FEATURE ARTICLE

Collaboration of Hospital Pharmacists and Hospitalists to Address Glycemic Control of General Medicine Patients: Implementation of a Pilot Inpatient Diabetes Management Program

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This study examined the clinical benefits of a collaborative pharmacist-physician inpatient diabetes management program that included daily blood glucose assessment and the recommendation and implementation of American Diabetes Association–recommended insulin regimens.

Inpatient hyperglycemia results in increased morbidity, increased lengths of stay, and increased risks of adverse events and medication errors (1,2). Despite this evidence, management of hyperglycemia during hospitalization is often inadequate and involves significant use of sliding-scale insulin (SSI) (3–5). The RABBIT 2 (Randomized Study of Basal-Bolus Insulin Therapy in the Inpatient Management of Patients With Type 2 Diabetes) and RABBIT 2 Surgery trials and other studies have shown that regimens that include basal insulin are superior to reliance on an SSI regimen for control of hyperglycemia (6–9).

To encourage evidence-based management of diabetes in the hospital, the American Diabetes Association (ADA), the American Association of Clinical Endocrinologists (AACE), the Endocrine Society, the Joint Commission, and the Society of Hospital Medicine have all put forth guidelines for the management of diabetes in hospitalized patients who are not in the intensive care unit (ICU) (10–14). Current ADA guidelines state that a regimen of basal plus correctional insulin is the preferred treatment for noncritically ill hospitalized patients with poor or no oral intake and that a regimen including basal, mealtime, and correctional (BMC) insulin is the preferred treatment when a patient has good oral intake (10).

The ADA also recommends the use of insulin order sets and insulin management algorithms because both are proven methods of increasing the use of basal insulin regimens and improving inpatient glycemic control (10,15,16).

Importantly, the use of basal insulin during hospitalization with continuation of a basal insulin regimen after discharge has been shown to decrease A1C (16,17). Current ADA guidelines suggest that tailored glucose management interventions such as dose adjustments and regimens that include basal insulin should be considered during hospital stays and that active glucose management should persist through transition out of the acute care setting (10). The Endocrine Society's guidelines similarly suggest that inpatients with A1C values >7% require intensification of their outpatient treatment regimen and may benefit from a regimen of basal plus correctional insulin or a BMC regimen (13).

Using our existing hospitalist and pharmacist interdisciplinary teaching team model, we implemented an inpatient diabetes care initiative for general internal medicine inpatients receiving insulin therapy during hospitalization. We conducted a prospective, randomized trial to evaluate whether daily target-based blood glucose assessment combined with insulin dose and regimen adjustments collaboratively managed by pharmacists and physicians could increase the use of ADA-recommended inpatient insulin regimens and promote active diabetes management through transition out of the acute care setting.

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Methods

This was an institutional review board–approved, prospective, randomized, open-label, parallel-group trial. The study was conducted over a 7-month period at our 1,400-bed tertiary care teaching hospital.

At our institution, hospitalists admit the majority of general internal medicine patients. Hospitalist teaching teams include an attending physician, a senior resident, an intern, and a medical student. Pharmacists stationed on individual nursing floors provide clinical services and order verification, including participating as a team member on medical rounds on the majority of hospitalist teams. Nurses join the medical team at patients' bedside.

Physicians order insulin via an electronic medical record system (Epic, Verona, Wisc.) using an insulin order set created by our institutional Diabetes Care Committee that presents multiple basal, mealtime, and pre-built correctional insulin (SSI) options. Types of insulins available during the trial included glargine, detemir, glulisine, NPH, regular, and mixed products. The order set includes blood glucose monitoring orders (with meals and at bedtime or every 6 hours) and a hypoglycemia protocol for blood glucose values <70 mg/dL. General insulin dosing information based on patient weight and type of diabetes is provided for all prescribers as part of the order set.

Before the study initiation, physicians in the Department of Hospital Medicine and participating pharmacists were introduced to the study and informed about ADA and ADA/AACE guidelines for insulin prescribing and the benefits of regimens containing basal insulin. The pharmacist-physician collaborative model and insulin dosing recommendation strategy were reviewed. Physicians gave informed consent to participate in the study. Hospitalist teams were prospectively randomized to usual care or collaborative intervention groups. Thirty-four hospitalists and nine pharmacists participated in the study.

