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Impact of Dosing Conversion From Basal Insulin to Follow-On Insulin Glargine

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Abstract

Background: Several basal insulins have recently come to market including follow-on insulin glargine (Basaglar®). Currently, there is no real-world data published on the implications of conversion to Basaglar on dosing or glycemic control. **Objective:** To identify differences in basal insulin dosing requirements, hemoglobin A1c (HbA1c), and incidence of hypoglycemia or weight gain when converting a patient to Basaglar from another basal insulin. **Methods:** Single-center, retrospective chart review at an academic medical center. All patients prescribed Basaglar between December 15, 2016, and August 31, 2017 were included for review if converted from another basal insulin. **Primary outcome:** Difference in basal insulin requirements in both units/d and units/kilogram (kg)/d after conversion to Basaglar. **Secondary outcome:** Change in HbA1c and weight. **Results:** Mean basal insulin dose was 38.4 ± 26.3 units/d pre-conversion and 40.5 ± 29.8 units/d post-conversion (P = .031). Results were significant for patients with type 2 diabetes mellitus (T2DM; pre-conversion basal dose 34.6 ± 24.3 units/d; post-conversion basal dose 37.6 ± 29.0 units/d; P = .009). Weight-based dosing changed from 0.37 ± 0.25 units/kg/d pre-conversion to 0.39 ± 0.29 units/kg/d post-conversion (P = .056) and was significant for patients with T2DM (P = .040). A nonsignificant decrease in HbA1c was seen (−0.14% ± 1.24%; P = .142). There was no difference seen in weight (111.6 ± 46.3 kg vs 111.7 ± 46.9 kg; P = .662). **Conclusion:** Patients with diabetes require similar basal insulin doses upon conversion to Basaglar. Clinicians should monitor blood glucose closely during basal insulin transition.

Keywords

Basaglar, insulin, long acting, follow-on insulin, hemoglobin A_{1c} protein, human, conversion

Introduction

Over the last 3 years, several new basal insulin products have come to market including insulin glargine (Toujeo®) approved in February 2015 and insulin degludec (Tresiba®) approved in September 2015. Most recently, the first follow-on insulin product, insulin glargine (Basaglar®) was approved for launch in the United States in December 2016. Basaglar is a long-acting human insulin analogue containing an amino acid sequence identical to its comparator agent, Lantus®. Prior to approval of these newer basal insulin products, the standard of care was to use insulin glargine (Lantus), insulin detemir (Levemir®), or insulin NPH (Humulin N®/Novolin N®) for treatment of type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM). The current American Diabetes Association and American Association of Clinical Endocrinologists guidelines do not preferentially recommend one basal insulin over another, and the choice of which basal insulin to use is often dictated by insurance coverage and cost.

Although Basaglar is considered a follow-on product to insulin glargine (Lantus), the products are not considered to be interchangeable according to the Food and Drug Administration (FDA) Orange Book. Currently, follow-on products are not viewed as generic agents and are approved through the FDA new drug application process.[1] Due to the complex nature of biologically derived products, the manufacturing processes for Lantus and Basaglar are different despite the identical amino acid sequences leading to slight variations in the final products.[2] When converting patients to Basaglar from other basal insulins, the manufacturer outlines specific recommended dose conversions for Lantus, Toujeo, and twice daily NPH insulin (Table 1). The recommendation when switching from once-daily NPH insulin or other long-acting

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Table 1. Basaglar® Manufacturer Dose Conversion Recommendations.[3]

Starting Insulin	Dose Conversion to Basaglar
Insulin glargine (Lantus®)	Unit-per-unit
Insulin glargine U-300 (Toujeo®)	Use 80% of total insulin glargine U-300 dose
Twice daily insulin NPH	Use 80% of total insulin NPH dose
Once-daily insulin NPH	Change in dose of basal insulin may be required
Other long-acting insulins Insulin detemir (Levemir®) Insulin degludec (Tresiba®)	Change in dose of basal insulin may be required

insulins (eg, insulin degludec) to insulin glargine (Basaglar) is less clear, and the manufacturer only states that a change in the dose of the basal insulin may be required.[3]

