DEMYSTIFYING INSULIN THERAPY

Frederick Banting
1923 Nobel Prize Winner
Breakthrough work led to insulin's discovery

Why, When, and How

to Use Insulin Analogs and Premixed Insulin Analogs in Patients with Type 2 Diabetes

A Continuing Education Monograph for Pharmacists, Nurses, and Dietitians

Supported by an educational grant from Novo Nordisk Inc. This program is accredited by AADE for pharmacists, nurses, and dietitians.

Program Goal

To increase the knowledge of healthcare providers regarding why, when, and how to utilize insulin analog and premixed insulin analog therapy in patients with type 2 diabetes.

Target Audience

This continuing education (CE) program is intended for pharmacists, nurses, and dietitians who work with or anticipate working with patients with diabetes requiring insulin.

Educational Objectives

After reading this monograph, the participant should be able to:

- Discuss how treatment of type 2 diabetes can be matched to the pathophysiology of the disease (ie, insulin deficiency and insulin resistance) and attempt to mimic the normal physiology of insulin secretion.
- Explain the importance of considering both fasting and postprandial glycemic control when designing treatment regimens.
- Identify when patients need to be placed on insulin therapy.
- Describe factors that influence the choice of insulin regimen and how insulin doses can be titrated and adjusted.
- Explain the advantages of insulin analogs and premixed insulin analogs over human insulin formulations.
- Describe how utilization of innovative insulin delivery devices can help overcome patient and healthcare provider concerns regarding insulin therapy.

Fee

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Introduction

Overview

Diabetes is a debilitating and costly disease that is reaching epidemic proportions in the United States. The prevalence of adults diagnosed with diabetes increased from 4.9% in 1990 to 7.9% in 2001.[1] In the United States, the total (direct and indirect) costs attributable to diabetes were estimated to be $132 billion in 2002.[2] Management of diabetes accounts for 10% of US healthcare costs.[2] In 2002, 18.2 million Americans (6.3% of the population) were estimated to have diabetes.[3] Based on the revised definition of prediabetes by the American Diabetes Association (ADA), it is now estimated that another 41 million Americans have prediabetes.[4]

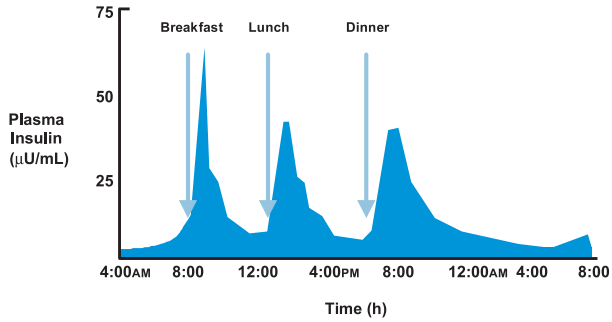
Although insulin is required by patients with type 1 diabetes from the time of initial diagnosis, the majority of patients with type 2 diabetes will eventually require insulin.[5] Therefore, it is imperative that healthcare professionals and patients with diabetes are educated about the progression of type 2 diabetes, the benefits and safety of insulin, and new advances in insulin formulations and delivery systems. Insulin is the most effective and safest therapy for diabetes when dosed properly.[6] Insulin analogs and premixed insulin analogs have overcome many of the shortcomings of the older human insulin formulations.[7-10] The aim of this monograph is to describe why, when, and how therapy with insulin analogs and premixed insulin analogs can be initiated in patients with type 2 diabetes.

Contributors to Hyperglycemia

In individuals without diabetes, basal secretion of insulin occurs at a steady rate that primarily limits hepatic glucose production and output while large peaks in insulin secretion occur after meals (Fig. 1). Diabetes is usually diagnosed by measuring fasting plasma glucose (FPG) levels. The long-term (>3 months) impact of hyperglycemia on glycemic control is monitored by measuring glycosylated hemoglobin (A1C) levels in the blood. A1C is usually <6% in individuals without diabetes. An increase of 1% in A1C corresponds to an increase in mean plasma glucose of ~35 mg/dL.[11]

Although postprandial glucose excursions (ie, high blood glucose [BG] levels after meals) are a substantial contributor to daytime hyperglycemia, most therapies are based on fasting glucose measures.[11] Data from several studies including the Third National Health and Nutritional Examination Survey (NHANES III) have shown that postprandial hyperglycemia is common even in those patients with type 2 diabetes who have good overall glycemic (A1C) control.[12]

Figure 1: Physiological Serum Insulin Secretion Profile in Individuals Without Diabetes



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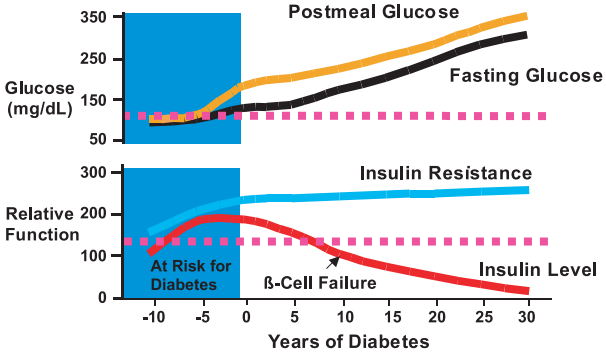
The Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE) study has shown that inadequate control of postprandial glycemia (PPG), which is primarily due to impaired first-phase insulin secretion, is a larger risk factor for cardiovascular disease and death from all causes than impaired fasting glucose.[13] The importance of PPG was reinforced by a study that showed that glucose excursions after breakfast were a major contributor to failed glycemic control in patients with type 2 diabetes on oral antidiabetic drug (OAD) therapy.[14] In another study of 290 patients with type 2 diabetes who were poorly controlled with two OADs, postprandial glucose excursions were predominant in those with mild or moderate hyperglycemia compared to patients with severe disease (ie, A1C >8.4%) where fasting glucose was the main contributor to overall hyperglycemia.[15] As patients get closer to their target A1C levels, elevations in PPG have a much greater role in glycemic control compared with FPG.[15] Therefore, both fasting and postprandial glucose excursions should be considered in the management of diabetes.

Why Insulin?

Type 2 Diabetes is a Progressive Disease

Autoimmune-mediated destruction of pancreatic ß-cells virtually abolishes endogenous insulin secretion in type 1 diabetes, although some patients will still produce some residual insulin.[7] In contrast, ß-cell deterioration in type 2 diabetes occurs progressively over many years; eventually the pancreas cannot synthesize and secrete sufficient insulin to meet the demands of insulin-resistant patients (Fig. 2). Although insulin secretion can be boosted with secretagogues, and the action of endogenous insulin can be enhanced with sensitizers, pancreatic ß-cell failure occurs over time.

