

Case Study Responses

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Note: Readers are encouraged to visit www.InsulinJournal.com to review the details of a Case Study published in the October 2008 issue of *Insulin*.

This was the case of a 50-year-old man with a 4-year history of type 2 diabetes mellitus (DM) that responded initially to lifestyle changes and again when combination glyburide/metformin was added. However, over the past 6 months, the patient's 2-hour postdinner blood glucose level had risen to 180 to 200 mg/dL and his glycosylated hemoglobin (A1C) level had risen to 7.5%.

Question 1. What is the most likely explanation for this patient's increase in A1C?

Answer: c. Progressive nature of type 2 DM

The patient demonstrated poor compliance with his diabetes treatment regimen in the past, but he now reports full compliance. He has also continued to follow a diet that resulted in weight loss of almost 40 lb since diagnosis. Therefore, noncompliance with lifestyle changes seems to be an inaccurate conclusion despite the 2-lb weight gain the patient experienced since his last visit. Studies have generally failed to show deterioration in blood glucose levels in patients with emotional stress,^{1,2} although it is difficult to design valid protocols for such studies. In contrast, many studies have documented the progressive decreases in β -cell function and concomitant increases in blood glucose values that typically occur in type 2 DM.^{3,4}

Question 2. What do you do now?

Answer: c. Add exenatide

Many treatment choices are available at this point. Although a visit with a registered dietitian or certified diabetes educator might be helpful, the patient continues to follow a previously successful dietary program. With regard to adding medications to the patient's treatment regimen, the consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes on the treatment of type 2 DM⁵ and the recent update of that statement⁶ place basal insulin therapy as the most validated choice (over pioglitazone or exenatide). However, the patient's clinical data are more important in determining the best choice. A head-to-head study of exenatide versus insulin glargine in patients whose treatment with oral agents had failed (baseline A1C, 8.2%) found equivalent lowering of A1C values.⁷ The main improvement in blood glucose levels with exenatide occurred after meals, which seems to be most beneficial for our patient, as opposed to the effect of basal insulin in lowering fasting blood glucose levels. Pioglitazone is another choice, although the possibility of weight gain and the heightened risk of bone fracture, maybe even in men,⁸ is diminishing some providers' enthusiasm for this class of medications.

Question 3. Exenatide therapy is best monitored by _____.

Answer: b. A1C and postprandial blood glucose values

The major metabolic effect of exenatide is controlling postprandial blood glucose levels because of enhanced glucose-dependent insulin secretion, lowered postprandial glucagon values, and slowed gastric motility.^{7,9} A common clinical situation in patients who only monitor fasting blood glucose levels is perceiving little improvement in glycemia when the change in A1C is substantial. A useful rule of thumb is to recommend that patients who use incretin therapy (glucagon-like peptide-1 [GLP-1] agonists and dipeptidyl peptidase-IV inhibitors) periodically monitor their postmeal blood glucose values.

Question 4. If exenatide is prescribed, you recommend that the patient's twice-daily glyburide 10-mg/metformin 500-mg regimen be _____.

Answer: d. Changed to glyburide 5 mg/metformin 1000 mg twice daily

GLP-1 regulates postprandial insulin and glucagon levels in a glucose-dependent fashion; hence, the risk of hypoglycemia with incretin therapy is modest.⁹ Indeed, the experience with exenatide has shown virtually no risk of hypoglycemia when used in combination with thiazolidinediones or metformin. The one exception is when exenatide is combined with a sulfonylurea.¹⁰ In that case, the general recommendation is to reduce the dosage of the sulfonylurea by 50%. That seems to be particularly important in our patient, whose pre-exenatide A1C is 7.5% and fasting blood glucose level is 100 to 120 mg/dL.

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