Case Report

A CASE REPORT OF CONTINUOUS SUBCUTANEOUS U-500 INSULIN ADMINISTRATION IN A PATIENT WITH INSULIN RESISTANT LIPODYSTROPHY

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ABSTRACT

Objective: To report the clinical outcome of a patient with lipodystrophy complicated by insulin-resistant diabetes mellitus who was changed from traditional multiple daily injection U-500 dosing to off-label continuous subcutaneous insulin infusion (CSII) of U-500 insulin in a V-Go® Disposable Insulin Delivery device (V-Go®).

Methods: Case report with literature review.

Results: After initiation of V-Go® the patient was able to reduce her total daily insulin dose from 415 U to 280 U with a concomitant reduction in glycated hemoglobin (HbA1c) from 9.3 to 6.8% over a 3-month period. The reported frequency of hypoglycemia was also significantly reduced. The patient reported increased satisfaction and improved insulin administration compliance.

Conclusion: U-500 delivered via CSII in patients with highly resistant type 2 diabetes, as can be seen in lipodystrophy, may be beneficial when patient becomes difficult to manage on insulin administered by multiple daily injections. The use of a V-Go® insulin delivery device can facilitate continuous insulin delivery in patients who are not able to use an insulin pump. **(AACE Clinical Case Rep. 2015;1:e45-e48)**

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Abbreviations:
CSII = continuous subcutaneous insulin infusion; **HbA1c** = glycated hemoglobin A1c

INTRODUCTION

Lipodystrophic syndromes are diseases of abnormal body fat distribution. There are several different types, each with different characteristics, but common features include impaired adipocyte distribution with loss of subcutaneous fat and ectopic lipid deposition resulting in lipotoxic effects including hyperlipidemia, hypertriglyceridemia, liver dysfunction, and insulin resistance (1). Most subjects with lipodystrophies demonstrate profound insulin resistance compared to traditional type 2 diabetic patients (2). Consequentially, high doses of insulin may be required to control diabetes secondary to lipodystrophic syndromes.

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Once U-100 insulin requirements exceed 200 U daily, transitioning to U-500 insulin can improve long-term glycemic control, be more cost effective, and provide higher patient satisfaction (3-5). U-500 insulin via continuous subcutaneous administration may provide improvement in glucose control without adverse effects in patients who have failed to achieve it with multiple daily injections (6). However, the pharmacokinetic profile of U-500 insulin is very different compared to U-100 analog insulin (7). Thus, the use of carbohydrate-adjusted bolus therapy may be less effective. This combined with the profound insulin resistance noted in these patients makes many features of insulin pump therapy redundant. Thus, it may be useful to evaluate more simplified continuous subcutaneous insulin injection (CSII) methods in this patient population. Here we report a case of U-500 insulin delivered through a V-Go® Insulin Delivery device (V-Go®).

CASE REPORT

A 58-year-old female with a history of Köbberling type of partial lipodystrophy (8) complicated by severe coronary artery disease, hypertriglyceridemia with several previous bouts of pancreatitis, and long-standing insulin-resistant type 2 diabetes mellitus using U-500 insulin, was seen for diabetes control. Prior evaluations had excluded hypercortisolism, use of medications such as antiretroviral therapy, and any other causes for her lipodystrophy or insulin resistance. She acknowledged regularly missing multiple insulin doses during the week. In the past, she had been assessed for an insulin pump but had failed to qualify with her insurance and thus continued to use multiple daily insulin injections. The patient reported at least 3 weekly symptomatic episodes of hypoglycemia, which she treated without checking her blood glucose and without requiring assistance, but otherwise was predominantly hyperglycemic. Her diabetes treatment regimen consisted of metformin (850 mg twice daily), 25 syringe units of U-500 insulin (equivalent to 125 U U-100 insulin) 3 times daily before meals, and an additional 40 U of glargine insulin at bedtime (which was added 3 years previously as the patient had fasting hyperglycemia that could not be corrected by increased supper time U-500 dosing due to the development of nocturnal hypoglycemia). Thus, her total daily insulin dose was 415 U. With regard to her hypertriglyceridemia, management consisted of omega-3-acid esters (2 g twice daily), ezetimibe (10 mg daily), niacin extended release (1,000 mg daily), and rosuvastatin (40 mg daily).