Prior Studies

Prior to approval by the US FDA, 2 phase III studies were conducted to determine whether insulin glargine (Basaglar) was equally safe and effective when compared to Lantus.[4,5] ELEMENT 1 was a randomized, open-label, 52-week trial comparing Lantus to Basaglar in 535 patients with T1DM who previously received basal-bolus insulin therapy for at least 1 year prior to screening.[4] The prestudy basal-bolus regimen had to contain one of the following basal insulins: once-daily insulin NPH, insulin glargine (Lantus), or insulin detemir (Levemir). Patients were randomized to once-daily Lantus or once-daily Basaglar and were initiated on the same dose as their prestudy basal insulin as determined by a unit-to-unit conversion. Dose adjustments were made to achieve the following glycemic targets: hemoglobin A_{1c} (HbA_{1c}) <7%, fasting plasma glucose (FPG) $\leq$108 mg/dL, and other preprandial blood glucoses between 70 and 130 mg/dL. The mean age of the patients included in the study was 41 years, and the mean duration of T1DM was 16 years in the Basaglar group and 17 years in the Lantus group. There were no statistical differences in HbA_{1c}, FPG, body weight, rate of hypoglycemia, and mean insulin dose between the 2 groups at 24 weeks nor at 52 weeks. However, a statistical difference in HbA_{1c} was seen earlier in the study at 12 weeks (7.31% in the Lantus group vs 7.42% in the Basaglar group; $P = .03$). The mean basal insulin dose achieved at 52 weeks was 28.46 units/d (0.38 units/kg/d) for the Basaglar group and 26.4 units/d (0.36 units/kg/d) for the Lantus group. The study concluded that Basaglar was an effective and safe option when used in combination with mealtime insulin for patients with T1DM.[4] The open-label study design potentially influenced the titration and adjustment of medications evidenced by a statistically but not clinically significant reduction in HbA_{1c} in patients in the Lantus group (7.31%) compared to the Basaglar group (7.42%) after 12 weeks of treatment. It was also noted that during the titration period, there were nonsignificant differences in insulin dose adjustments which may explain the significant reduction in HbA_{1c} between the 2 groups at 12 weeks. Investigators were aware of the treatment and therefore could have been more aggressive in titrating Lantus compared to Basaglar due to familiarity.

The ELEMENT 2 trial was a randomized, active-controlled, double-blind 24-week treatment period of 756 patients with T2DM.[5] Patients in the study had to be receiving 2 or more oral antihyperglycemic medications at stable doses for 12 weeks prior to screening (with or without Lantus) and then were randomized to receive Basaglar or Lantus. Those who were on Lantus prior to the study were converted to Basaglar at a dose that was equivalent to their prestudy basal insulin dose (1:1 unit per unit dose conversion), and those who were insulin-naive were initiated on 10 units per day. Basal insulin doses were titrated by increasing by 1 unit daily until FPG was <100 mg/dL. The mean age of patients included in the study was 59 years and mean duration of diabetes was 12 years in the Basaglar group and 11 years in the Lantus group. At 24 weeks, there was no statistical difference in HbA_{1c}, FPG, insulin dose, weight change, or rates of hypoglycemia between the 2 groups.[5] These results also held true when stratified by those who were insulin-naive and those who were on basal insulin at baseline. The study concluded that both Lantus and Basaglar provided similar blood glucose control when used in combination with oral antihyperglycemic medications in patients with T2DM as Basaglar fulfilled the requirements of noninferiority.[5] Although nonsignificant, the total insulin dose per kilogram per day was lower in the Lantus group (0.53 units/kg/d) compared to the Basaglar group (0.60 units/kg/d) in patients who were on Lantus prior to the study. The study was not powered to detect a difference within the subgroups. Therefore, further studies are warranted to investigate whether higher doses of Basaglar are needed compared to Lantus to achieve similar glycemic control in patients previously taking Lantus.

