EFFECT OF GLARGINE INSULIN DELIVERY METHOD (PEN DEVICE VERSUS VIAL/SYRINGE) ON GLYCEMIC CONTROL AND PATIENT PREFERENCES IN PATIENTS WITH TYPE 1 AND TYPE 2 DIABETES

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ABSTRACT

Objective: To evaluate the effects of two different glargine insulin delivery methods (pen device vs. vial/syringe) on glycemic control and patient preferences in a randomized, open-label, crossover, comparative effectiveness study.

Methods: Thirty-one patients discharged from the hospital were recruited for this study. In the hospital, all patients were treated with a basal-bolus insulin regimen. Upon discharge, 21 patients received glargine by pen device for 3 months and were then switched to vial/syringe for the next 3 months (group 1). Group 2 consisted of 10 patients discharged on vial/syringe and converted to pen device after 3 months. Hemoglobin A_{1c} (HbA_{1c}) was measured at enrollment and at 3 and 6 months. A questionnaire assessing patient preference was administered at 3 and 6 months.

Results: Groups 1 and 2 had similar baseline HbA_{1c} (10.7 ± 2.2% and 11.2 ± 2.5%, respectively) and similar reduction in HbA_{1c} at 3 months (7.8 ± 1.7% and 7.3 ± 1.4%, respectively; $P<.001$ vs. baseline). However, after crossover, the changes in HbA_{1c} from 3 to 6 months were significantly different between groups. HbA_{1c} increased to 8.5 ± 2.0% at 6 months in group 1 after switching to the vial/syringe but remained unchanged (7.1 ± 1.6%) in group 2 after switching to a pen device ($P<.01$, group 1 vs. group 2). Patient questionnaires after each phase of the trial revealed that patients found the pen device more convenient and were more likely to recommend this insulin delivery method to someone else.

Conclusion: Patients switching to a glargine pen device achieved lower HbA_{1c} at the 6-month follow-up. Patients in both groups overwhelmingly preferred glargine pens over vials/syringes. **(Endocr Pract. 2014;20:536-539)**

Abbreviation:
HbA_{1c} = hemoglobin A_{1C}

INTRODUCTION

A number of well-designed studies have demonstrated both the accuracy and convenience of insulin pen devices for treatment of type 1 and type 2 diabetes (1-5). Prefilled and disposable pens are now being used widely around the world by patients with diabetes on insulin treatment. However, due to both perceived and sometimes actual higher costs associated with use of insulin pens relative to the traditional vial/syringe method, many institutions and insurance plans often disincentivize the use of pen devices by their patients. Real or perceived cost issues deprive many uninsured and underinsured patients with diabetes of the opportunity to use a more convenient and possibly more efficacious device for administration of insulin (4).

The key question is whether insulin pen devices provide a therapeutic advantage over the vial/syringe method of insulin delivery, particularly among patients at higher risk for poor glycemic control and diabetes complications. Therefore, we conducted a crossover study among indigent and Medicaid-covered patients with type 1 or type 2 diabetes who were discharged from the University of Colorado Hospital on a basal-bolus insulin regimen. The aim of this study was to evaluate the effects of two different glargine insulin delivery methods (pen device and vial/syringe) on glycemic control and patient preference in indigent patients with type 1 or type 2 diabetes with poor glycemic control.

Submitted for publication September 27, 2013
Accepted for publication November 19, 2013
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Published as a Rapid Electronic Article in Press at http://www.endocrinepractice.org on December 10, 2013. DOI:10.4158/EP13404.OR

This was a randomized, open-label study with a crossover design, a real-life comparative effectiveness trial. We recruited 41 patients with type 1 and type 2 diabetes, either indigent or receiving Medicaid, who were discharged from the hospital on a basal-bolus insulin regimen (glargine and humalog). Twenty-three subjects were randomized to group 1 and received glargine by pen device for 3 months and were then switched to vial/syringe for the next 3 months. Eighteen subjects were randomized to group 2 and received glargine insulin via vial/syringe for the first 3 months and then by pen device for an additional 3 months. Randomization was performed using odd-even last digit medical record numbers. Patients whose medical record number ended with an odd numeral were randomized into group 1, whereas those whose record number ended with an even numeral were randomized into group 2. None of the patients in either group had been exposed to any pen device before this study. The study design is outlined in Figure 1.

Two subjects in group 1 and 8 subjects in group 2 were lost to follow-up at 3 or 6 months and were excluded from the final analysis. Thirty-one subjects completed the study: 21 in group 1 and 10 in group 2.