Patients with diabetes who were ≥18 years of age, admitted to the adult hospitalist teaching services, and receiving subcutaneous insulin therapy for >48 hours were eligible for inclusion in the study. Patients receiving diabetes medications other than insulin, patients in active diabetic ketoacidosis (DKA) or hyperosmolar hyperglycemic state, and pregnant patients were excluded.

In the usual care group, target blood glucose levels and insulin dosing were left to the discretion of the medical team. No daily blood glucose review or insulin adjustment recommendations were routinely provided by the study pharmacists.

In the intervention group, nursing unit–based pharmacists reviewed blood glucose results daily. Pharmacists made recommendations to the hospitalist teams to adjust insulin doses and insulin regimens according to patients' blood glucose values during the previous 24 hours based on the study diabetes management guide (Appendix). The insulin adjustment strategy was modeled on the insulin dose adjustment protocol used in the RABBIT 2 trials (6,7). This strategy and other similar dosing algorithms have been used successfully in trials of insulin use in the inpatient setting (9,15). If the morning fasting blood glucose or the previous day's mean blood glucose was >140 mg/dL, initiation of basal or mealtime insulin was recommended. Alternatively, a basal or mealtime insulin dose adjustment of 20% was recommended. Recommendations could be modified based on patient-specific situations, and more than one adjustment could be made daily. Medical teams retained the clinical discretion to decline a recommendation.

In the intervention group, daily goals were to actively manage diabetes, encourage the use of either a basal-plus-correctional insulin regimen or a BMC insulin regimen, and minimize sole use of an SSI regimen. Target blood glucose levels were fasting and premeal values of 70–14 mg/dL and random blood glucose values <180 mg/dL.

The usual care group and the intervention group used the same insulin order set and had access to our institution's standard insulin dosing recommendations. The only difference between the usual care group and the intervention group was daily blood glucose result review and criteria-based insulin dosing recommendations by the study pharmacists per the study's diabetes management guide.

Data were collected for the duration of the hospital stay while patients were on an insulin regimen. Data collected included demographics, use of corticosteroids, transfers to an ICU, surgical procedures, and days patients were on NPO status. Daily blood glucose readings, insulin doses administered, insulin regimen type, and insulin dose recommendations were recorded. Insulin regimens prescribed before admission and at discharge were documented. All hypoglycemia and DKA events were reviewed daily. Hypoglycemia was defined as blood glucose <70 mg/dL (10). Severe hypoglycemia was defined as blood glucose <40 mg/dL (11). Insulin

regimens were classified as basal-plus-correctional, BMC, or sole use of an SSI regimen.

Statistical Analysis

Study data were analyzed on an intention-to-treat basis. All statistical analyses were performed at the $\alpha = 0.05$ level using SPSS, version 11, software (IBM, Armonk, N.Y.). Fisher's exact test was used to evaluate differences in percentages, and *t* tests were used to compare normally distributed data between two independent groups. Analysis of covariance was performed to analyze changes in blood glucose measures between study arms by adjusting for baseline blood glucose. A sample size of 183 subjects in each group provided 80% of the statistical power to detect a 15% difference in mean blood glucose between groups.

Results

A total of 193 subjects were enrolled in the usual care (UC) group, and 190 subjects were enrolled in the intervention (INV) group over a period of 29 weeks. There were no statistically significant differences between the two groups in patient-specific characteristics such as age, height, weight, race, sex, or BMI. Additionally, there was no difference in number of monitored inpatient days, type of diabetes, lengths of stay, case severity index, number of ICU transfers, surgical procedures, or use of corticosteroids. NPO status occurred more often in the INV group than in the UC group (37.9 vs. 17.1%, $P < 0.001$) (Table 1).