Despite these 2 phase III clinical trials demonstrating the noninferiority of Basaglar compared to Lantus, there is currently no real-world clinical data published on the implications on dosing, glycemic control, hypoglycemia, or weight gain when converting to insulin glargine (Basaglar) from another basal insulin. The objective of this study was to identify differences in dosing requirements of insulin glargine (Basaglar) as well as differences in glycemic control and incidence of hypoglycemia and weight gain when converting a patient previously taking another basal insulin to insulin glargine (Basaglar) in a real-world clinical setting.

Research Design and Methods

A single-center, retrospective chart review was conducted between December 15, 2016, and August 31, 2017, to assess dose conversion from an intermediate or long-acting basal insulin to follow-on insulin glargine (Basaglar) within the outpatient setting of a large academic medical center. The study was approved by the health-system institutional review board. Patients with T1DM or T2DM who received at least 1

prescription for follow-on insulin glargine (Basaglar) during this timeframe were identified. Patients had to previously be prescribed insulin glargine U-100 (Lantus), insulin glargine U-300 (Toujeo), insulin NPH (Humulin N/Novolin N), insulin degludec (Tresiba), or insulin detemir (Levemir) prior to being prescribed follow-on insulin glargine (Basaglar) to be included. Patients less than 18 years and those who had not previously been on basal insulin prior to receiving a prescription for insulin glargine (Basaglar) were excluded.

The primary outcome was the difference in basal insulin dosing requirements in both units per day and units per kilogram per day from baseline to postconversion to follow-on insulin glargine (Basaglar). The baseline dose was determined by collecting the last dose the patient was on prior to conversion and the postconversion dose was the last dose the patient was on closest to the end of the defined study time frame. Secondary outcomes included change from baseline to postconversion for the following: total insulin dose requirements including both basal and bolus insulin, change in HbA1c, and change in weight. Safety of the conversion was also evaluated through assessment of the incidence of hypoglycemia and weight gain thought to be associated with the conversion to follow-on insulin glargine (Basaglar). Outcomes were analyzed using paired *t* tests and were examined for normality and statistical outliers. We ran a sensitivity analysis to determine the minimum effect size detectable assuming 80% power, using the formula in G*Power, an online power calculation tool. Our primary outcome was the change in basal dose (units/d), computed both for type 1 and type 2 DM samples. Based on the G*Power formula we also computed an achieved power. Data were stratified between T1DM and T2DM for additional analyses. McNemar's chi-square test with continuity correction was used to test for the association of pre–post paired binary variables. Statistical tests were performed with R version 3.5.1[6] and G*Power 3.1.9.2.[7,8]

Results

A total of 250 patients were prescribed follow-on insulin glargine (Basaglar) between December 15, 2016, and August 31, 2017, and 177 patients were included in the final analysis. The breakdown of the number of patients for each reason for exclusion can be found in Figure 1. The primary reason for exclusion was that patients had been prescribed Basaglar within the electronic medical record (EMR) but had no documented follow-up after conversion.

Of the 177 patients included in the final analysis, 110 (62.1%) patients had T2DM and 67 (37.8%) patients had T1DM. Baseline characteristics can be found in Table 2. The mean age was 51 years, and the majority of the population had a duration of diabetes of 5 years or longer. In general, patients had uncontrolled diabetes with a mean baseline HbA_{1c} of 8.5%. Baseline antihyperglycemic medications for the total study population can be found in Figure 2. The most common medication taken in conjunction with insulin was metformin (n = 65). Other medications included sulfonylureas (n = 16), dipeptidyl peptidase 4-inhibitors (n = 12), glucagon-like peptide-1 receptor agonists (n = 9), sodium-glucose cotransporter-2 inhibitors (n = 2), α-glucosidase inhibitors (n = 1), and thiazolidinediones (n = 1). The primary reason identified for patients switching from one basal insulin product to follow-on insulin glargine (Basaglar) was formulary changes by the patient's insurance company.