Figure 2: Progression of Type 2 Diabetes



Exogenous insulin is needed when insulin resistance is present, when ß-cell capacity falls below a critical threshold, and when glycemic control is no longer adequate with OADs.[16] In some patients with type 2 diabetes, OADs may be ineffective or not tolerated; therefore, insulin therapy must be initiated at the time of diagnosis. This is particularly important in patients who present with severe symptomatic hyperglycemia. Due to the progressive nature of type 2 diabetes that leads to insulin deficiency, many patients will eventually require insulin therapy. The United Kingdom Prospective Diabetes Study (UKPDS) showed that more than half the patient population with type 2 diabetes required insulin at the end of the 10-year study; the investigators predicted that most of the patients would need insulin during their lifetimes.[5]

Treatment Should Address the Underlying Pathophysiology

Treatment should be matched to the pathophysiology of the disease (ie, ß-cell deficiency and insulin resistance) and mimic physiological (basal and prandial) secretion of insulin.[17] Exogenous insulin corrects the insulin deficiency; if dosed properly, it is the most effective and safest medication for treating uncontrolled diabetes.[6,18] Given the potentially devastating consequences of uncontrolled diabetes, it is imperative that patients be treated with the most effective agents for maintaining glycemic control.

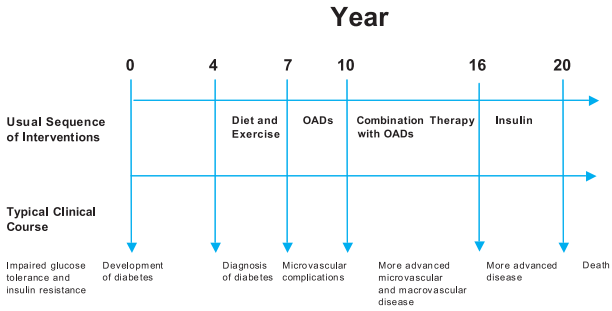
Treatment Goals are Not Being Met

In the United States, most patients with diabetes are not meeting treatment goals for glycemic control, blood pressure, and lipids. The number of patients meeting the ADA goal of A1C <7.0% has declined from 44.5% in 1994 to 35.8% in 2000.[19] Furthermore, the majority of patients are not being monitored for glycemic control and complications at the recommended frequency. This was shown by an analysis of data collected from 1988 to 1994 from 1,026 participants with diabetes in NHANES III and in 3,059 patients with diabetes in the Behavioral Risk Factors Surveillance System study.[20] Each participant had a physician diagnosis of diabetes: 34% had hypertension and 58% had elevated low-density lipoprotein cholesterol. During a 1-year observation period, however, only 29% had an A1C test, 63% a dilated eye examination, and 55% a foot examination.[20] These data suggest that more aggressive management of diabetes is necessary and that treatment should be modified as soon as patients fail to meet glycemic targets.

Current Stepwise Approach is Not Working

Although specific treatments may differ, treatment usually progresses in a stepwise manner from lifestyle modification (diet and exercise) as the initial strategy, to monotherapy with an OAD, combination OAD therapy, and finally insulin therapy, either in combination with an OAD or alone (Fig. 3). Long periods of inadequate control often occur before the next step (agent) is introduced.[21] Success of the stepwise approach depends on aggressive monitoring and changing the therapy when the targeted goals are not met.[22] Since the number of patients meeting the goal for A1C (see next section) continues to decline in the United States, it seems that the stepwise approach as currently utilized is not working.

Figure 3: Stepwise Approach Used for the Treatment of Type 2 Diabetes



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OADs lower A1C by 1.0% to 2.0% as monotherapy or when added as a second or third agent.[23,24] However, insulin can lower A1C to a desired target; its main limitation is the potential to cause hypoglycemia, which can often be overcome by careful monitoring of BG and adjustments of insulin doses or the meal plan. Patients should be referred to diabetes self-management training programs to learn skills to prevent and treat hypoglycemia, monitoring of BG, and insulin dose adjustment. Depending on the nature of the glucose excursions and severity of the disease, insulin can be used in combination with OADs or alone.

Limiting Diabetes-related Complications

The importance of maintaining stringent glycemic control to reduce the risk of complications is well documented. Many patients with type 2 diabetes will have some type of macrovascular or microvascular complication by the time they are diagnosed with diabetes.[25] Several landmark trials have demonstrated the importance of intensive insulin therapy to achieve glycemic control and reduce microvascular complications such as neuropathy, retinopathy, and nephropathy.[19,26,27] Epidemiological analyses of the UKPDS showed that each percentage point reduction in A1C correlated with substantial reductions in the risk for both microvascular and macrovascular complications; 21% for any end point related to diabetes including death.[28] Based on these landmark trial findings,[26-28] both the ADA[29] and the American Association of Clinical Endocrinologists (AACE)[30] have set aggressive targets for control of BG. The ADA recommends an A1C target of <7.0%, whereas the AACE goal for A1C is ≤ 6.5%.

Development of Insulin Analogs and Premixed Insulin Analogs

The development of insulin analogs has been one of the greatest advances in diabetes therapy in the last decade.[7] As shown in Table 1, several formulations of insulin analogs and premixed insulin analogs are available. Insulin analogs were developed to more closely mimic physiological secretion; they have a more predictable onset and duration of action compared with human insulin formulations. The development and use of insulin analogs has also increased flexibility for dosing and mealtimes.[7] Insulin aspart and insulin lispro are rapid-acting analogs that are administered just prior to meals while insulin glargine is a long-acting analog used for basal control (Table 1). Insulin glulisine, a rapid-acting analog, was recently approved by the US Food and Drug Administration (FDA) but is not yet available in the United States. Insulin detemir is a long-acting analog that is available in Europe and is awaiting FDA approval in the United States.

Table 1. Time-Action Profiles of Insulin Analogs and Premixed Insulin Analogs Currently Available in the United States

Formulation	Time to Onset of Action (hr)	Time to Peak Action (hr)	Duration of Action (hr)
Rapid-Acting Analogs			
Insulin lispro (Humalog®)	0.25-0.5[31]	0.8-4.3[32]	4-6[31]
Insulin aspart (NovoLog®)	<0.5[33]	1-3[34]	3-5[34]
Long-Acting Analogs			
Insulin glargine (Lantus®)	1[35]	Peakless[35]	10.8-24[35]
Premixed Insulin Analogs			
Biphasic insulin lispro 75/25 (Humalog® Mix75/25)	<0.5[36]	1-6.5[36]	~22[36]
Biphasic insulin aspart 70/30 (NovoLog® Mix 70/30)	<0.5[37]	1-4[37]	≤24[37]

Wide interindividual variation in time to onset of action, time to peak action, and duration of action can occur.