Before admission, 44.5% of subjects in the UC group and 45.8% of subjects in the INV group were treated with a regimen that included basal insulin ($P = 0.918$). During hospitalization, such regimens were used on 52% of patient days in the UC group and 58.9% of patient days in the INV group ($P < 0.001$). SSI monotherapy regimens were used 46.2% of patient days in the UC group and 40% of patient days in the INV group ($P = 0.002$). On the day before discharge, 53.9% of patients in the UC group were on a regimen containing basal insulin compared to 67.4% of patients in the INV group ($P = 0.018$). Patients were discharged on a regimen that included basal insulin more frequently in the INV

TABLE 1 Patient Characteristics

	UC Group ($n = 193$)	INV Group ($n = 190$)	*P*
Age, years, mean (SD)	64.7 (16.0)	62.2 (17.1)	0.156
Male sex, %	45.6	43.9	0.758
Race, %			0.928
White	44.3	44.2	
African American	52.4	52.6	
Hispanic	1.1	0.6	
Other	2.2	2.6	
Weight, kg, mean (SD)	93.3 (30.5)	95.8 (37.1)	0.464
BMI, kg/m^2, mean (SD)	32.9 (10.7)	33.6 (12.5)	0.580
Type of diabetes, %			0.151
Type 1	5.1	9.2	
Type 2	94.9	90.8	
ICU admission, *n* (%)	3 (1.6)	4 (2.1)	0.722
Surgery, *n* (%)	9 (4.7)	19 (10.0)	0.051
NPO during admission, *n* (%)	33 (17.1)	72 (37.9)	<0.001
Corticosteroid during admission, *n* (%)	31 (16.1)	39 (20.5)	0.291
Case severity index, mean (SD)	2.0 (2.1)	2.2 (2.7)	0.240
Length of stay, days, mean (SD)	7.0 (5.1)	7.0 (6.0)	0.936
Insulin therapy, days, mean (SD)	6.5 (3.7)	6.4 (4.0)	0.857

TABLE 2 Insulin Regimens and Adjustments

	UC Group	INV Group	*P*
Insulin regimens			
Basal-containing regimen, patient-days (%)	642/1,234 (52)	713/1,211 (58.9)	<0.001
Sliding-scale regimen, patient-days (%)	570/1,234 (46.2)	484/1,211 (40)	0.002
Basal-containing regimen before admission, *n* (%)	86/193 (44.5)	87/190 (45.8)	0.918
Basal-containing regimen before discharge, *n* (%)	104/193 (53.9)	128/190 (67.4)	0.018
Basal-containing regimen on discharge, *n* (%)	110/193 (57.0)	130/190 (68.4)	0.026
Regimen changes, admission to discharge	***n* = 193**	***n* = 190**	
Remain on non-basal regimen, *n* (%)	79 (40.9)	58 (30.5)	0.011
Change to basal regimen, *n* (%)	28 (14.5)	48 (25.3)	
Change to non-basal regimen, *n* (%)	10 (5.2)	4 (2.1)	
Remain on basal regimen, *n* (%)	76 (39.4)	80 (42.1)	
Insulin adjustments	***n* = 179**	***n* = 399**	<0.001
Stop basal, mealtime, or correctional, *n* (%)	12 (6.7)	26 (6.5)	
Decrease dose, *n* (%)	37 (20.7)	53 (13.3)	
Increase dose, *n* (%)	76 (42.5)	186 (46.6)	
Add basal, mealtime, or correctional, *n* (%)	51 (28.5)	106 (26.6)	
Other, *n* (%)	3 (1.6)	28 (7.0)	

group than in the UC group (68.4 vs. 57.0%, $P = 0.026$) (Table 2).

A total of 179 insulin therapy adjustments were made in the UC group (0.9 adjustments per subject) compared to 399 treatment adjustments in the INV group (2.1 adjustments per subject) ($P < 0.001$) (Table 2). In the UC group, insulin treatment was adjusted 23% of the times that subjects met criteria for adjustment (176/766) compared to 48.6% of the times that criteria for adjustment were met in the INV group (371/763) ($P < 0.001$).