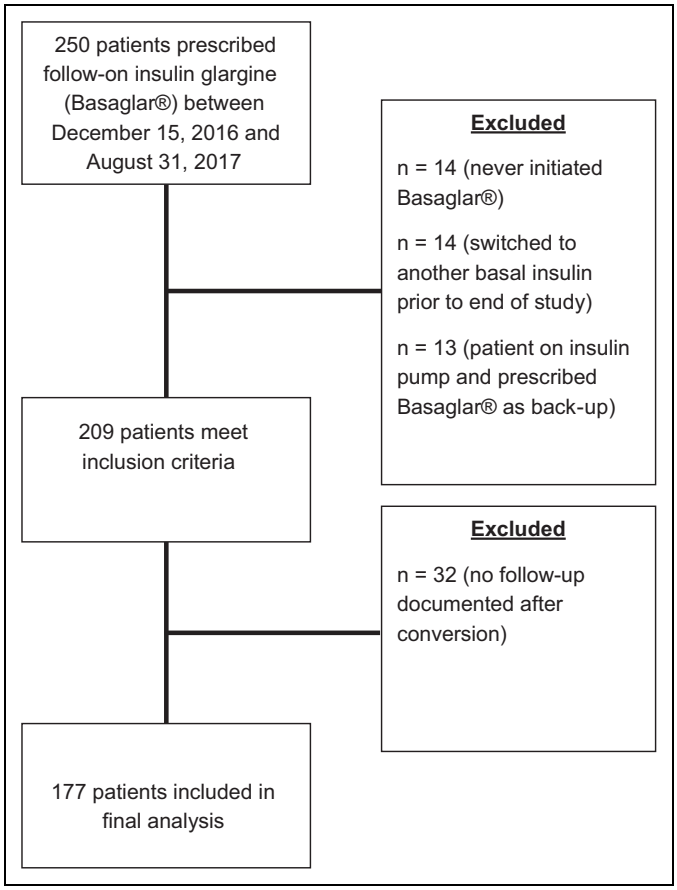

Figure 1. Identification of included patients.

The majority of patients (n = 166, 93.8%) were converted from Lantus to Basaglar, although there were 11 (6.2%) patients who were converted from an alternative basal insulin including Levemir, Toujeo, or Humulin N/Novolin N. No patients were transitioned from Tresiba to Basaglar. The most common method used for conversion to Basaglar from another basal insulin was converting directly based on a 1:1-unit-per-unit conversion. A total of 107 (60.4%) patients were converted using a 1:1-unit-per-unit conversion, 45 (25.4%) patients were converted to a higher dose of Basaglar, 22 (12.4%) patients were converted to a lower dose of Basaglar, and 3 (1.7%) patients did not have clear documentation of the initial conversion dose.

With regard to the primary end point, the mean basal insulin dose at baseline was 38.4 ± 26.3 units/d (0.37 ± 0.25 units/kg/d), and the mean basal insulin dose postconversion at the end of the study period was 40.5 ± 29.8 units/d (0.39 ± 0.29 units/kg/d). The difference between preconversion and

Table 2. Baseline Characteristics of Study Participants.[a]

Characteristic	Value
Female sex, n (%)	71 (40.1)
Race, n (%)	
Caucasian	149 (84.2)
African American	17 (9.6)
Asian	2 (1.1)
American/Native Indian	3 (1.7)
Other	6 (3.4)
Age	
Type 1 (18-67 years)	36 ± 15.4
Type 2 (28-86 years)	61 ± 10.6
Diabetes mellitus type, n (%)	
Type 1	67 (37.8)
Type 2	110 (62.1)
Duration of diabetes, n (%)	
<5 years	14 (7.9)
5-9 years	63 (35.6)
10-14 years	28 (15.8)
≥15 years	72 (40.7)
Followed by endocrinology in past year, n (%)	
All patients	123 (69.5)
Type 1 diabetes	59 (88.1)
Type 2 diabetes	64 (58.2)
Followed by PharmD in past year, n (%)	
All patients	35 (19.8)
Type 1 diabetes	4 (6.0)
Type 2 diabetes	31 (28.2)
Attended diabetes education class in past year, n (%)	
All patients	43 (24.3)
Type 1 diabetes	24 (35.8)
Type 2 diabetes	19 (17.3)
Mean baseline A_{1c}, %	
All patients	8.53 ± 1.94
Type 1 diabetes	8.32 ± 1.82
Type 2 diabetes	8.67 ± 2.01
Mean baseline weight, kg	
All patients	111.6 ± 46.3
Type 1 diabetes	113.7 ± 42.1
Type 2 diabetes	110.4 ± 49.0
Preconversion basal insulin, n (%)	
Lantus® (insulin glargine)	166 (93.8)
Toujeo® (insulin glargine)	3 (1.7)
Levemir® (insulin detemir)	5 (2.8)
Humulin N®/Novolin N® (insulin NPH)	2 (1.1)
Other (lispro used in pump)	1 (0.6)
Reason for conversion, n (%)	
Insurance	160 (90.4)
Other	17 (9.6)