Premixed insulin analogs provide both basal and prandial coverage in one injection; they are suitable for starting insulin therapy in patients who desire a simple and convenient regimen or are not willing to administer multiple daily injections (MDIs). Two products are currently available: (1) biphasic insulin aspart 70/30 (70% insulin aspart protamine suspension and 30% insulin aspart); and (2) biphasic insulin lispro 75/25 (75% insulin lispro protamine suspension and 25% insulin lispro). The rapid-acting components of premixed analogs are more rapidly absorbed and provide better postprandial coverage compared with human insulin premixed formulations.[10] Because of their more physiological time-action profiles, insulin analogs and premixed insulin analogs also lower the risk for hypoglycemia, especially overnight, compared with human insulin formulations.[8-10,38]

When to Initiate Insulin Therapy

Insulin should be prescribed when it is likely to be the most effective agent, rather than waiting until patients fail to reach normal A1C levels with lifestyle modifications and OADs. Insulin therapy should be considered as initial therapy in patients with severe hyperglycemia (FPG >350 mg/dL), ketonuria, or intolerance or contraindications to OADs.[39] At present, many patients have had type 2 diabetes for 10 to 15 years (and may have developed complications) before insulin therapy is initiated.[21]

Because of the progressive decline in endogenous insulin secretion, insulin is eventually required by the majority of patients with type 2 diabetes. Some authorities advocate that type 2 diabetes be treated aggressively by introducing insulin earlier in the treatment plan.[23,40] Availability of insulin analogs and premixed insulin analogs, as well as development of more convenient insulin delivery systems, has alleviated some barriers and fears associated with insulin use.[40]

Poorly controlled patients have high morbidity and mortality rates, low quality of life, and incur higher healthcare costs.[23] Therefore, it is essential that glycemic control be maintained and that patients be treated with the safest and most effective regimens in a timely manner. The following case study provides an example of a patient not achieving adequate glycemic control on OADs.

Case 1: Patient was not maintaining glycemic control on combination OAD therapy and premixed insulin analog therapy was initiated

CJ is a 59-year old female. She was diagnosed with type 2 diabetes 10 years ago. Her body mass index (BMI) is currently 25 with a weight of 168 pounds and height of 5'9''. CJ works full time and commutes 40 to 60 minutes per day depending on traffic. CJ works in the sales department and her mealtimes are not set. CJ has also stated that she has no time for exercise and that she is really too tired to even consider it.

CJ was initially treated with metformin 500 mg BID and then repaglinide 2 mg TID was added. Two years ago, pioglitazone 15 mg QD was started. With each additional OAD, CJ had a 0.5% to 1% reduction in her A1C values. Her most recent OAD regimen included metformin 1000 mg BID, repaglinide 4 mg with meals, and pioglitazone 45 mg QD.

At a regular visit several months ago, CJ complained of nocturia, polyuria, and polyphagia. Her body weight had also increased 15 pounds over the last 6 months. CJ's fasting blood glucose (FBG) level was 180 mg/dL and postprandial values were over 300 mg/dL. Her A1C value was 8.2%.

Messages

This patient is now at the final phase of the conventional stepwise approach (Fig. 3). Control is inadequate on combination OAD therapy. While FBG is high, the postmeal readings are markedly abnormal. The A1C of 8.2% suggests that the hyperglycemia may be related to the high postmeal excursions.[15] Meals are inconsistent in both timing and portions, with dinner the largest meal. What treatment options could be recommended for this patient who was reluctant to commence insulin therapy?

Options for initiating insulin therapy

Plan A

Prescribe premixed analog at dinnertime (eg, biphasic insulin aspart 70/30 or biphasic insulin lispro 75/25) with the option to add a second injection if needed.

i. Provides both prandial and overnight basal insulin coverage with a single injection
ii. Insulin can be administered by pen or doser within 15 minutes before meal
iii. Premixed analog eliminates mixing errors
iv. Fixed ratio of rapid- and intermediate-acting analogs precludes the independent adjustment of the basal and prandial components
v. Requires a fixed meal size and a bedtime snack to prevent nocturnal hypoglycemia
vi. Retain metformin and pioglitazone. Use of repaglinide based on PPG values at breakfast and lunchtime; discontinued at dinnertime.

Plan B

Prescribe long-acting insulin analog (eg, insulin glargine) with the option to add a rapid-acting insulin analog if PPG is not controlled.

i. Provides basal insulin coverage for up to 24 hours with a single injection
ii. Reduces the risk of hypoglycemia related to eating less than planned
iii. Does not remedy the postmeal excursions
iv. Retain all OADs especially secretagogues to help with endogenous insulin release with meals

Plan C

Prescribe mealtime rapid-acting insulin analog (eg, insulin aspart or insulin lispro) with the option to add a long-acting insulin analog if FPG is not controlled.

i. Requires a dose of insulin before each meal
ii. This regimen does not provide basal coverage
iii. Insulin can be administered using a pen or doser
iv. Lowering the postmeal readings should lower the FBG and impact the A1C
v. Allows CJ to decide when she wants to eat and to alter the insulin dose based on the food she plans to eat
vi. Retain metformin and pioglitazone and discontinue repaglinide

The healthcare provider and the patient decided to try Plan A because it is a simple regimen that has the potential to control both the postprandial and basal glucose excursions in one injection. CJ decided to administer one injection of a premixed insulin analog just prior to dinner (her largest meal) and to consume a bedtime snack to minimize the risk of nocturnal hypoglycemia. The diabetes educator helped CJ with dinner choices to ensure a consistent carbohydrate intake and identified a realistic plan to increase physical activity. After 3 months on Plan A, CJ's FPG level had decreased to 110 mg/dL and her PPG readings were usually <140 mg/dL. Her A1C had decreased to 6.9%. CJ was asked to check her BG levels 2 hours after breakfast and lunch. CJ reported that she has reduced her portions of food, has more energy, and is now walking 30 minutes three times a week. CJ was also counseled that she may have to use two injections of the premixed analog to lower her A1C further.

How to Initiate Insulin Therapy

Individualized BG targets are usually established for each patient. The aim of insulin therapy is to achieve optimal glycemic control without causing hypoglycemia or excessive weight gain. When initiating insulin therapy, many patients remain on their OADs but the doses are gradually reduced. The insulin dose can be titrated slowly over several weeks as necessary to achieve optimal glucose levels. The regimen should be simple and tailored to match the patient's needs and lifestyle. The contributions of fasting and postprandial glucose excursions to overall hyperglycemia should also be considered.

Other issues that need to be addressed when initiating insulin therapy include the type(s) of insulin formulation, the number of injections, and the insulin delivery system that is appropriate for a particular patient. The following points should be considered when choosing an insulin formulation: how rapidly it works (onset); when it works at maximum capacity (peak); how long it works (duration); and impact on lifestyle. The predictability of these properties and the stability of the different formulations in various insulin delivery systems should also be considered. Variable absorption of human insulin formulations has been a major limitation.[7] This is less of an issue with insulin analogs and premixed insulin analogs because they have more predictable time-action profiles.

