

Case Studies in Insulin Therapy: The Last Arrow in the Treatment Quiver

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Because type 2 diabetes is a progressive disease, its natural course requires initiation of insulin in a significant proportion of patients, especially when oral agents fail to achieve glycemic targets. Most practicing physicians and endocrinologists acknowledge that neither the transition to nor the journey with insulin treatment is often as smooth as one would hope. Most have occasionally met with patients who plead for help in controlling their blood glucose levels with oral drugs alone. Often, doctors struggle to persuade such patients to start insulin.

In this article, we share some of our experiences—some common throughout the world and others unique to our country—in caring for patients who are prescribed insulin. It is important to learn from these experiences with insulin because it represents, more often than not, the last arrow in our treatment quiver.

Case Study 1

The patient was a 45-year-old man who has had type 2 diabetes for the past 6 years and had been taking insulin for the past 2 years. His body weight was 50 kg (BMI 24 kg/m²). He presented with uncontrolled and recently increased blood glucose levels and a dramatic increase in insulin dose during the past 5 months without any apparent cause. He had no history of fever, infections, or steroid use. He had had multiple hospital visits during the past few months.



Figure 1. Discoloration with hypertrophy on medial aspects of both thighs on the site where the patient described in Case Study 1 was injecting insulin.

The patient appeared to be well educated and concerned about this situation. To our surprise, however, we found he was injecting insulin on the medial aspect of his thighs. Examination showed lipohypertrophy with swelling in that region (Figure 1). The crowded clinic with its lack of trained diabetes educators and nurses was the perfect setting for this gross oversight in checking injection sites.

Case Study 2

The patient was a 55-year-old obese (BMI 28 kg/m²) man with known type 2 diabetes for 12 years who had been taking insulin for the past 6 months. He presented with haywire blood glucose levels over several visits, with gradually increasing doses of insulin. There were no documented episodes of hypoglycemia.

The patient was injecting his own insulin, and his injection technique was confirmed to be good. The insulin injection sites were healthy.

Insulin was properly stored at his home, and he was using a 40 IU syringe and a compatible vial.

Surprisingly, his A1C level was 7.2%, which was discordant with his venous blood glucose readings. He was not performing self-monitoring of blood glucose at home because of logistical issues. What was perplexing was that, although his dose of premixed insulin before breakfast had increased from 12 to 36 units in the past 6 months, his morning fasting levels were controlled with a predinner dose of 6 units, and although his post-breakfast values crept up from 200 to 340 mg/dl during the past four visits, his fasting blood glucose had decreased from 98 to 66 mg/dl in the same time period.

Through detailed questioning, we learned that dietary irregularities on the days of the test were at the heart of the matter. On a normal day, the patient injected insulin at about 7:40 a.m., ate breakfast at 8:00 a.m., and ate lunch at noon. However, on the

days of the test, he had an extended fast, skipping breakfast. He then performed SMBG and took insulin at noon and, instead of a normal lunch, ended up overeating with a large meal essentially comprising both breakfast and lunch. Hence, his insulin dose was always insufficient, and his postprandial glucose values were always high. This would not have happened if the test center had been closer to his house or had opened at 8:00 a.m., which would have allowed him the flexibility to follow his normal dietary routine on test days.

The patient was asked to divide his meals, take voglibose before breakfast and lunch, and perform SMBG at the proper time. We split his doses, with 16 units of regular insulin before breakfast and 16 units before lunch and 6 units of premixed insulin before dinner. His blood glucose was then controlled.

Case Study 3

A man with type 2 diabetes who had been taking insulin for the past 4 years with good glycemic control was started on twice-daily premixed insulin with a pen device for the past month. Although he was happy with the convenience and ease of using a pen device, his blood glucose levels became erratic. We decided to confirm his injection technique and asked him to bring his pen device to the clinic. He brought along a pen device with the cartridge in place, but the needle was missing. On questioning, we learned that the patient was injecting insulin without a needle. He thought it normal that he would not feel anything because pen devices were supposed to be painless. In actuality, he was trying to give himself insulin transdermally rather than subcutaneously. This case illustrates that a combination of less-than-adequate education and aggressive marketing by device sales companies

can lead to misconceptions on the part of patients.

Case Study 4

A woman with type 2 diabetes who had been taking insulin for the past 6 years with reasonable glycemic control presented with high glucose levels and injection site abscesses for the past month (Figure 2). Through thoughtful questioning, we learned that she had been wiping the insulin injection tip with a cotton swab before and after injecting.



Figure 2. Insulin site abscess in patient described in Case Study 4.

Case Study 5

A 46-year-old man with type 2 diabetes started noticing nodular swellings and subsequent discharging sinuses from these swellings at the insulin injection site for the past 6 months (Figure 3). These swellings continued



Figure 3. Chronic granulomatous infection at injection site in patient described in Case Study 5.

to appear when he took insulin from a particular vial. When that vial got finished, new lesions did not appear.

Patient was treated with multiple courses of different antibiotics with minimal response. Grams stain and multiple bacterial cultures performed on the discharge were negative for any growth. A fine needle aspiration cytology was positive for acid-fast bacilli. The patient refused a biopsy. He was started on anti-tubercular treatment with which the lesions began to regress.

