complications of diabetes.

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