Mean daily blood glucose was 177.5 mg/dL in the UC group and 180.9 mg/dL in the INV group ($P = 0.508$). There were 163 blood glucose values <70 mg/dL (3.6%) in the UC group and 144 (3.2%) in the INV group ($P = 0.417$). Sixteen severe hypoglycemia events occurred in the UC group (0.3%) compared to 19 such events in the INV group (0.4%) ($P = 0.613$) (Table 3).

Discussion

The effectiveness of a target-based approach to glycemic control in non–critically ill hospitalized patients was demonstrated in the RABBIT 2 trials (6,7). SSI monotherapy was compared to BMC insulin regimens actively titrated to reach blood glucose targets of 90–130 mg/dL. BMC regimens controlled blood glucose more effectively than SSI monotherapy and reduced the risk of hypoglycemia. The Basal-Plus trial (9) compared the glycemic control achieved using BMC, basal-plus-correctional insulin, or SSI monotherapy in 351 hospitalized patients with type 2 diabetes. Glycemic control in both

TABLE 3 Blood Glucose Outcomes

	UC Group	INV Group	*P*
Daily blood glucose, mg/dL, mean (SD)	177.5 (51.3)	180.9 (48.6)	0.508
Blood glucose results <70 mg/dL, *n* (%)	163/4,582 (3.6)	144/4,447 (3.2)	0.417
Blood glucose results <40 mg/dL, *n* (%)	16/4,582 (0.3)	19/4,447 (0.4)	0.613

basal-containing regimen groups was superior to sole treatment with SSI.

The AACE/ADA consensus statement on inpatient diabetes control recommends basal-plus-correctional and BMC regimens and discourages prolonged use of SSI monotherapy for control of hyperglycemia in hospitalized patients (11). Current ADA standards of care for hospitalized, noncritically ill patients with diabetes have both an inpatient and a care transition component (10).

Baldwin et al. (16) implemented a medical resident reeducation project to actively manage diabetes during inpatient admission and eliminate the use of SSI. A1C in the intervention group was reduced compared to the control group 12 months after discharge. Umpierrez et al. (17) studied a basal insulin discharge algorithm in subjects who participated in the previously reviewed Basal-Plus trial. A1C was reduced 12 weeks after discharge in study participants who received a basal insulin regimen in place of or in addition to their previous diabetes treatment. Wu et al. (18) studied outcomes in patients with type 2 diabetes and an A1C >8% who had insulin therapy initiated during hospitalization and then either continued or discontinued insulin treatment at discharge. A1C <7% was achieved more often in the group who maintained the new insulin treatment after discharge. Of those patients with an A1C >9%, continuation of insulin was associated with lower all-cause mortality as well as fewer diabetes-related readmissions.

Achieving blood glucose targets requires a systematic, multidisciplinary approach involving physicians, pharmacists, nurses, and other health care providers (HCPs) (10,13). Our research shows that a collaborative approach to inpatient diabetes management between physicians and pharmacists positively affects both inpatient care and the transition to the primary care setting. Daily review of blood glucose results and insulin adjustment recommendations by pharmacists reduced reliance on the sole use of SSI. Prescribing basal insulin-containing regimens as recommended by ADA, AACE, and Endocrine Society guidelines increased without increasing the incidence of hypoglycemia.

Management of diabetes with basal-containing insulin regimens before admission was similar in both groups. At discharge, prescribing of basal-containing regimens increased 12.5% in the UC group. Physician-pharmacist collaborative management achieved a 22.6% increase in insulin use after discharge, a statistically significant difference. Daily, focused, collaborative, target-based review of blood glucose values identified additional patients who would benefit from treatment intensification.

The study did not reveal a significant difference in mean daily blood glucose between the UC and INV groups. There may be several explanations for this finding. Before study initiation, all participating hospitalists received information about the study and current standards for inpatient care, which may have encouraged the use of basal insulin regimens in the UC group. Delay in implementation of recommendations occurred when insulin was administered before daily recommendations were made, which may have lessened the immediate impact of an insulin intervention. NPO status and surgical procedures were noted more frequently in the INV group, which may have caused blood glucose variability, making insulin regimens more difficult to adjust.