In clinical studies and in everyday practice, many clinicians empirically start with a low fixed dose of insulin. Algorithms used to estimate insulin doses vary.[7,18,24,41-44] The starting regimen is determined primarily by the degree of hyperglycemia as measured by BG monitoring and the A1C value. Body weight is also usually used to calculate the appropriate starting insulin dose. Based on home glucose monitoring, the dose is then titrated every few days or weekly by the physician via telephone or during brief office visits.[45] Beginning at a low dose and slowly titrating to higher doses helps avoid hypoglycemia and builds patient confidence when initiating insulin therapy. Healthcare providers should explain that the dose will be raised over time as the disease progresses. They should also point out that some degree of disease progression is normal and not due to "failure" of the patient to adhere to the treatment plan. The following characteristics and issues can be considered when calculating the starting insulin dose and making dose adjustments.[18]

Blood Glucose Levels

BG monitoring is essential for evaluation of the prescribed regimen. A reasonable plan involves checking at least one fasting and one postprandial BG value and recording each result. The frequency and timing of BG testing depends primarily on the insulin regimen. The patient can record each result, preferably using a meter with memory and download capability. The frequency of monitoring also depends on the severity of hyperglycemia, magnitude of glucose

excursions, and patient willingness. Those using MDIs may need to check the BG level before each meal, 2 hours postprandial, and at bedtime each day. BG levels should be checked if the individual has signs or symptoms of hypoglycemia. Patterns of highs or lows indicate that a dose adjustment may be needed.

Carbohydrate Counting and Adjustment of Mealtime Insulin Doses

Carbohydrate counting is an advanced skill that adds flexibility to meal planning. Patients using MDIs or an insulin pump can adjust the mealtime insulin dose based on the estimated carbohydrate content of the meal as well as the BG reading.[43] For example, 1 unit of a rapid-acting analog can be given for every 10 to 15 grams of carbohydrate consumed.[46] This strategy works for basal-bolus therapy but is not appropriate for patients using a premixed analog formulation.

An obese individual may need a ratio of 1:5 (1 unit of a rapid-acting insulin analog for every 5 grams of carbohydrates to be consumed), while a thin, insulin-sensitive individual may require a ratio of 1:20. BG should be checked 2 hours after the meal to determine if the dose is correct. Postprandial BG should be within 30 points of the preprandial value when the insulin to carbohydrate ratio is optimal.

If the premeal glucose is high, more (supplemental) insulin may be given in addition to the normal prandial insulin dose. The extra insulin will vary according to a patient's sensitivity to insulin. For example, patients may require an additional 1 to 2 units for every 50 mg/dL the premeal glucose level is above the target.[43]

For example, patient DM uses an insulin to carbohydrate ratio of 1:15. He is about to eat dinner which he estimates contains 90 grams of carbohydrates. Although his premeal BG target is 100 mg/dL, the actual reading was 200 mg/dL. Therefore, he may have underestimated the carbohydrate content at the previous meal resulting in a high predinner reading. DM will take 6 units of insulin aspart to cover the 90 grams of carbohydrates plus another 2 units of insulin aspart to correct for being 100 mg/dL over his target glucose. His total insulin dose with dinner will be 8 units.

Body Weight

Overweight patients require higher doses of insulin, probably because of greater insulin resistance and deficiency. Although 0.4 to 0.8 units/kg can be used as an initial daily dose in overweight patients, many patients with type 2 diabetes need a total daily dose of 1.0 to 1.2 units/kg to achieve an A1C <7.0%.[42] The initial dose is increased by 2- to 4-unit increments (or by 5- to 10-unit increments in patients with severe insulin resistance) every 3 to 4 days until the desired level of control is achieved.[44]

Special Considerations

Dose adjustments may be required if the patient is taking certain medications that affect carbohydrate metabolism or responses to insulin. Liver or renal disease can also affect the pharmacokinetics of insulin. Exercise, illness, stress, aberrant eating patterns, alcohol, and travel may also necessitate dose adjustments.

Examples of Insulin Regimens and Other Case Studies

Coverage of PPG and FPG with a Premixed Insulin Analog

Since the main aim of insulin therapy is to correct the physiological deficit and mimic endogenous secretion without causing hypoglycemia,[38] both PPG and FPG should be targeted. Premixed insulin analogs enable both PPG and FPG to be covered with the same injection. A premixed formulation can be administered once or twice a day, sometimes in conjunction with OAD therapy.

Case 2: Patient was successfully treated with a premixed insulin analog formulation and both PPG and FPG were monitored

RP, a 57-year-old female with a BMI of 33.2 was diagnosed as having type 2 diabetes 9 years ago. She was referred to an endocrinologist for management of uncontrolled hyperglycemia and diabetes-related complications including retinopathy and nephropathy. RP described several weeks of increased polyuria and polydipsia. Random BG levels measured at home were in the 347- to 514-mg/dL range. Her physical activity was limited by comorbid osteoarthritis. She had recently seen a registered dietitian and was trying to follow her dietary recommendations. At presentation, RP's medications included lisinopril 5 mg QD and glipizide 10 mg BID. Previous gastrointestinal side effects experienced with metformin precluded its use. Her A1C at this visit was 11.5% (normal <6.0%), whereas the last available measurement 1 year ago was 7.8%. Serum chemistry tests revealed normal renal and liver function.

RP was started on a premixed insulin analog formulation beginning with 10 units, 15 minutes before breakfast, and 10 units, 15 minutes before dinner. This premixed insulin analog formulation

contains 70% intermediate-acting insulin aspart protamine suspension, which provides basal coverage, and 30% rapid-acting insulin aspart, which has prandial action. Her glipizide was discontinued and the insulin dose was titrated, based on BG monitoring results given to the physician by telephone, to 20 units in the morning and 22 units in the evening. She returned to the office a few weeks later with the decreased BG levels reported in Table 2. Six months later, her A1C value was 7.4%.

Table 2. Blood Glucose Levels in Case 2 Patient

Day	Before Breakfast (mg/dL)	Before Lunch (mg/dL)	Before Dinner (mg/dL)	Bedtime (mg/dL)
Sunday	213	147	166	193
Monday	146	108	115	84
Tuesday	260	129	*	98
Wednesday	130	70	*	129

*Blood glucose checks not performed.

Messages

This patient with long-standing type 2 diabetes with microvascular complications presented with severe, symptomatic hyperglycemia. Due to the severity of her BG elevation, her physician prescribed a BID regimen of a premixed insulin analog. The initial low dose was empirically selected to avoid hypoglycemia and was titrated effectively by telephone and subsequent office consultations.

In retrospect, earlier initiation of insulin therapy in this patient may have prevented or delayed the diabetes-related complications. Additional dose titration will be necessary to reduce the A1C further. The patient needs to be instructed not to skip meals as the prandial component of her insulin regimen may cause hypoglycemia.