The patient denied having used an insulin syringe that was used earlier for Bacillus Calmette-Guérin vaccination. However, he was sure that a particular vial of insulin was associated with these lesions because no new lesions appeared after he changed vials. Unfortunately, the vial in question could not be retrieved.

The patient was thoroughly evaluated but was not found to have any tubercular foci elsewhere in the body. Although tuberculosis is endemic in our country, tuberculosis at insulin injection sites caught us by surprise. There are no similar case reports or descriptions, although we did find case reports from Columbia of cutaneous tuberculosis after subcutaneous injections for cosmetic mesotherapy.¹

Case Studies 6 and 7

A young woman with diabetes and uncontrolled blood glucose was found to be injecting insulin into her forearm (Figure 4), and yet another man was found to be injecting insulin intradermally on his thigh with residual post-inflammatory hyperpigmentation (Figure 5).

QUESTIONS

1. What are some of the causes of insulin therapy failure?
2. How can clinicians be vigilant in identifying patients with nonad-



Figure 4. Forearm injection sites of the female patient described in Case Study 6.



Figure 5. Post-inflammatory hyperpigmentation in the thighs of the male patient described in Case Study 7.

- herence to or problems carrying out their insulin regimen?
3. What are the consequences of nonadherence to insulin therapy?
 4. How can we ensure better adherence to insulin therapy?

COMMENTARY

Incomplete or incorrect initial education and a lack of continuing education are at the root of all of the cases reported above. Apart from the obvious effects they have on glycemic status, incidents such as these leave an indelible trauma in the minds of patients and act as strong deterrents to continuing insulin therapy.

Doctors and patients expend great effort to start insulin, and the manner in which we use this last arrow in our treatment quiver matters. In a busy outpatient department, the easiest thing to do for

patients with uncontrolled blood glucose levels is simply to increase the dose of insulin. However, this not only destroys patients' confidence in insulin, but also leads to decreasing self-confidence and depression in patients on insulin. Hence, it would seem prudent and rewarding to devote some time to educating patients and using every visit to reinforce their knowledge and verify their insulin therapy practices. Logistical issues and test conditions need to be factored in when interpreting blood glucose data. This also highlights the importance of the role of diabetes educators and paramedical staff in care of diabetes patients. Unfortunately, these professionals and the services they provide are missing in most diabetes clinics in underdeveloped or developing countries, where the gap between the disease burden and the availability of care providers is widening rapidly.

Recent reviews on insulin adherence in Western countries show adherence rates as low as 62–64%.² Estimates of diabetes medication adherence in our country (India) are even worse, especially in populations in which illiteracy and poverty levels are very high. Nonadherence rates as high as 74% (95% CI 69.2–78.3) have been reported from south India.³

Insulin nonadherence has been shown to be a significant risk factor for increased mortality and increased costs of therapy in the diabetic population.^{4,5} Many factors determine adherence to insulin. Misinformation and miscommunication between doctors and patients is one of the foremost causes. Illness and treatment perceptions have also been shown to be an important determinant of adherence.⁶ Among various suggestions to improve treatment adherence is a participatory model in which patients are made an integral part of decision-making. This has been shown to

improve adherence to insulin and antidiabetic drugs and, hence, to improve outcomes.⁷

All insulin-requiring patients must learn to position the needle perpendicular to their skin when injecting insulin, rotate injection sites, discard syringes after a single use, inject at appropriate sites, inject subcutaneously into fat, count to 10 after injections, store insulin in a cool and airy place away from direct sunlight, and discard open vials after 1 month or the prescribed shelf life indicated on the vial.⁸ Apart from this basic education, they should be taught methods that may reduce the pain of injection, such as allowing the insulin to come to room temperature before injecting, making sure there are no air bubbles in the syringe, and keeping underlying muscles relaxed. This information may help to boost patients' morale.⁸

A change in temperature can change the concentration of insulin in the cartridge of a pen device.⁹ Hence, it is recommended to remove the needle from the pen immediately after use so the temperature of the insulin is not affected by the leak in thermo insulation caused by the attached needle.¹⁰ Another common mistake is using a 100 IU/ml pen cartridge but injecting insulin through a 40 IU/ml syringe. Patients also should be educated about the color coding of syringes and vials of different insulin concentrations (e.g., a red syringe is 40 IU/ml, whereas an orange syringe is 100 IU/ml).

Although the cases described here expose our shortcomings in diabetes care, highlighting such unusual clinical scenarios might alert other health care providers to recognize similar instances in their practice and enable better outcomes from insulin therapy.

CLINICAL PEARLS

- Unexplained deterioration in glycemic control and discrepancies

between plasma glucose, SMBG values, and A1C test results should alert physicians to the possibility of patients' nonadherence with or poor practices in carrying out their insulin regimen.

- Nonadherence is associated with a significantly higher mortality, higher complication rates, low self-confidence, poor self-image, and adverse disease-related perceptions.
- In addition to patient illiteracy and poverty, failure on the part of the health care system to ensure a proper, planned, and staged patient education and confidence-building program before instituting insulin therapy is a major barrier to successful insulin therapy.
- A few hours spent by physicians, nurses, or other diabetes educators with patients initiating insulin may save many years of life for these patients.

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