Prevalence of and Characteristics Associated With Overbasalization Among Patients With Type 2 Diabetes Using Basal Insulin: A Cross-Sectional Study

Kevin Cowart,[1,2] Wendy H. Updike,[1,3] and Rashmi Pathak[4]

This article describes a cross-sectional analysis of 655 patients to determine the prevalence of and patient-specific characteristics associated with overbasalization in patients with type 2 diabetes. Overbasalization was defined as uncontrolled A1C (>8%) plus a basal insulin dose >0.5 units/kg/day. The period prevalence of overbasalization was found to be 38.1, 42.7, and 42% for those with an A1C >8, ≥9, and ≥10%, respectively. Those with an A1C ≥9% had the greatest likelihood of experiencing overbasalization. These results suggest that overbasalization may play a role in patients not achieving optimal glycemic control in type 2 diabetes.

Overbasalization is defined as the titration of basal insulin beyond an appropriate dose in an attempt to achieve glycemic targets (1). Current clinical practice guidelines suggest treatment intensification to address postprandial hyperglycemia when a patient's A1C target is not being achieved at a basal insulin dose >0.5 units/kg/day (2,3). However, the strength of this recommendation is based on expert opinion because few studies have investigated the maximum effective dose of basal insulin at which treatment intensification is indicated (4). Overbasalization is not well studied as a barrier to achieving glycemic targets. The aim of this study was to identify the prevalence of and patient-specific characteristics associated with overbasalization in patients with type 2 diabetes.

Research Design and Methods

This was a cross-sectional study conducted at the University of South Florida Department of Family Medicine between 1 January 2015 and 31 December 2018. Inclusion criteria were age 18–80 years, diagnosis of type 2 diabetes for at least 12 months, and at least one clinic visit with a medical provider. The first clinic visit within the study time frame at which a prescription for a basal insulin (glargine U-100, glargine U-300, detemir, degludec U-100, degludec U-200, regular U-500, or NPH insulin) was generated was defined as the index date. The basal insulin dose must have been included on the prescription for inclusion in the study.

The most recent A1C prior to 90 days of the index date was used for the analysis. If an A1C was not available within this time frame, the subject was excluded. Prisoners, pregnant women, and individuals prescribed prandial insulin, a noninsulin injectable (glucagon-like peptide-1 [GLP-1] receptor agonist or pramlintide), or a fixed ratio combination of a basal insulin and a GLP-1 receptor agonist were excluded.

Baseline demographics were analyzed using descriptive statistics. Overbasalization was defined as an A1C >8% plus a basal insulin dose >0.5 units/kg/day. The period prevalence of overbasalization was calculated by determining the number of patients with uncontrolled type 2 diabetes (A1C >8%), and who had a basal insulin dose >0.5 units/kg/day, as compared with patients with the same A1C but without a basal insulin dose >0.5 units/kg/day. The period prevalence was also calculated for those with an A1C of ≥9 and ≥10%.

Univariate logistic regression analysis was performed to determine the significance of several baseline patient characteristics (age, BMI, sex, A1C, race/ethnicity, and type of basal insulin) with the dependent variable (overbasalization). Variables found to be significant in

[1]Department of Pharmacotherapeutics & Clinical Research, Taneja College of Pharmacy, University of South Florida, Tampa, FL; [2]Department of Internal Medicine, Morsani College of Medicine, University of South Florida, Tampa, FL; [3]Department of Family Medicine, Morsani College of Medicine, University of South Florida, Tampa, FL; [4]College of Public Health, University of South Florida, Tampa, FL

Corresponding author: Kevin Cowart, kcowart2@usf.edu

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the univariate analysis were then included in a backward-elimination multivariate regression model. The concentrated insulin products (regular U-500, glargine U-300, and degludec U-200) were excluded from the multivariate regression model to minimize confounding by indication because they may be indicated for people with a basal insulin dose >0.5 units/kg/day. Statistical significance was defined as $\alpha < 0.05$ for all analyses. The analysis was conducted using SAS, v. 9.4 (SAS Institute, Cary, NC). This study was certified exempt by the University of South Florida's institutional review board.