We recognize that daily dose adjustments and treatment intensification at discharge is not necessary for all patients. Reasons to decline recommendations could include inconsistent oral intake, NPO status for surgery or a medical or diagnostic procedure, blood glucose near target, or other reasons. By the trial design, as in actual clinical practice, medical teams were not required to follow all recommendations, but rather could use their clinical judgment while making insulin changes.

Most importantly, diabetes was more actively managed in the INV group; when subjects in that group met criteria for adjustment, an adjustment was made 49% of the time—more than double the 23% rate of adjustment in the UC group. When pharmacists in the INV group initiated the recommendations according to the insulin adjustment strategy, recommendations were accepted 55% of the time. Nevertheless, a higher rate of acceptance of pharmacists' recommendations or a more rigorously applied insulin adjustment strategy could have improved blood glucose results in the INV group.

This trial examined a collaborative insulin management intervention compared to usual care in acutely ill patients with diabetes who were prescribed the full range of insulin regimens. Previous landmark studies (6,7,9) demonstrating the efficacy and safety of basal insulin regimens compared to SSI monotherapy and forming the basis of current inpatient insulin treatment standards excluded patients with ICU stays, surgical procedures, renal failure, hepatic disease, and corticosteroid use. The present study was conducted to measure the impact of collaborative, active insulin management of typical inpatients without excluding these conditions. Inclusion of high-acuity subjects with many comorbidities

may make our results somewhat different than those found in previous important trials but perhaps more reflective of results that can be obtained in actual clinical practice.

Draznin et al. (19) highlight the need for more randomized controlled trials of innovative glycemic control efforts. Newton and Young (20) demonstrated the benefits of a collaborative hospital-wide program to employ inpatient BMC regimens. Our randomized controlled study demonstrates that collaborative, active inpatient diabetes management by pharmacists and physicians produces a change in therapy that lasts beyond hospital discharge. Such a change has been associated with improvement in A1C (16,17) and decreased diabetes-related hospital readmissions (18).

Current diabetes care standards encourage HCPs to collaborate and use inpatient admissions as opportunities to actively manage diabetes (10,13). Such management should persist after transition to the outpatient setting. Brunton (21) exhorts physicians and other HCPs to be "armed with the guidelines, insights, and recommendations of the ADA Standards of Care" to improve the care of patients with diabetes. Most patients with diabetes will be treated with insulin during hospitalization, so the use of guideline-recommended regimens is necessary. Current guidelines do not recommend insulin treatment at discharge for all patients. However, treatment intensification is both crucial and beneficial for patients whose diabetes is not in good control. Inpatient admissions are appropriate times to consider and implement insulin adjustment for such patients. Additional research is needed on dosing algorithms, guideline-based diabetes management strategies for inpatients and the transition back to primary care, and the type of patients who will benefit from active inpatient diabetes management.

Expanding pharmacist responsibilities to include inpatient diabetes management as part of the inpatient care team is a safe and effective way to improve diabetes treatment. Current evidence-based diabetes management guidelines emphasize the importance of insulin dose and regimen optimization. Hospital pharmacists can provide daily blood glucose review and diabetes management services to the medical team via a diabetes management program or collaborative practice agreement. Implementation of diabetes management services can be achieved using existing pharmacist staff.

In this pilot program, we designed an insulin adjustment strategy that translates the findings of bedrock clinical trials and current diabetes standards of care for hospitalized patients into a pharmacist-physician collaborative diabetes care activity. Daily blood glucose assessment and insulin adjustments managed by pharmacists and physicians is a safe and effective way to increase the use of guideline-recommended insulin regimens in the hospital and at discharge. This strategy accomplishes the goal of active inpatient diabetes management with a potential benefit that lasts beyond the inpatient admission, as recommended by ADA, AACE, and Endocrine Society guidelines.

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DUALITY OF INTEREST

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

AUTHOR CONTRIBUTIONS

J.M.K. designed the study, obtained funding, supervised the research, and wrote the manuscript. E.J.Y. managed the data and performed statistical analysis. S.S. contributed to the study design and execution, contributed to the discussion, and reviewed and edited the manuscript. J.M.K. is the guarantor of this work and, as such, had full access to all the data in this study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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