Her physical examination was significant for obesity (body mass index, 34.31 kg/m^2) with truncal deposition of adipose tissue and minimal adiposity associated with the extremities. A monofilament exam demonstrated a mild decrease in fine touch in the distal left toes. She otherwise had a normal examination including normal cognition and judgment. Her glycated hemoglobin A1c (HbA1c) value was 9.3%, which had increased from 7.7% over the course of 1 year despite continued uptitration of her insulin. Review of her blood glucose monitor revealed high variability with blood glucose values between 170 and 450 mg/dL. Other laboratory studies demonstrated elevated triglycerides (309 mg/dL) and slightly elevated creatinine (1.2 mg/dL). All other laboratory evaluations were within normal limits.

Given the deteriorating glycemic control with high variability in her glucose readings, as well as the inability to obtain insurance approval for provision of an insulin pump, we recommended insulin delivery via a V-Go® device. Training on the device was provided by a certified diabetic educator including instructions on filling the device with insulin, applying the device, and use of the insulin bolus function for mealtime insulin. Initial dosing consisted of 40 U of U-500 insulin (200 U insulin) given via continuous subcutaneous administration over 24 hours in the V-Go® and use of the device's bolus function to give an additional 12 U of U-500 insulin (60 U insulin) per meal. Given that the device was limited to a capacity of 76 U insulin/day (380 U insulin daily) Glargine (40 U at night) was initially continued to maintain the same total daily insulin dose (this sums to 420 U of insulin daily) (9). Due to reduced hyperglycemia and decreased glucose variability, glargine was discontinued within 1 week, and over the next 3 months the patient's basal insulin dose was reduced to 20 U of U-500 insulin (100 U of insulin) with continued 10 to 12 units of U-500 with meals (50-60 U insulin). Thus, her total daily insulin dose decreased from 415 U/day to approximately 280 U/day. After 3 months, her HbA1c decreased to 6.8%, and she reported that symptomatic hypoglycemic events had decreased to less than 1 per week, with no hypoglycemia documented by blood glucose monitoring. Her triglycerides remained elevated at 425 mg/dL despite improved glycemic control. Her weight increased by 7 lbs in the 12 months after starting the V-Go®, but this fluctuation was within the same range of weight she has maintained for the past 10 years.

The patient reported greater satisfaction with her insulin administration due to convenience of the device and ease of use. She also reported decreased fatigue and subjective improvement in short-term memory with normalization of glucose. It was specifically noted by the patient that her compliance with the therapy was much improved as she no longer had to remember to take her insulin with her or administer shots outside of the home. The patient was continued on V-Go® device without further insulin adjustment. Her HbA1c values were 7.8%, 7.6%, and 6.6% at her following appointments over the next 12 months (Fig. 1). She continued to endorse subjective improvement and compliance with diminished hypoglycemia over the 12 months of using the insulin delivery device.

DISCUSSION

We report a patient with marked insulin resistance as a complication of lipodystrophy. Over the course of her management, she had multiple adjustments in her insulin dosing in an attempt to improve overall glucose control. The increased complexity of her insulin regimen resulted in varying compliance with continued poor control and glucose variability. Upon the initiation of the V-Go® device, the patient reported an immediate subjective improvement in compliance with diminished hypoglycemia. Her overall insulin dose was reduced within 3 months of initiation of the insulin delivery device. The patient sustained improvement in her glycemic control, glucose variability, and overall satisfaction with her diabetic management over the 12 months of follow-up. Although her dyslipidemia did not improve with better glycemic control, this could be explained by dietary indiscretions and/or poor compliance with her multiple lipid-lowering medications. Her