Case 3: Patient had experienced adverse events with OADs and was switched to a premixed insulin analog formulation

LJ is a 66-year-old female with a BMI of 27.0 and a 7-year history of type 2 diabetes. Her most recent A1C was 9.9% and, as a result, metformin 500 mg BID was added to glyburide 10 mg BID. Because she was experiencing gastrointestinal side effects from the metformin after 1 month, her therapy was changed. It was assessed that LJ was following her meal plan and that she has very routine mealtimes with fixed amounts of food. LJ's day-to-day activities do not vary much. She monitors her BG levels 2 to 3 times daily and reports that her FPG levels average 147 mg/dL, premeal levels average 173 mg/dL, and postmeal levels average 235 mg/dL. In discussing therapeutic options with this patient, it was decided to try a premixed insulin analog BID (biphasic insulin lispro 75/25) and discontinue OADs. After 4 weeks, her doses were stabilized at 20 units, 15 minutes before breakfast and dinner. After 3 months of this regimen, the patient's FPG levels averaged 125 mg/dL, her PPG levels averaged 180 mg/dL, and her A1C decreased to 7.5%.

Messages

Premixed insulin analogs can be an appropriate choice for patients who have a routine lifestyle. The A1C value should be checked in another 3 months and a dose adjustment or change in her treatment regimen may be required if the A1C goals are not met.

Initial Coverage with a Long-acting Insulin Analog

Another common way to begin insulin therapy is to add a long-acting insulin analog to OAD therapy at bedtime. Problems of nocturnal hypoglycemia with neutral protamine Hagedorn (NPH) insulin therapy may be overcome by using a long-acting insulin analog instead; this is because the pharmacokinetic profile is relatively peakless compared with NPH insulin.[45,47] Because individual dose requirements can vary considerably depending on the degree of endogenous insulin deficiency, dosing should be based on treatment goals (ie, FPG levels between 90 and 130 mg/dL).[44] As these basal regimens do not cover the postprandial glucose excursions, OADs or a rapid-acting insulin analog may need to be added. Furthermore, basal insulin analogs such as insulin glargine do not last for 24 hours in all patients.[9]

Case 4: Patient with elevated A1C and neuropathy on high doses of OADs was successfully treated with a long-acting insulin analog formulation

JT is a 53-year-old male with a 3-year history of type 2 diabetes. He is 5'11'' with a BMI of 30. His A1C value is 8% on high doses of OADs, which include metformin 1000 mg BID, glyburide 10 mg BID, and rosiglitazone 4 mg BID. JT is very concerned because a recent eye examination showed early retinopathy. Because he travels frequently with his job, mealtimes, exercise, and BG monitoring are erratic. A review of his meter's memory revealed that he had checked his BG levels only 7 times in the past month. JT is now willing to do whatever it takes to get his BG levels under control. After explaining the therapeutic options, his medications were changed to a long-acting insulin analog at night and OADs during the day. He also met with the registered dietitian to design a meal and exercise plan to fit his lifestyle.

After 1 month of this new regimen (metformin 1000 mg BID, rosiglitazone 4 mg BID and insulin glargine 10 units at bedtime), the patient's average BG levels were an FPG of 120 mg/dL and PPG of <180 mg/dL. After 3 months of this regimen, the patient's A1C was 6.8%. The patient will need to continue monitoring his BG levels because over time he may eventually need a rapid-acting insulin analog to keep his PPG under control.

Messages

In patients with erratic schedules or unpredictable activity, a long-acting insulin analog may be less likely to result in hypoglycemia versus an intermediate-acting insulin such as NPH. Since postprandial hyperglycemia can significantly contribute to his A1C value, JT may eventually require a rapid-acting insulin analog after each meal or a twice-daily premixed insulin analog if the OAD therapy does not provide optimal PPG control.

Case 5: Patient was successfully treated with a long-acting insulin analog formulation but required an OAD for prandial control

CZ is an obese (BMI of 46) 56-year-old female who presented with a 6-year history of type 2 diabetes and insulin resistance. Her FPG (161 mg/dL) and A1C (9.6%) levels at presentation were both elevated. She was taking a combination of glyburide 10 mg and metformin 1000 mg BID as well as medication for hypercholesterolemia and hypertension. Given the level of hyperglycemia, a long-acting insulin analog was prescribed at bedtime and glyburide was discontinued. Her meal plan was also modified to reduce portions and improve variety. After 2 weeks, her FPG levels were consistently <130 mg/dL. One month later at her diabetes education class, CZ's postprandial blood glucose was measured after she drank a regular soft drink. The reading of 327 mg/dL shocked her as she was accustomed to fasting readings <130 mg/dL. CZ learned more about food choices and portions and began PPG monitoring. Even when her food choices were within her meal plan, her postprandial readings were out of range and repaglinide 4 mg was initiated at breakfast and dinner. After 3 months, her FPG range was 100 to 114 mg/dL, PPG range was 141 to 157 mg/dL, and A1C was 7.2%.

Messages

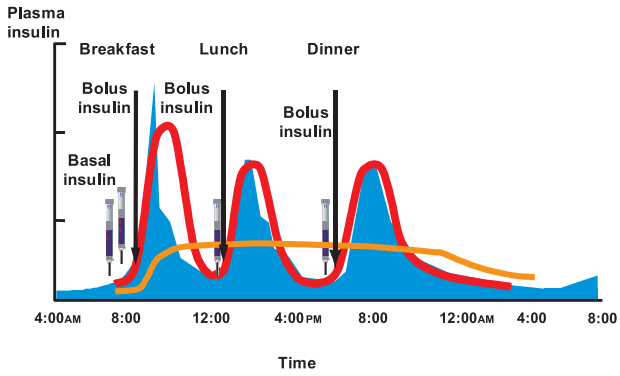
A bedtime long-acting insulin analog for this insulin-resistant patient combined with diabetes self-management education was an appropriate introduction to insulin therapy. However, this case also illustrates the importance of postprandial blood glucose monitoring. Patients often need to see elevated postprandial readings before they are convinced to make further changes in their therapy. Even with careful adherence to her meal plan, treatment of postprandial hyperglycemia was necessary in this case to control PPG levels. The patient preferred to start with a prandial secretagogue rather than administer additional injections of insulin. In retrospect, therapy with repaglinide may not have been necessary if glyburide was not discontinued when insulin therapy was initiated.

Basal-Bolus (MDI) Therapy

Basal-bolus therapy attempts to mimic basal and postprandial insulin secretion. Many physicians and healthcare providers are now prescribing these regimens in patients with type 2 diabetes to aggressively control BG levels in patients with advanced ß-cell deficiency and complications. Successful use of basal-bolus therapy requires comprehensive patient education. Patients also need to learn carbohydrate counting and how to use a correction factor for insulin dose adjustment.

