Improving Glycemic Control in Medical Inpatients: A Pilot Study

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BACKGROUND: Inpatient hyperglycemia is associated with poor patient outcomes. Current guidelines recommend that in an inpatient non-ICU setting there be treatment to achieve a glucose level below 180 mg/dL.

METHODS: Objectives of this prospective quality-improvement pilot study were to implement a subcutaneous insulin protocol on a general medicine service, to identify barriers to implementation, and to determine the effect of this protocol on glycemic control. Eighty-nine patients with a preexisting diagnosis of type 2 diabetes or inpatient hyperglycemia were eligible. Study outcomes included resident acceptance of the protocol, insulin-ordering practices, and mean rate of hyperglycemia (glucose > 180 mg/dL) per person. Results were compared with those of a previously conducted observational study.

RESULTS: Residents agreed to use the protocol in 56% of cases. Reasons for declining the protocol included severity of a patient’s other disease states, desire to titrate oral medications, and fear of hypoglycemia. Basal and nutritional insulin were prescribed more often in the pilot group compared with at baseline (64% vs. 49% for basal, \( P < .05 \); 13% vs. 0% for nutritional, \( P < .001 \)). Basal insulin was started after the first full hospital day in 42% of patients, and only one-third of patients with any hypo- or hyperglycemia had any subsequent changes in their insulin orders. The mean rate of hyperglycemia was not significantly different between groups (31.6% of measurements per patient vs. 33.3%, \( P = .85 \)).

CONCLUSIONS: Adherence to a new inpatient subcutaneous insulin protocol was fair. Barriers included fear of hypoglycemia, delays in starting basal insulin, and clinical inertia. Quality improvement efforts likely need to target these barriers to successfully improve inpatient glycemic control. Journal of Hospital Medicine 2008;3:55–63. © 2008 Society of Hospital Medicine.

KEYWORDS: diabetes mellitus, hyperglycemia management, outcomes measurement, subcutaneous insulin protocol.

Diabetes mellitus is a common comorbid condition in hospitalized patients. In 2003, diabetes was listed as a diagnosis in 17.2% of hospital discharges in the United States.1 Because these diagnosis codes do not account for undiagnosed diabetes or hospital-related hyperglycemia, the true prevalence of diabetes or hyperglycemia in hospitalized patients is likely higher and has been estimated to be as great as 38%.2 Hypermelcemia has been associated with adverse outcomes among hospitalized patients, including infectious complications, increased length of stay, and increased mortality.2–7 However, because hyperglycemia is not usually the primary reason patients with diabetes are hospitalized, its management is often not a focus in the inpatient setting. Sliding-scale insulin alone continues to be commonly prescribed
despite clinical evidence showing it to be ineffective in achieving glycemic control.8,9

Recent randomized controlled trials have demonstrated that aggressive treatment of inpatient hyperglycemia improves outcomes in surgical and medical intensive care units10,11 and in patients admitted for myocardial infarction.12,13 Based on this clinical evidence and strong observational data linking hyperglycemia to poor patient outcomes in the non-ICU setting,2–7 the American Diabetes Association (ADA) now advocates good metabolic control, defined as preprandial glucose levels of 90-130 mg/dL and peak postprandial glucose levels < 180 mg/dL in hospitalized non-ICU patients with hyperglycemia14 (note that these targets are less aggressive than those for ICU patients, for whom randomized controlled trials showed the benefits of reduced mortality provided by tight glucose control).11 To reach these targets, the ADA and American College of Endocrinology suggest that multidisciplinary teams develop and implement hyperglycemia management guidelines and protocols.15 Protocols should promote the use of continuous intravenous insulin or scheduled subcutaneous insulin as opposed to the use of sliding-scale insulin alone. Subcutaneous insulin protocols should include target glucose levels; basal, nutritional, and supplemental insulin; and daily adjustments based on previous glucose levels, insulin sensitivity, nutritional intake, illness, and medications.6,15 To date, few published protocols or algorithms for inpatient subcutaneous insulin have been shown to be effective.16,17 It is therefore not known how best to design and implement an inpatient diabetes management protocol that is effective, efficient, and self-perpetuating. The aims of our pilot study were to develop and implement a subcutaneous insulin protocol on a general medicine service, to identify barriers to implementation, and to determine the effect of this protocol on glycemic control.