[a]Data are no. (%) of patients or mean (SD).

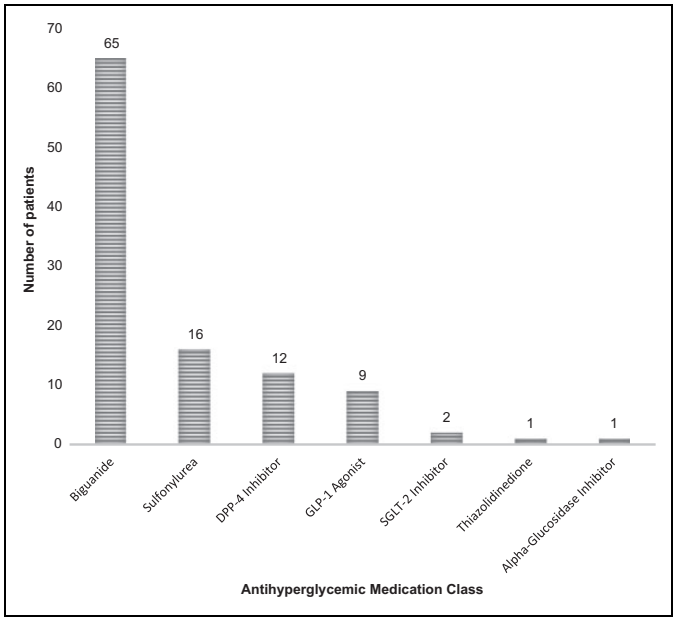

Figure 2. Noninsulin antihyperglycemic medications at baseline.

postconversion basal insulin doses in units/d was significant (difference 2.0 ± 12.5 units/d; $P = .031$). The difference in basal insulin doses in units/kg/d was not significant (difference 0.02 ± 0.13; $P = .056$).

When stratified by diabetes type, the results were nonsignificant for patients with T1DM in both units/d (pre-conversion basal dose = 44.7 ± 28.5 units/d; post-conversion basal dose = 45.1 ± 30.7 units/d; difference 0.4 ± 13.4 units/d; $P = .785$) and units/kg/d (preconversion basal dose =0.43 ± 0.29 units/kg/d; postconversion basal dose = 0.43 ± 0.32 units/kg/d; no difference -0.02 to 0.04; P=0.691). However, in patients with T2DM, there was a statistically significant increase in basal insulin dose from preconversion to postconversion in units/d (preconversion basal dose = 34.6 ± 24.3 units/d; postconversion dose = 37.6 ± 29.1 units/d; difference 3.0 ± 11.9; $P = .009$) and units/kg/d (preconversion basal dose = 0.33 ± 0.21 units/kg/d; postconversion 0.36 ± 0.27 units/kg/d; difference 0.03 ± 0.13; $P = .040$).