Results

A total of 655 patients (mean age 57 ± 13.4 years) were included in this analysis. The mean BMI was 32.4 kg/m^2 (SD ± 8.7), and 48% of the subjects were male. The majority of patients (57.3%) were White, followed by 24.4% being Black or African American. The mean A1C was 8.4% (SD ± 2.2) and the mean dose of basal insulin was 0.4 units/kg/day (SD ± 0.4). The majority of patients were prescribed insulin glargine U-100 (63.2%), followed by insulin detemir U-100 (21.4%). The period prevalence of overbasalization in this population was found to be 38.1, 42.7, and 42% for those with an A1C >8, ≥9, and ≥10%, respectively. Mean BMI did not differ clinically between these groups (A1C >8%: 32.1 kg/m^2 [SD ± 8.8]; A1C ≥9%: 31.5 kg/m^2 [SD ± 8.4]; A1C ≥10%: 31.5 kg/m^2 [SD ± 8.1]).

In the univariate regression analysis, the following patient characteristics were independently associated with overbasalization: age 35–54 years (odds ratio [OR] 1.89, 95% CI 1.24–2.88), age 65–80 years (OR 0.44, 95% CI 0.27–0.73), A1C ≥9% (OR 13.97, 95% CI 8.43–23.14), A1C ≥10% (OR 6.04, 95% CI 3.93–9.29), and prescription for insulin glargine U-100 (OR 0.62, 95% CI 0.41–0.93). In the multivariate analysis, only A1C ≥9% remained significant; thus, all other variables were eliminated from the model.

Discussion

This is the first report to our knowledge describing the prevalence of overbasalization in a primary care setting among patients with type 2 diabetes. Just under half of the population sampled in this cross-sectional study experienced overbasalization. It is worth mentioning that, regardless of the degree to which A1C was elevated, the prevalence of overbasalization remained similar (~40%). This finding suggests that a large number of patients with type 2 diabetes who are using basal insulin without prandial insulin or a GLP-1 receptor agonist may benefit clinically from treatment intensification. Because the degree of fasting versus postprandial hyperglycemia varies by level of A1C and the prevalence of overbasalization was similar across varying A1C levels, it cannot be determined from this study whether individuals not meeting glycemic targets need additional basal insulin or postprandial coverage. Therefore, these preliminary findings are hypothesis-generating and support the need for additional investigation into the optimal dose of basal insulin at which to initiate postprandial coverage.

Several patient-specific characteristics were found to be independently associated with overbasalization, although when adjusted for potential confounders, an A1C ≥9% was the strongest predictor of overbasalization. These findings suggest that overbasalization may play a role in patients with type 2 diabetes not achieving optimal glycemic control, although this hypothesis requires additional investigation in a larger sample. Additionally, studies are needed to determine the association of hypoglycemia with overbasalization because that was not measured as a variable in this study and is an expected adverse outcome associated with overbasalization.

Limitations to this analysis include the limited independent variables that were measured to predict the dependent variable. Furthermore, oral antidiabetic medication use and length of time basal insulin was prescribed were not captured, and both may affect treatment decisions. Additionally, we did not exclude patients using steroids, which may transiently increase insulin requirements. Future work should also evaluate the following characteristics to define overbasalization: postmeal blood glucose >180 mg/dL, A1C not at goal despite attaining fasting blood glucose targets, or a bedtime-morning blood glucose differential ≥50 mg/dL (1). There may also be patients seen in clinical practice whose basal insulin dose is much larger than their prandial insulin dose (i.e., >50% of their total daily insulin dose) who may also be overbasalized (5–8), although such patients were not accounted for in the present analysis because prandial insulin use was an exclusion criterion. An additional consideration in light of high basal insulin doses in patients with suboptimal glycemic control is the potential for poor insulin injection technique. Given the retrospective nature and limited variables available for collection in the electronic medical record, we could not assess this, although it should be considered in future prospective evaluations. Additional limitations include the observational design (lack of temporality) and low external validity because analyzed data were from one academic family medicine practice. However, the study's

strengths include its large sample size and an adjusted analysis for potential confounders affecting the dependent variable.

In conclusion, our findings are hypothesis-generating but suggest that overbasalization may play a role in patients with type 2 diabetes not achieving optimal glycemic control. The results highlight the need for additional investigation into therapeutic strategies that ascribe to a physiologic approach in the management of patients with type 2 diabetes using basal insulin. These strategies may involve continuous glucose monitoring or having shorter intervals between routine clinic visits to appropriately titrate basal insulin without delay in treatment intensification when warranted in those not meeting glycemic goals.

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DUALITY OF INTEREST

No potential conflicts of interest relevant to this article were reported.

AUTHOR CONTRIBUTIONS

K.C. contributed to the conception, study design, and statistical analysis and wrote the first draft of the manuscript. W.H.U. contributed to the acquisition and interpretation of the data and provided critical revisions to the manuscript for important intellectual content. R.P. contributed to the statistical analysis. K.C. is the guarantor of this work and, as such, had full access to all the data in the project and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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