

BEST PRACTICES IN: Overcoming Patient Challenges Associated With Basal-Bolus Insulin Therapy in Type 2 Diabetes

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Introduction: Diabetes is a major and growing public health problem. According to 2011 statistics from the Centers for Disease Control and Prevention, an estimated 25.6 million people over 20 years of age in the United States have diabetes; between 90% and 95% of these individuals have type 2 diabetes.¹ Diabetes is associated with substantial morbidity and mortality—it was the seventh leading cause of death in the US in 2010—and direct and indirect costs are estimated in the hundreds of billions of dollars.^{1,2}



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Despite the many oral anti-diabetic therapeutic options available to adult patients with type 2 diabetes, as many as 40% eventually require subcutaneous insulin.³ Insulin therapy is an established, effective method for glycemic control and known to prevent the microvascular and macrovascular complications typically associated with type 2 diabetes.³ Basal insulin injections can provide steady glycemic control; however, prandial insulin

injections are also eventually required by many patients to maintain normal or near-normal glucose levels.^{3,4}

Unfortunately, reproducing physiologic basal and prandial insulin replacement requires patients to take multiple daily injections.³ This presents a formidable challenge to successful diabetes management: conventional insulin therapy—although available in many formulations—is cumbersome for patients, as well as potentially embarrassing and intimidating, and adherence to insulin therapy is a major obstacle to successful glucose control (Table).^{5,6} Consequently, and despite the established benefits of insulin replacement, many patients, even in well-controlled clinical trials, do not

TABLE

Reasons for reluctance to start or intensify insulin therapy in order of decreasing importance

- Fear of hypoglycemia
- Embarrassment of injections in public
- Feeling of dependence on regular injections
- Trepidation about dietary adherence
- Trepidation about the perceived careful organization required to work insulin therapy into daily schedule
- Fear of pain with injections
- Fear of injections in general

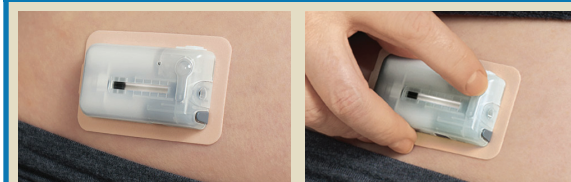
Adapted from Petrak F, et al.⁵ and Kapitza C, et al.⁶

achieve optimal levels of glycosylated hemoglobin A1C (HbA1c).⁷⁻¹⁰ Suboptimal treatment is often attributable to administration and adherence issues, suggesting that developing easier and better-controlled administration methods may help improve adherence and outcomes.

Insulin Delivery: The V-Go is a disposable insulin delivery device that provides basal and bolus insulin infusions that mimic physiologic biphasic insulin metabolism (Figure). The small, discreet device, which is affixed with an adhesive strip to a patient's abdomen or any place that insulin can be injected or infused, supplies a continuous and predictable infusion of insulin at a preset basal rate for 24 hours and on-demand delivery of insulin for mealtime boluses. The device measures 2.4 x 1.3 x 0.5 inches and weighs 0.7 to 1.8 ounces (depending on dosage) and is completely mechanical. No programming or batteries are required. The prandial bolus is delivered by pressing 2 buttons (which can be done through clothing) prior to a meal. It is indicated for adult patients (age 21 years and over) requiring insulin therapy.

In a proof of concept trial, Kapitza and colleagues eval-

FIGURE: The V-Go Device



The V-Go is applied using the adhesive patch and is activated by pushing the needle button. Prandial insulin is delivered by pushing both the bolus release button and the bolus delivery button.

uated the device in 6 patients with type 2 diabetes taking ≥ 15 U/day of insulin glargine with or without oral therapy.⁶ Patients had a mean age of 59.5 years ± 5.2 years, a mean HbA1c level of 7.7% $\pm 1.2\%$ (range, 6.6% to 9.6%), and no known diabetes-related complications.⁶ Glargine was discontinued 3 days prior to affixing the V-Go device. Once it was in place, patients used the device under supervision during study days 1-4 (inpatient phase) and continued to use the device as outpatients for days 4-7. Continuous glucose monitoring assessments were conducted during each study phase and capillary blood glucose concentrations were measured daily at multiple timepoints.⁶ Measurements included fasting blood glucose (FBG) and 1- and 2-hour postprandial glucose concentrations.*

Although the study sample size (N=6) was not large enough to assess the product's safety or efficacy, the V-Go device was generally well tolerated and there was 100% compliance.⁶ Importantly, there were no serious adverse events or difficulties keeping the device affixed to the skin.⁶ Mean total insulin doses with daily subcutaneous glargine prior to the study were comparable to those infused during the inpatient and outpatient phases of the study with the V-Go device (33.3 vs 31.5 vs 32.3 U, respectively). Likewise, FBG values were comparable between baseline and study periods, and overall glycemic control, measured with continuous glucose monitoring, improved with non-statistically significant decreases from 173 mg/dL at baseline to 157 mg/dL and 156 mg/dL during the inpatient and outpatient phases, respectively.⁶

Patients and physicians appear to have positive perceptions of the device as well, reporting that the V-Go is convenient, comfortable, and easy to use, and that it may provide better glucose control than conventional insulin therapy.¹¹⁻¹³ A recent publication described patient experience with the device as well as a retrospective analysis of glucose control before, during, and after device use. The analysis included 23 patients with type 2 diabetes who had been using insulin therapy for an average of 7 years. Patients were surveyed via telephone and rated their overall experience with the V-Go at 12 weeks as 9.1 on a 10-point scale, with 10 being the most positive.¹³ Clinical data collected retrospectively support the product's potential to improve outcomes. For example, the following results show the product's potential benefit. At baseline, mean HbA1c was 8.8%. After 12 weeks of insulin therapy delivered via the V-Go, there was a statistically significant decrease in HbA1c to 7.6% ($P=0.002$). Twelve weeks after device discontinuation, there was a statistically significant increase in HbA1c to 8.2% ($P=0.011$). Fasting blood glucose followed a similar, albeit non-statistically significant, trend, decreasing from baseline during treatment and increasing after removal of the device (205 vs 135 vs 164 mg/dL before, during, and after treatment, respectively).¹³ Such findings suggest that the regulated and predictable basal insulin infusions and discreetly administered prandial boluses facilitated by the V-Go device may optimize total daily insulin dosage. The fact that the boluses can be administered without withdrawing from social situations and without disrobing may make patients more adherent to therapy.

Towards Improved Adherence: In the past, physicians have prescribed insulin therapy in a stepwise fashion, beginning with basal insulin alone and progressively adding bolus doses as each step proved ineffective.^{3,4} This was not done for safety and/or efficacy. Stepped-insulin therapy was done because it appeared easier and patients were more receptive to initiating therapy with a single injection versus multiple daily injections. The V-Go Disposable Insulin Delivery Device, by providing predictable and easily administered physiologic insulin replacement, may have the potential to change the paradigm of stepped-insulin therapy and improve adherence and outcomes.

If regular adjustments or modifications to the basal rate of insulin are required in a 24-hour period, or if the amount of insulin used at meals requires adjustments of less than 2-Unit increments, use of the V-Go Disposable Insulin Delivery Device may result in hypoglycemia. The following conditions may occur during insulin therapy with the V-Go: hypoglycemia (low blood glucose) or hyperglycemia (high blood glucose). Other adverse reactions associated with V-Go use include skin irritation from the adhesive pad or infections at the infusion site. The V-Go should be removed before any magnetic resonance imaging testing.

*This proof of concept study in 6 patients was not intended to provide clinical evidence of the product's safety or efficacy.

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