An MDI regimen often includes a rapid-acting insulin analog before each meal and a long-acting insulin analog once a day (Fig. 4). Therefore, patients can coordinate the timing of injections with meals, giving them more flexibility with mealtimes and lifestyle. Patients should monitor their BG levels frequently (morning and nighttime fasting and 2 hours after each meal) and determine the impact of meal content, particularly carbohydrates, on the dose of insulin required. An insulin pump can be used in place of MDI in patients who are suitable candidates for continuous subcutaneous insulin infusion therapy.

Figure 4: Representation of Rapid-Acting and Long-Acting Insulin Analog Time-Action Curves



Case 6: Patient with elevated A1C despite aggressive OAD therapy reluctantly started basal insulin therapy, and ultimately required MDI therapy to achieve optimal glycemic control

SM is a 60-year-old female with a BMI of 26.5 (height, 5'5''; weight, 159 pounds). She was diagnosed with type 2 diabetes 6 years ago. SM reported that her BG levels, checked at home upon waking and at bedtime as well as after each meal, ranged from 200 to 350 mg/dL before and after meals, respectively. She had a regular exercise routine that included walking 4 to 5 times a week for 30 minutes and made healthy food choices. She described burning pains in both feet at night. Medications at presentation included glyburide 10 mg BID and metformin 500 mg BID; she reported that higher doses of metformin had caused diarrhea. Pioglitazone 30 mg had been prescribed in the past, but was discontinued because of pedal edema. Her A1C was 9.3%.

SM was reluctant to start insulin therapy but agreed to one injection of insulin glargine, 10 units, once daily at bedtime. The dose was titrated based on BG monitoring results given to the physician over the telephone by the patient. At follow-up 3 weeks later, she reported administering insulin glargine 30 units at bedtime and continuing OADs. FPG levels were between 70 and 100 mg/dL, but PPG levels were all >250 mg/dL. Her physician suggested supplementing with insulin aspart, starting with one injection of 10 units with her largest meal of the day. She agreed and subsequently discovered that her BG excursions were better controlled if she administered the insulin aspart with all of her meals. Glyburide was discontinued.

SM met with a diabetes educator and learned how to use a pen device for delivering insulin aspart. She also learned how to estimate the carbohydrate content of her meals so that she may adjust the insulin aspart dose and SM also discussed healthy meal choices and ways to minimize weight gain. She carries her insulin pen with her wherever she goes and is very pleased with her ability to manage her BG levels and does not mind administering insulin 4 times per day. After 3 months, her FPG levels averaged 113 mg/dL and her PPG levels averaged 153 mg/dL. Her A1C had decreased to 6.9%.

Messages

Patients who need multiple injections of insulin can begin with a once-daily injection of a long-acting insulin analog with subsequent addition of a rapid-acting insulin analog at mealtimes. Working with a diabetes-care team and an easy-to-use insulin delivery system helped this patient transition to an MDI regimen. The improvements in glycemic control, flexibility, ownership, and general well-being have also helped this patient accept the regimen.

Case 7: Patient using a premixed human insulin formulation presented with hypoglycemia and was switched to a basal-bolus regimen

DT is a 57-year-old African American male who was diagnosed with type 2 diabetes 12 years ago. He travels frequently with his job and finds it difficult to eat his meals on time and make dose adjustments for the amount of food that he eats at each meal. DT's last A1C was 9.0%. He was injecting 60 units of premixed human insulin 70/30 before breakfast and an additional 30 units before dinner. DT presented to his physician with complaints of hypoglycemia in the afternoon. His insulin regimen was changed to an MDI regimen with insulin analogs to allow more flexibility at mealtimes and in his lifestyle.

The physician started the patient on 40 units of a long-acting insulin analog at bedtime and followed the registered dietitian's recommendation to initially use 1 unit of a rapid-acting insulin analog for every 15 grams of carbohydrate eaten at each meal. After 3 weeks, his average BG values were as shown in Table 3. To determine if the insulin to carbohydrate ratio is correct, DT was advised that the 2-hour PPG level should be within 30 to 40 mg/dL of the premeal value.

Table 3. Blood Glucose Levels in Case 7 Patient

Blood Glucose Checks	Values (mg/dL)
Fasting Blood Glucose	123
2 hrs after breakfast	155
Before lunch	103
2 hrs after lunch	185
Before dinner	115
2 hours after dinner	169

DT was concerned because his 2-hour PPG values were still greater than his target goal of 140 mg/dL 2 hours after a meal. He contacted his primary care physician and registered dietitian and they recommended 1 unit of rapid-acting analog for every 12 grams of carbohydrate. It was also recommended that he keep a food diary and compare BG levels after meals so the optimal insulin to carbohydrate ratio could be determined. The patient followed these recommendations and met his fasting, premeal, and postprandial blood glucose goals. After 3 months, his A1C had been reduced to 8.1%. The more rapid action and duration of activity of the rapid-acting analog formulation may have helped resolve his problems with hypoglycemia.

Messages

Patients with irregular mealtimes and schedules often need to use flexible insulin dosing with a MDI regimen to achieve optimal glycemic control. Furthermore, it is important that the prandial doses are adjusted by calculating the carbohydrate content of the meal and by monitoring PPG levels. Further adjustments will be necessary to get A1C to <7.0% or ≤ 6.5%.

Case 8: Patient using premixed insulin analog regimen improved glycemic control after switching to an MDI regimen

MS is a 65-year-old recently retired businessman who was diagnosed with type 2 diabetes nearly 10 years ago. For the last 2 years he has been injecting insulin. He has a history of hypertension and hyperlipidemia which are well controlled. At the last ophthalmology visit, he was found to have pre-proliferative retinopathy. His A1C at a recent visit was 7.9%.

MS is using a premixed insulin analog (biphasic insulin aspart 70/30). He takes 47 units in the morning with breakfast and 35 units with his evening meal. His wife comes with him to every clinic visit and prepares most of his meals and snacks. He follows a meal plan with consistent carbohydrate content except on the days when he plays golf with his friends.

His BG levels over a one-week period are shown in Table 4.

On Monday, MS played golf and had a larger than usual lunch with his friends. He took extra units of the premixed insulin analog to cover his high predinner glucose but awoke in the middle of the night with symptoms of hypoglycemia, for which he ate a snack with some juice.

MS and his physician agreed he needed to intensify his insulin therapy to prevent progression of diabetes-related complications. He has trouble with hyperglycemia following lunch and has occasional hypoglycemia at other times. He would also like to play golf more often, providing it would not negatively affect his glycemic control.

His physician started him on a basal-bolus MDI regimen. His current total insulin dose was 82 units a day. The physician prescribed insulin glargine, 40 units every evening, and insulin aspart, 10 to 15 units with each meal. This provided him with about half of his total insulin dose as basal insulin and the other half as prandial insulin, which could be adjusted according to the carbohydrate content of each meal after he and his wife learned advanced carbohydrate counting skills.