Hemoglobin A_{1c} (HbA_{1c}) was measured at enrollment and at 3 and 6 months using the same assay. A questionnaire assessing patient preferences was administered at 3 months (the end of the initial treatment period) and at 6 months (at the end of the crossover period). The unvalidated questionnaire consisted of 3 questions, with a satisfaction scale ranging from 0 (very dissatisfied) to 6 (very satisfied):

Q1: How satisfied are you with your current treatment?

Q2: Would you recommend this form of treatment to others?

Q3: How satisfied would you be to continue your present form of treatment?

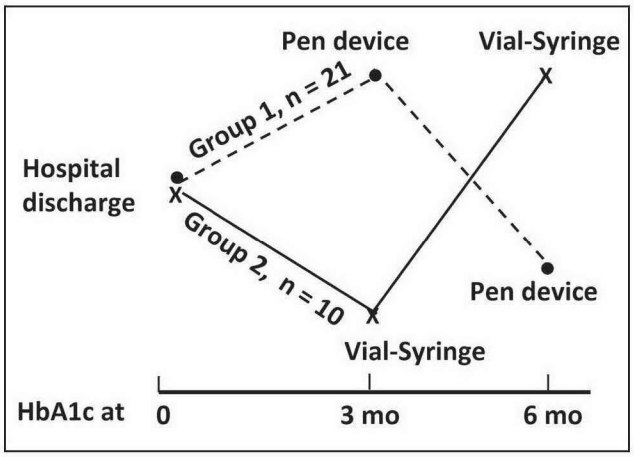

Fig. 1. Crossover study design for group 1 (X) and group 2 (•).

were combined for each treatment modality in the final analysis. The numerical scores of the answers (0 to 6) were tabulated and the mean ± SEM were compared using the Student's *t* test.

All subjects self-administered insulin lispro by vial/syringe throughout the study. All study medications were provided to subjects free of charge. Pen devices were given to group 1 upon discharge from the hospital and to group 2 at the 3-month follow-up visit by one of the authors. Instruction on how to use the pen device was provided at the same time. Insulin lispro adjustments were made at the 3-month follow-up visit as well. Compliance with the prescribed insulin regimen was evaluated at each visit by reviewing the insulin administration log and meter download. The study was approved by the Colorado Multiple Institutional Review Board prior to any study procedures being performed.

RESULTS

The characteristics of the 31 subjects who enrolled and completed this study are shown in Table 1. The average age of subjects was 49 ± 11 years in group 1 and 46 ± 15 years in group 2 (not significant). There were 3 subjects with type 1 diabetes in each group, and the gender and ethnic distributions were similar.

One of the most revealing observations was the high drop-out rate, despite receipt of free long-acting insulin supplies for 6 months. A total of 10 subjects (24.4%) dropped out, including 2 subjects in group 1 (8.7%) and 8 in group 2 (44.4%). There were no differences in education, socioeconomic, or demographic characteristics between the dropouts and nondropouts, nor were there any differences between groups with respect to the clinical course of diabetes or any other comorbidity. Because of

Table 1
Clinical Characteristics of Patients Enrolled in the Study[a]

	Group 1 (n = 21)	Group 2 (n = 10)
Age (years) Mean ± SD	49.3 ± 10.8	46.2 ± 14.9
Men/Women	13/8	6/4
Caucasian Hispanic African American	11 5 5	6 3 1
Type 1 diabetes Type 2 diabetes	3 18	3 7

[a] There were no statistically significant differences between the groups in any of the parameters presented.

dropout rate was not significant between the groups.

A second important observation is that subjects who completed all study procedures and were compliant with their study medications demonstrated dramatically improved metabolic control, regardless of the mode of insulin administration (Fig. 2). The HbA_{1c} in group 1 dropped from 10.7 ± 2.2% to 7.8 ± 1.7% at 3 months and from 11.2 ± 2.5% to 7.3 ± 1.4% in group 2 ($P<.001$ between baseline and 3 months for both groups). Neither the basal nor 3-month HbA_{1c} were statistically different between the groups. However, following the crossover period, subjects using the pen device remained in better control (group 2 HbA_{1c}, 7.1 ± 1.6%) than the subjects who switched to vial/syringe (group 1 HbA_{1c}, 8.5 ± 2.0%; $P<.01$).

The results of the patient satisfaction questionnaire are summarized in Table 2. Subjects using the pen device clearly preferred this mode of insulin administration, reporting a significantly higher level of satisfaction for all 3 questions ($P<.0001$ compared with vial/syringe use).

