

Insulin Therapy: Questions This Issue

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Note: The goal of this section of *Insulin* is to provide answers to frequently asked questions regarding insulin therapy in diabetes. Readers are encouraged to submit their own questions by visiting www.InsulinJournal.com or by e-mailing insulin@elsevier.com. One or more questions will be addressed each issue.

QUESTION:

Apart from clinical findings, how can I tell my patient with certainty that he has type 1 diabetes mellitus (DM)? I ask this question because last week I saw a 27-year-old male patient who, 3 months earlier, had received an initial diagnosis of diabetes and was started on oral hypoglycemic agents. Last week he was admitted to our hospital with diabetic ketoacidosis. This problem could have been prevented if initially the patient's diabetes had been categorized as type 1 DM and he had been started on insulin therapy.

ANSWER:

Many patients have diabetes that is difficult to characterize for various reasons: an increasing prevalence of both types of diabetes, onset of type 2 DM at a much younger age, onset of autoimmune diabetes at a later age, and increasing longevity of patients with type 1 DM. About 10% of patients who are diagnosed with type 2 DM may have a pathologic process similar to that found in patients with type 1 DM (ie, autoimmune destruction of β -cells); these patients have latent autoimmune diabetes in adults (LADA). Clinical features that are often helpful in differentiating between the 2 types of diabetes (but not always possible to obtain) are presented in **Table I** (type 1 DM) and **Table II** (type 2 DM).

It is important to identify the type of diabetes correctly because it will clearly affect treatment decisions and will prevent problems similar to this case. The author likes to develop a clinical suspicion based on clinical features (**Tables I and II**) for all of his patients with diabetes at the initial visit and chooses to further evaluate those patients who cannot be clearly categorized as having type 1 or type 2 DM. Two types of tests are helpful in characterizing such borderline cases:

- Diabetes-related autoantibodies: The presence of antibodies like islet-cell cytoplasmic autoantibodies, glutamic acid decarboxylase autoantibodies (GADs), or insulin autoantibodies suggests type 1 DM or LADA. The author typically checks anti-GAD antibodies only, because other antibodies typically do not provide any additional information.
- β -Cell function: C-peptide levels can be used to assess β -cell function and characterize the type of diabetes. Patients with type 1 DM have very low C-peptide levels, whereas patients with type 2 DM have insulin resistance and, hence, elevated or high-normal C-peptide levels. Some caveats to consider when using this test include the following:
 - It is a common error to check the C-peptide level without checking the serum glucose level. It is imperative to check the C-peptide level when the serum glucose level is high to distinguish between the 2 types of diabetes. The C-peptide level will be low in any patient with a low or low-normal serum glucose level.
 - If a patient has had very high glucose levels (>250 mg/dL) over the past several weeks or is having symptoms of hyperglycemia (eg, polyuria, polydipsia, weight loss, blurred vision), the patient's C-peptide level may be low even if the patient has type 2 DM. Marked hyperglycemia and hyperlipidemia can cause β -cell toxicity and cause significant β -cell dysfunction with low insulin and C-peptide levels. Thus, C-peptide levels should be interpreted with caution in that setting.

Table I. Features favoring type 1 diabetes mellitus (DM).

Younger age (<30 years)
 No family history of type 2 DM
 No hypertension
 No typical diabetic dyslipidemia
 Normal body weight
 Abrupt onset of symptoms/hyperglycemia, with or without diabetic ketoacidosis

Table II. Features favoring type 2 diabetes mellitus (DM).

Older age (≥ 30 years)
 Family history of type 2 DM
 Hypertension
 Diabetic dyslipidemia
 Overweight/obesity
 Slow onset of symptoms/hyperglycemia

It may take several days to receive the results of these tests. In the meantime, if the patient is acutely symptomatic, catabolic, or ketotic, insulin therapy should be started.

QUESTION:

Many patients with type 1 DM have increased insulin requirements due to insulin resistance. They may have a family history of type 2 DM. Would the addition of an oral diabetes medication be effective in a patient with type 1 DM?

ANSWER:

It is worthwhile to consider using oral diabetes medications in certain patients with type 1 DM. Given the increasing prevalence of DM, it is likely that 7% to 8% of patients with type 1 DM will also have type 2 DM with insulin resistance. Patients with a family history of type 2 DM are likely to have insulin resistance. Furthermore, patients who need >40 units of insulin per day are likely to have insulin resistance. The author uses the term *double diabetes* to refer to these patients with type 1 DM who, over time, gain weight, have increased insulin requirements, and develop dyslipidemia and other features of type 2 DM.

Metformin has been shown to reduce insulin requirements in patients with type 1 DM. It has been shown that insulin receptor binding is reduced in patients with type 1 DM, probably due to higher insulin levels in peripheral blood. Metformin might improve insulin binding and action. Pioglitazone and rosiglitazone have been shown to be useful in patients with type 1 DM as well as in those with type 2 DM. Most of these agents tend to have a more pronounced effect on postprandial blood glucose levels than on fasting glucose levels.

The author typically considers using metformin or a thiazolidinedione in certain patients with ≥ 1 of the following characteristics: a need for >50 units of insulin per day, a strong family history of type 2 DM, being overweight, and having the type of dyslipidemia that is commonly found in type 2 DM. The author typically uses these medications in patients with suboptimal control and higher levels of glycosylated hemoglobin; hence, the author does not reduce the dose of insulin. However, for patients who are close to their glycemic goal, a reduction of 10% to 20% in the doses of basal and bolus insulin may be warranted to prevent hypoglycemia.