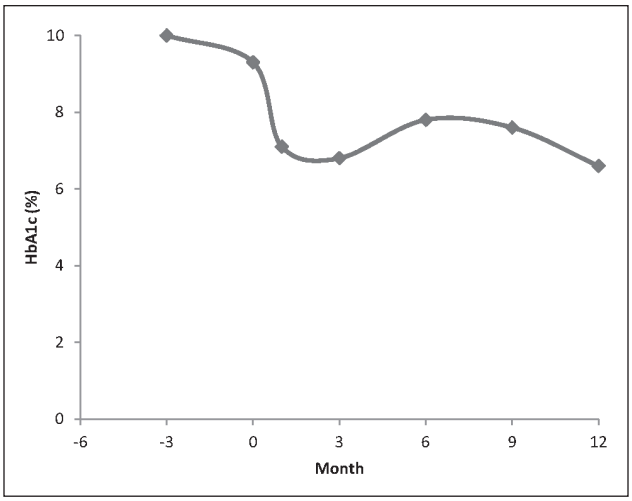

Fig. 1. HbA1c over the course of 1 year of use of the V-Go® insulin delivery device (beginning at 0 months) in our patient. *HbA1c* = glycated hemoglobin.

triglyceride levels remained <500 mg/dL, and no further episodes of pancreatitis have occurred since she started using the V-Go®.

Several small studies (with subjects numbers ranging from 4 to 21) have shown that CSII with U-500 insulin via insulin pumps has a significant benefit in overall glycemic control and total daily insulin dose, with no significant increase in adverse outcomes including hypoglycemia (10-12). While these studies suggest that CSII therapy with U-500 is an effective strategy, there remain several potential barriers to the use of insulin pump therapies in type 2 diabetics including access to specialist care, insulin pump and supply expenditures, complexity of the technology, and adaptation to the lifestyle interruptions of wearing an insulin pump (13). Furthermore, most payers (including Medicare) restrict insulin pump therapy coverage, which provides another barrier to patients who may benefit from CSII.

One potential solution to these issues is the use of a simplified continuous insulin delivery device such as the V-Go®. This is a mechanical subcutaneous insulin delivery device that is worn for 24 hours prior to disposal, at which time it is replaced with a new V-Go®. It is available in 20-, 30-, and 40-U containers, which reflect the amounts of insulin delivered over 24 hours. In addition, it provides the ability to give a total of 36 U insulin in the form of bolus administration in 2-U increments at the push of a button. A retrospective analysis of diabetic patients who switched from traditional injection insulin regimens to the V-Go® demonstrated an overall improvement in average glycated hemoglobin (HbA1c) from 8.8% to 7.6% over 12 weeks, with an overall positive affirmation reported regarding ease of use of the device, ability to administer insulin discreetly, and improved adherence to insulin therapy while using the V-Go® (14). Thus, the V-Go® device appears to offer many of the benefits associated with CSII while decreasing many of the pitfalls noted with traditional insulin pump therapy.

CONCLUSION

Our patient's outcome with V-Go® was consistent with the outcomes reported in a study of the V-Go® utilizing U-100 insulin (14). In addition to improved glucose control, she had a significant decrease in total daily insulin requirements. While this potential for diminished total daily dose is consistent with some of the smaller studies that examined U-500 insulin delivered via CSII, there was no significant change in dose in patients followed out over 9.5 years (6). Thus, the larger contributor to this reduction in total daily insulin dose was likely the patient's reported overall improvement in compliance once the device was initiated. The use of the V-Go® device also led to a greater emphasis on continuous basal insulin, which may have contributed to her improved glycemic control. This continuous insulin action and improved glycemic control could reduce beta cell toxicity (resulting from glucose toxicity or lipotoxicity), further contributing to the observed improvement in glucose control and decreased insulin requirements (15). Also given the off-label use of the V-Go®, the patient may have received increased attention through outpatient correspondence, which may have contributed to improvement in control. Regardless, the combination of improved physiologic delivery and ease of use makes the V-Go® a potentially effective tool in the treatment of highly insulin-resistant patients including those utilizing U-500 insulin.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

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