Messages

In patients with type 2 diabetes and advanced ß-cell dysfunction, an MDI insulin regimen provides the most physiological insulin replacement. With an MDI basal-bolus regimen, near-normal glycemia can be achieved with less hypoglycemia. Most patients benefit from using a rapid-acting analog with each meal and the ability to vary the timing and the dose to account for changes in schedules and size of meals. Various easy-to-use insulin delivery systems can be used to administer the rapid-acting insulin analog in a convenient and discreet manner.

Points to Consider When Implementing Insulin Therapy

Addressing Concerns about Insulin Therapy

As BG and A1C continue to increase, insulin therapy may be required; however, patients resist for a variety of reasons.[48] The healthcare provider can assist patients in making an informed decision by understanding their concerns and providing the

Table 4. Blood Glucose Levels in Case 8 Patient

Day	Before Breakfast (mg/dL)	Before Lunch (mg/dL)	Before Dinner (mg/dL)	Bedtime (mg/dL)	3:00AM (mg/dL)
Friday	180	60	215	150	*
Saturday	125	85	191	*	*
Sunday	203	*	225	*	*
Monday	162	*	348	*	47
Tuesday	226	92	185	*	*
Wednesday	170	*	*	82	*
Thursday	123	*	*	*	*

*Blood glucose checks not performed.

Table 5. Common Concerns in Patients Starting Insulin Therapy

Concern	Resolution
Initial anxiety	More education and support about the role of insulin in treating diabetes.
Feeling of personal "failure"	Inform patient that diabetes is a progressive disease and explain ß-cell failure.
Hypoglycemia	Educate about the signs and symptoms as well as prevention and treatment.
Injection phobia	Teach self-injection with saline. Explain devices including those that conceal the needle as well as availability of fine needles.
Weight gain	Explain improved metabolic control and efficiency. Adjust diet and physical activity. Carefully plan snacks and incorporate into the meal plan.
Lifestyle factors	Explain flexible and multiple insulin regimens and devices that allow discreet dosing. Insulin administration can enhance lifestyle flexibility because dosing can be adjusted to accommodate activity and changes in meal plans.
Lack of support	Explain role of the diabetes care team and education for family and friends.
Myths about insulin	Explain treatment options and progressive nature of the disease at initial diagnosis. Use evidence-based literature to dispel myths.
Preventing complications	Explain how insulin can reduce the risk of further microvascular and, perhaps, macrovascular complications.

information they require.[48] Table 5 shows some common concerns and strategies that can help patients overcome these issues. Patients should be referred to a diabetes team to increase their knowledge and learn the various skills required to manage diabetes.

Using a Diabetes-care Team Approach

Because diabetes is a multifaceted disease, a multidisciplinary team approach to disease management is recommended. However in primary care practice, where the majority of patients are treated, the physician may lack the time and resources to instruct and educate patients. Collaboration with diabetes educators and other healthcare professionals should be part of the standards of care for patients with diabetes.

The patient should be intimately involved in all aspects of care including the choice of therapy. Many concerns about insulin therapy are manageable and can be prevented by careful monitoring and dose adjustments.

Healthcare professionals working with patients with diabetes are more than just teachers and providers; these individuals are expert coaches that lead the patient through the complexities of insulin therapy and help them problem solve. Apart from insulin administration skills and options, patients also need to learn recognition, prevention, and treatment of hypoglycemia, exercise guidelines and precautions, meal planning and carbohydrate counting, and weight management. The skills involved in making adjustments for exercise, travel, during sickness, and when under stress are part of a diabetes education curriculum.

Weight gain with insulin can occur because of improved glycemic control, less glucosuria, or overinsulinization, not necessarily because insulin is anabolic. Furthermore, snacking, to prevent hypoglycemia or feed the peaks of human insulin, can add unnecessary calories. Patients can work with registered dietitians to minimize any weight gain due to more efficient metabolism or snacking.

Improvements in Insulin Delivery Systems

Delivery of insulin by vial and syringe has been a considerable barrier to patient acceptance and adherence with insulin therapy.[49] Patients who were once limited to the single option of vial and syringe delivery now have the choice of reusable "durable" or prefilled "disposable" insulin pens, insulin jet injectors, insulin dosers, or an external insulin pump. The ideal insulin delivery system is one that provides accurate dosing while being comfortable and convenient for the patient. Other considerations for choosing the ideal delivery system include patient safety, social acceptability, affordability, and environmental issues. The fear of pain and other concerns with injections have been diminished by the availability of finer and smaller needles, and utilization of insulin pens and dosers. Development of insulin pumps that are no larger than a pager enables doses of insulin to be delivered as needed (basal-bolus) without the need for multiple injections.

Summary and Recommendations

- Because ß-cell deficiency is an inevitable consequence of type 2 diabetes, insulin therapy should be initiated when patients are not able to meet glycemic goals with OADs.
- Since basal and postprandial glucose excursions both contribute to overall glycemic control, both FPG and PPG levels need to be targeted and monitored if patients are to meet goals.
- Goals for glycemic control and insulin doses should be individualized. Although various algorithms for calculating insulin dosage can be used as guidelines, most clinicians start with a low dose based on body weight and titrate up every 3 to 4 days based on BG readings and meal carbohydrate content until goals are achieved.
- The insulin regimen is prescribed to achieve glycemic control and minimize risk of hypoglycemia and other metabolic disturbances. The regimen should be easy to follow and adjusted when necessary based on BG readings and the carbohydrate content of meals.
- The more predictive onset and duration of action of insulin analogs and premixed insulin analogs can lower the risk of hypoglycemia.
- Basal-bolus therapy, with a rapid-acting analog 15 minutes before meals and a long-acting insulin analog for basal coverage, is effective in patients with advanced ß-cell dysfunction and provides patients with flexible insulin dosing based on their lifestyle needs.
- Insulin pens, dosers, and pumps have overcome many concerns associated with vial and syringe delivery. These devices should be explained and offered to each patient.
- Where possible, patients should work with a diabetes-care team and be encouraged to take an active role in managing their disease.

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Post-Test

1. Which of the following variables should be considered when prescribing treatments for type 2 diabetes?

   a. Lifestyle
   b. Insulin resistance
   c. ß-cell function
   d. All of the above

2. All of the following are true about postprandial glucose excursions EXCEPT _____.

   a. They are *primarily* due to impaired first-phase insulin secretion
   b. They *do not* contribute significantly to overall glycemic control
   c. They *usually* peak 2 hours after a meal
   d. They *can be* controlled by administering a rapid-acting insulin analog

3. Compared to impaired fasting glucose, the DECODE study showed that inadequate postprandial glucose control is a _____ contributor to cardiovascular risk.

   a. Larger
   b. Smaller
   c. Similar

4. All the following statements are true about insulin therapy EXCEPT _____.

   a. Insulin can be administered via a pen device
   b. Human insulin formulations have more physiological time-action profiles compared with insulin analogs
   c. Insulin therapy is typically initiated after patients do not meet goals with OADs
   d. Risk of hypoglycemia limits the dosage of insulin