The mean HbA_{1c} was similar before and after conversion to Basaglar (8.53% vs 8.39%; $P = .142$). The difference in HbA_{1c} was nonsignificant for patients with T1DM (difference 0.04% ± 1.13; $P = .763$) and significant for patients with T2DM (difference −0.25% ± 1.3; $P = .048$; Table 3). Patients were on Basaglar for an average of 4.4 months (±2.3 months) at the end of the study period. Incidence of patient-reported hypoglycemia was similar before and after conversion to Basaglar. There were 62 (35%) patients who reported hypoglycemia preconversion and 53 (29.9%) patients who reported hypoglycemia postconversion (McNemar chi-square with continuity correction statistic 1.489, $P = .223$, at $\alpha = 0.05$ no statistical difference between proportions; Table 3). There was no significant difference in weight throughout the study population from preconversion to postconversion (111.6 kg ± 46.3 to 111.7 kg ± 46.9; difference 0.2 ± 5.7; $P = .662$), a finding that remained when comparing patients with T1DM and T2DM (Table 3).

The detectable effect size (d) of the primary end point (units/d) for the T1DM sample (n = 67) was 0.347, and for the T2DM sample (n = 110) it was 0.270. Our actual effect size for T1DM was 0.030 (mean 0.4/sd 13.4), which was much smaller than the minimum detectable size of 0.347. The achieved effect size for T2DM was 0.252 (mean 3.0/sd 11.9), which was much closer to the necessary effect size of 0.270. A post hoc power

Table 3. Primary and Secondary Outcomes.[a]

		Pre-Conversion	Post-Conversion	Difference	*P* Value
Change in basal dose, unit	All	38.42 CI (34.55-42.29)	40.46 CI (36.07-44.85)	2.04 CI (0.20 to 3.88)	.031
	Type 1	44.67 CI (37.86-51.48)	45.12 CI (37.77-52.47)	0.45 CI (−2.76 to 3.66)	.785
	Type 2	34.62 CI (30.09-39.15)	37.62 CI (32.21-43.03)	3.00 CI (0.78 to 5.22)	.009
Change in unit/kg/d- unit/kg/d	All	0.37 CI (0.33-0.41)	0.39 CI (0.35-0.43)	0.02 CI (0.00 to 0.04)	.056
	Type 1	0.43 CI (0.36-0.50)	0.43 CI (0.35-0.51)	CI (−0.02 to 0.04)	.691
	Type 2	0.33 CI (0.29-0.37)	0.36 CI (0.31-0.41)	0.03 CI (0.01 to 0.05)	.04
Change in A_{1c}%	All	8.53 CI (8.24-8.82)	8.39 CI (8.11-8.67)	−0.14 CI (−0.32 to 0.04)	.142
	Type 1	8.32 CI (7.88-8.76)	8.36 CI (7.88-8.84)	0.04 CI (−0.23 to 0.31)	.763
	Type 2	8.65 CI (8.27-9.03)	8.40 CI (8.06-8.74)	−0.25 CI (−0.49 to −0.01)	.048
Change in weight, kg	All	111.55 CI (104.73-118.37)	111.74 CI (104.82-118.66)	0.19 CI (−0.65 to 1.03)	.662
	Type 1	113.75 CI (103.66-123.84)	113.63 CI (103.28-123.98)	−0.12 CI (−1.26 to 1.02)	.837
	Type 2	110.21 CI (101.09-119.33)	110.59 CI (101.39-119.79)	0.38 CI (−0.79 to 1.55)	.529
Incidence of patient-reported hypoglycemia, n (%)	All	62 (35.0%)	53 (29.9%)	–	.223[b]

[a]Data are no. (%) of patients or mean (95% CI).
[b]McNemar chi-square test with continuity correction.

analysis for the T1DM sample showed a power of 0.057 and for the T2DM sample showed a power of 0.745.

Discussion

We evaluated the impact of conversion from intermediate or long-acting basal insulin to follow-on insulin glargine (Basaglar) on dosing, glycemic control, incidence of hypoglycemia, and weight change. In the present study, similar weight-based doses of follow-on insulin glargine (Basaglar) were needed after conversion from another basal insulin (primarily Lantus) in order to achieve similar glycemic control when evaluating the patient population as a whole including patients with T1DM and T2DM. A statistically significant increase in the dose of Basaglar was seen after conversion from another basal insulin in patients with T2DM. There was no difference in weight change or incidence of hypoglycemia after conversion to Basaglar.