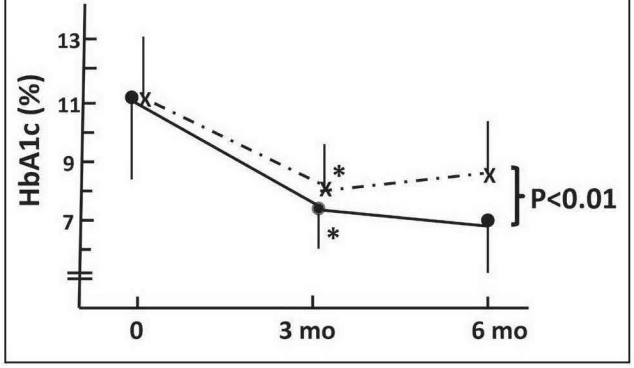

Fig. 2. Hemoglobin A_{1c} at the initiation of the study and at 3 and 6 months in group 1 (X) and group 2 (•). *$P<.001$ versus initial values.

DISCUSSION

In general, adherence to chronic drug regimens, including those for diabetes management, is frequently inadequate (6-9). Furthermore, lower socioeconomic status is associated with greater barriers to adherence with therapeutic regimens (7). Most of the studies using objective measures of medication adherence (as opposed to self-reported adherence) support its association with better glycemic control in patients with diabetes (7,9,10-13). Our results support this notion as well. Adherence to glargine insulin administration as prescribed (review of insulin administration log and meter downloads by the staff) greatly improved metabolic control in indigent patients in our study, regardless of the mode of administration. HbA_{1c} was reduced robustly and precipitously (Fig. 2). We did not evaluate potential reasons for previous poor compliance, but the results from this study clearly show that compliance with a prescribed insulin regimen is critical for improvement in metabolic control.

The dropout rate in our study (24.4%) is certainly disturbing. The 10 subjects who dropped out made up a quarter of those initially enrolled and were lost to follow-up even when given glargine insulin at no financial cost. This is likely to represent a behavioral barrier to medication adherence, although a financial component (e.g., the cost of transportation) cannot be ruled out. Further studies are needed to understand the causes of nonadherence and dropout. Interestingly, there were more subjects who dropped out during the vial/syringe phase than among patients in the pen-device phase.

After the crossover phase, subjects using pen devices maintained good metabolic control, whereas those switching to the vial/syringe mode of glargine administration

Table 2
Questionnaire Results[a]

	SoloSTAR (n = 31)	Vial/syringe (n = 31)	*P* value
How satisfied are you with your current treatment?	5.5 ± 0.6	3.1 ± 0.6	<.0001
Would you recommend this form of treatment to others?	5.4 ± 0.4	3.0 ± 0.9	<.0001
How satisfied would you be to continue your present form of treatment?	5.8 ± 0.4	2.7 ± 0.7	<.0001

[a]Answer scale: 6 = "very satisfied;" 0 = "very dissatisfied."

Subject satisfaction with treatment after switching to the vial/syringe mode also dropped significantly.

Recently, Grabner et al (14) examined clinical and economic outcomes among patients with diabetes using a glargine pen versus those using a vial/syringe in a large retrospective administrative claim study. Following initiation of glargine therapy, patients using a pen device were more adherent to their medication ($P<.001$) and had lower HbA_{1c} during follow-up ($P<.001$) compared with patients using a vial/syringe. Similarly, Davis et al (15) observed that among 3,842 patients with type 2 diabetes (n = 1,921 per group), those who initiated glargine therapy with a disposable pen showed better treatment persistence and less hypoglycemia in comparison with those using a vial/syringe.

The results of our crossover study among indigent and Medicaid-covered patients with type 1 or type 2 diabetes are consistent with many previous assessments of patient preference in favor of pen devices (1-5). The use of disposable pens for administration of insulin in Europe, Canada, and Australia was accompanied by higher efficacy, adherence to therapy, and patient satisfaction (4,16). It appears that the use of pen devices might actually lower the overall treatment cost as a consequence of better control and higher treatment adherence rates (17,18).

CONCLUSION

In conclusion, our data from a high-risk, transitional population of patients crossing over from one form of insulin glargine delivery to another strongly suggest that both metabolic control and patient preference are significantly improved in patients using disposable pens as compared with those using vials/syringes. These data support more widespread use of pen devices for insulin administration to improve medication adherence and glycemic control.

ACKNOWLEDGMENT

This study was supported by Sanofi and the Foundation for Biomedical Education and Research.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

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