5. SW is a 46-year-old female diagnosed 10 years ago with type 2 diabetes. She now has symptoms of nocturia, polyuria, and polyphagia and reports that she is not feeling well. She is overweight and is currently taking high doses of metformin, pioglitazone, and repaglinide. Her A1C is 8.2%, while her FPG levels average 180 mg/dL and her PPG levels average 310 mg/dL. She also has an erratic meal schedule and does not exercise. With a suitable adjustment in OAD therapy, an appropriate starting regimen for insulin therapy would be_____.

   a. A rapid-acting insulin analog
   b. A premixed insulin analog formulation before dinner
   c. A long-acting insulin analog at bedtime
   d. Any of the above

6. All the following are usually considered when initiating insulin therapy EXCEPT _____.

   a. Blood glucose levels and A1C
   b. Time-action profile of insulin formulation
   c. Family history of insulin use
   d. Type of insulin delivery system

7. Common concerns for patients starting insulin therapy include _____.

   a. Type of insulin formulation
   b. Hypoglycemia
   c. Weight gain
   d. Both b and c

8. Which of the following statements is FALSE about insulin analogs and premixed insulin analogs?

   a. Three premixed insulin analog formulations are currently available in the United States.
   b. They have a more predictable onset of action compared with human insulin.
   c. Insulin aspart is a short-acting analog.
   d. Insulin glargine is a long-acting analog.

9. Patients with hyperglycemia and _____ should be placed on insulin therapy initially.

   a. FPG >250 mg/dL
   b. Ketonuria
   c. Hypocalcemia
   d. Either a or c

10. DJ is a 50-year-old female with a BMI of 27.3. She was diagnosed with type 2 diabetes 10 years ago and has been using human insulin formulations for nearly 5 years. DJ's blood pressure is 135/85 mm HG and she also has signs of retinopathy. Although DJ's A1C level has been reduced to 7.6% with a basal-bolus regimen, she has also experienced wide glucose excursions and nocturnal hypoglycemia. These glycemic problems are most likely related to _____.

    a. Inappropriate insulin dosing
    b. Poor control of blood lipids
    c. Poor control of hypertension
    d. Either a or b

11. The patient in question 10 also lives a very demanding and unpredictable lifestyle. She is also very motivated to improve her A1C value. Is she an appropriate candidate for an insulin pump?

    a. Yes
    b. No

12. Patient concerns regarding insulin therapy can be addressed by_____.

    a. Explaining choices of insulin delivery systems
    b. Devising strategies to reduce risk of hypoglycemia and weight gain
    c. Working with a diabetes care team
    d. All of the above

13. EH is a 43 year-old male with a BMI of 33.5. He was diagnosed with type 2 diabetes 5 years ago and has been on OADs for nearly 5 years. Because EH's A1C level has increased to 9.1%, his physician recommends that he commence insulin therapy. However, EH is very anxious about injections and wants to start with a simple regimen. Based on EH's needs and concerns, which of the following would be a good starting regimen for providing both basal and postprandial coverage?

    a. A long-acting insulin analog QD using a vial and syringe
    b. A rapid-acting insulin analog BID using a pen device
    c. A premixed insulin analog formulation BID using a pen device
    d. A basal-bolus regimen using an injection device or insulin pump

14. EH is now 48 years old with a BMI of 36.5. Although he had maintained good glycemic control with his insulin regimen that was prescribed 5 years ago, his BG patterns have become more irregular and A1C has increased from 6.9% 1 year ago to 8.6%. Since the diabetes educator determined that EH had been adhering to his treatment and he no longer feared injections, he may benefit if his regimen was now changed to _____.

    a. A long-acting insulin analog QD using a vial and syringe
    b. A rapid-acting insulin analog BID using a pen device
    c. A premixed insulin analog formulation BID using a pen device
    d. A basal-bolus regimen using an injection device or insulin pump

Program Evaluation [069-999-04-188-H04]

Demystifying Insulin Therapy: Why, When, and How to Use Insulin Analogs and Premixed Insulin Analogs in Patients with Type 2 Diabetes

How many hours ____ and minutes ____ did it take you to complete this CE program? Please indicate date of completion _____
DIRECTIONS: Please rate the following on a scale of 1 - 5 (1 = Poor, 5 = Excellent)

EFFECTIVENESS OF TEACHING/LEARNING METHOD (Please circle one response per line.)

How well did this program achieve the following objectives?	Poor				Excellent
Discuss how treatment of type 2 diabetes can be matched to the pathophysiology of the disease (ie, insulin deficiency and insulin resistance) and attempt to mimic the normal physiology of insulin secretion.	1	2	3	4	5
Explain the importance of considering both fasting and postprandial glycemic control when designing treatment regimens.	1	2	3	4	5
Identify when patients need to be placed on insulin therapy.	1	2	3	4	5
Describe factors that influence the choice of insulin regimen and how insulin doses can be titrated and adjusted.	1	2	3	4	5
Explain the advantages of insulin analogs and premixed insulin analogs over human insulin formulations.	1	2	3	4	5
Describe how utilization of innovative insulin delivery devices can help overcome patient and healthcare provider concerns regarding insulin therapy.	1	2	3	4	5
	Strongly Disagree				**Strongly Agree**
The relationship of the learning objectives to the overall purpose/goal of this independent study was effective.	1	2	3	4	5
The teaching/learning resources were effective.	1	2	3	4	5
This home study has contributed to my professional effectiveness and improved my ability to:					
■ Optimize patient care	1	2	3	4	5
■ Communicate with patients	1	2	3	4	5
■ Manage my practice	1	2	3	4	5
■ Improve my clinical skills	1	2	3	4	5

Other _____

_____

	Poor				Excellent
The overall program was:	1	2	3	4	5

Did you feel this program covered the topic adequately?	❑ Yes	❑ No
Do you feel that the program was balanced, objective, and free of commercial bias?	❑ Yes	❑ No
Will you change your clinical practice based on this activity?	❑ Yes	❑ No

If so, how?_____

Suggested topics for future programs: _____

_____

General comments/suggestions: _____

_____

_____

Post-Test Answer Key

(Circle the correct answer.)

1.	a	b	c	d
2.	a	b	c	d
3.	a	b	c	
4.	a	b	c	d
5.	a	b	c	d
6.	a	b	c	d
7.	a	b	c	d
8.	a	b	c	d
9.	a	b	c	d
10.	a	b	c	d
11.	a	b		
12.	a	b	c	d
13.	a	b	c	d
14.	a	b	c	d

Demystifying Insulin Therapy: Why, When, and How to Use Insulin Analogs and Premixed Insulin Analogs in Patients with Type 2 Diabetes

To obtain a statement of credit, you must complete the post-test with a score of at least 70%, complete the program evaluation, and mail or fax both the evaluation form and the answer key to Program Management Services. Your statement of credit will be mailed in 4-6 weeks.

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Fax: (631) 563-1907

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