With the approval of several newer basal insulins over the last few years, a significant number of patients are being converted between the available basal insulin products in clinical practice. Insulin has been associated with a number of medication errors in both inpatient and outpatient settings and is a leading drug class involved in harmful medication errors.[9] Given the high risk nature of insulin use, it is essential that providers know how to appropriately dose and monitor patients when converting between basal insulins. Previous trials evaluating the conversion between basal insulins are mostly limited to phase III trials. The EDITION series compared Toujeo (insulin glargine U-300) and Lantus and found that patients required approximately 10% to 17% higher doses of insulin glargine U-300 to achieve similar glycemic control.[10-12] In contrast, in the phase III trial comparing concentrated Tresiba (insulin degludec U-200) and Lantus, there was an 11% lower dose required in patients in the Tresiba arm in order to achieve similar glycemic control.[13] While the manufacturer provides dose recommendations when converting to newer basal insulins, the recommendations do not fully reflect what was seen in the phase III trials. In addition to phase III trials, there are limited studies evaluating the conversion to either Levemir or Toujeo in real-world settings. The findings from these trials also suggest different dosing requirements when converting between available basal insulin products, and converting outside manufacturer recommendations may be warranted.[14,15] Therefore, it is important to assess the impact of conversion on dosing, glycemic control, and safety in a real-world clinical setting. The current study sought to specifically evaluate the conversion to Basaglar over the conversion to other newer agents, as several patients in our clinical practice are being converted to Basaglar due to formulary changes. Additionally, there is limited information about the true "equivalency" of follow-on biologic products.

Our findings suggest that conversion to Basaglar from another basal insulin (particularly Lantus as this was the basal insulin that the vast majority of our population was taking preconversion) in a real-world clinical setting requires similar dosing in order to achieve similar glycemic control. This aligns with the manufacturer recommendations of converting on a 1:1-unit-per-unit basis when switching to Basaglar from Lantus.[3] While there was a higher dose of Basaglar postconversion seen in patients with T2DM that was statistically significant, this finding may not be clinically significant as the mean difference was 2 units and only accounted for approximately 5% of the total basal insulin dose. Additionally, the mean HbA_{1c} was statistically lower in patients with T2DM postconversion compared to preconversion. The slightly higher basal insulin dose may have contributed to the small decrease of 0.25% in HbA_{1c} in these patients.

These findings are similar to the results of the ELEMENT 1 and ELEMENT 2 trials which were the phase III studies conducted evaluating Basaglar compared to Lantus. The ELEMENT 1 trial, which only included patients with T1DM, found no statistical differences in HbA_{1c}, weight, rates of

hypoglycemia, and mean insulin doses between patients on Lantus and patients on Basaglar at 24 and 52 weeks after conversion from a prior basal insulin.[4] The present study differs from the ELEMENT 1 trial in that the conversion from Lantus to Basaglar was assessed in a more real-world setting. In the ELEMENT 1 trial, clinic visits occurred at week 0, 2, 6, 12, 18, 24, 30, 36, 44, and 52 which allowed for closer monitoring and dose titrations. However, this follow-up regimen is not always realistic in real-world clinical practice. Our findings suggest that conversion from Lantus to Basaglar can be accomplished safely from a hypoglycemia perspective and that similar doses are needed to achieve similar glycemic control in patients with T1DM even without frequent clinic follow-up.

The ELEMENT 2 trial which evaluated patients with T2DM similarly found no statistical difference in HbA_{1c}, insulin dose, weight change, and rates of hypoglycemia between patients treated with Basaglar and patients treated with Lantus. This study differs from the current study in that it included both patients who were insulin naïve and patients who had been treated with insulin prior to the study. However, when the data were stratified by patients who were insulin-naive and those who were not, the results were the same.[5] Although not statistically significant, patients who were in the Basaglar group were on higher unit/kg doses at the end of the study compared to those in the Lantus group (0.60 units/kg/d vs 0.53 units/kg/d). This finding parallels our findings of higher unit/kg/d doses needed in the postconversion Basaglar group compared to the preconversion basal insulin group (0.36 units/kg/d vs 0.33 units/kg/d; $P = .04$) which was statistically significant. More studies are needed to further investigate whether patients converted from Lantus to Basaglar truly require higher doses over time to achieve similar glycemic control.

There are currently no other published studies to date evaluating the conversion from Lantus or other basal insulins to follow-on insulin glargine, Basaglar in a real-world clinical setting. Our study is the first to evaluate this in clinical practice and supports the findings of the phase III clinical trials. Based on these findings, it appears appropriate to convert patients using a 1:1 unit-per-unit dose when switching from Lantus to Basaglar in both patients with T1DM and T2DM. During the transition phase, more frequent monitoring and dose titration may be warranted, as there was a trend toward higher dosing requirements in patients who are switched to Basaglar in the ELEMENT 2 trial and a statistically higher dose achieved postconversion to Basaglar in our study for patients with T2DM. Further studies are warranted to assess appropriate conversions from other basal insulins (insulin detemir, insulin NPH, insulin glargine U-300, and insulin degludec) to Basaglar as our study primarily included patients converted from Lantus to Basaglar.

There are several limitations to our study. First, the study was retrospective and reliant on what was documented in the EMR. Therefore, titration of insulin doses could have occurred that were not documented in the EMR. Changes in weight may not have always been documented which could have also impacted our assessment of changes in unit/kg/d dosing. Adherence to antihyperglycemic medication regimens could not be assessed. However, we were able to capture insulin doses that were titrated over the phone in between office visits based on review of chart notes even if the change made was not documented on the medication list or an updated prescription generated. Second, the HbA_{1c} at the end of the study period may not be fully reflective of the dose changes that occurred. Given that the HbA_{1c} reflects an average of blood glucose over a period of 2 to 3 months, dose changes that occurred close to the follow-up HbA_{1c} check would likely not have significantly impacted the HbA_{1c} yet. Additionally, the time to follow-up for HbA_{1c} was not captured in this study. Third, diabetes is progressive, and the majority of the patients in the study had a duration of diabetes greater than 5 years and would be expected to require higher doses of insulin over time to achieve similar glycemic control. However, this likely has a minimal impact on our results given the short duration of our study. Fourth, we did not have a comparator group to assess change in basal insulin dosing in those patients who remained on Lantus during the study period. We chose not to have a comparator group as our objective was to evaluate the change within individual patients who were converted to Basaglar. Fifth, we were unable to account for the addition or adjustments of other antihyperglycemic agents that could have impacted provider decisions in adjusting basal insulin doses as well as overall glycemic control. Finally, while our results did show some statistical significance, the moderately high effect sizes in the study with 80% power (0.347 and 0.270), were not reached, which may be viewed as a potential limitation to our study. An inherent limitation in our sensitivity analysis is that we also included post-hoc power estimates to illustrate the achieved effect size. After analyzing the data, we realized that our estimate was lower than the minimum effect size and so we were not surprised that the P value in the T1DM sample was high. However, since our observed effect size in the T2DM population was much closer to the estimated threshold, we were not surprised to find statistical significance. Because post hoc power is computed after the data has been analyzed, it is directly related to the P values achieved and should not be confused with a true power estimate. We include its values as a tertiary measure to supplement the confidence intervals of the outcome variables and the sensitivity analysis showing the effect sizes needed for 80% power. Despite these limitations, our study is truly reflective of patient conversion to Basaglar from another basal insulin in a real-world clinical setting where many of these factors cannot be controlled for.

Conclusion

Patients with diabetes converted from basal insulin, particularly insulin glargine (Lantus), to follow-on insulin glargine (Basaglar) required similar doses to achieve similar glycemic control. Patients with T2DM required a slightly higher dose of basal insulin after conversion, though the clinical significance of this is uncertain. There were no differences in HbA_{1c}, incidence of hypoglycemia, or weight change from preconversion to postconversion to Basaglar. The manufacturer

recommendation of converting patients from Lantus to Basaglar in a 1:1 unit-per-unit manner appears appropriate based on our findings in a real-world clinical setting.

Declaration of Conflicting Interests

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