METHODS
Setting and Participants
This prospective quality-improvement pilot study was conducted at Brigham and Women’s Hospital (BWH) from January 10, 2005, through June 23, 2005. Patients were eligible to participate if they were admitted to either of 2 General Medicine Service (GMS) teams with either a known diagnosis of type 2 diabetes or inpatient hyperglycemia (random laboratory glucose level > 180 mg/dL) and at least 1 fasting point-of-care glucose reading > 140 mg/dL. Patients were excluded if they had diabetic ketoacidosis, hyperosmolar hyperglycemic state, another absolute indication for intravenous insulin, or fasting glucose < 60 mg/dL on no insulin or if they were pregnant. Each GMS team consisted of a teaching attending, a junior or senior resident, 2 interns, and a clinical pharmacist. Twenty-six physicians attended on these 2 teams during the study period, 13 of whom were hospitalists. This study was approved by the BWH Institutional Review Board; patient consent to participate in this study was deemed not necessary because of the relatively nonsensitive nature of the data (eg, glucose control, insulin orders), the noninvasive means of data collection (eg, chart review), and the steps taken by research personnel to minimize any breach in patient confidentiality.

Intervention
A multidisciplinary team composed of a diabetologist (M.L.P.), a hospitalist (J.L.S.), and a pharmacist (J.M.T.) developed a subcutaneous insulin protocol that was approved by the BWH Pharmacy and Therapeutics Diabetes Subcommittee. The protocol consisted of a set of treatment recommendations made by a pharmacist to be carried out by the medical team. The primary components are shown in Table 1 (a full description can be found in the Appendix). The main emphasis of the protocol was on discontinuing oral antihyperglycemic agents during hospitalization, initiating basal insulin in most patients, and adjusting basal insulin daily as needed.

All medical residents received general instructions regarding inpatient diabetes control by the research team’s diabetologist (M.L.P.) through a 1-hour department-wide didactic lecture. The standards of care taught were identical to those in the protocol. In addition, the research team’s hospitalist (J.L.S.) contacted each medical resident assigned to the 2 GMS teams electronically to introduce the protocol and describe the purpose and logistics of the pilot study.

A research assistant prospectively identified eligible patients each weekday by screening all patients admitted to the 2 GMS teams using the daily computerized sign-out system used by all medical residents. Specifically, laboratory random glucose levels, inpatient medications, and medical history were reviewed to determine if each patient met eligibility criteria. Eligibility criteria were confirmed
by medical record review. The pharmacist recommended to the primary team that the protocol be initiated for eligible patients. In addition, the pharmacist recommended daily adjustment of the insulin dose according to the protocol as appropriate. A chronologically organized summary of clinical data relevant to glycemic management for each patient, including bedside blood glucose measurements, general dietary intake, use of intravenous dextrose solutions, and administration of systemic steroids, oral diabetes medications, and all insulins, was provided to the team each day by the research assistant.

**Measurements**

The resident’s acceptance of the protocol or reasons for declining it were recorded by the pharmacist on the day the protocol was recommended. Protocol acceptance was categorized as yes, no, or partial. Partial acceptance was defined as resident agreement to use the protocol, but with stated caveats or modifications. Clinical data were collected on each eligible patient for up to 7 days on GMS. Several data sources were used, including physician admission notes, the hospital’s computerized clinical data system, vital-sign sheets, medication administration records, and personal communication with nurses regarding any missing or discrepant data.

All insulin use (prescribed drug, dose, route, schedule and actual administered drug, dose, route, and time) was recorded each day by the research assistant. Use of basal and nutritional insulin and daily dose adjustments if previous hypo- or hyperglycemia (categorized as yes, no, or not applicable for each patient each day) were determined by the study pharmacist (J.M.T.) through retrospective review of all orders.

Up to 4 routine bedside blood glucose measurements were recorded each day: for patients eating discrete meals, these were the measurements taken before meals and at bedtime; for patients not eating or receiving continuous nutrition, these were the measurements taken closest to 6 AM, noon, 6 PM, and midnight. Additional measurements were not recorded to avoid ascertainment bias caused by follow-up testing of abnormal glucose values. Glucose readings on the day of admission were excluded from analysis because these values are not amenable to inpatient ordering practices.

Study outcomes included overall protocol acceptance rate, insulin prescribing practices including use of basal insulin (ie, long-acting agents such

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**TABLE 1**

Major Components of Subcutaneous Insulin Protocol

| Oral agents | 1. Stop oral agents in most patients |
| Glucose testing | 2. Check bedside blood glucose before meals and at bedtime if eating, or every 6 hours if not eating |
| Insulin | 3. Start basal insulin Patient’s home dose or NPH 0.1 units/kg before breakfast and at bedtime or insulin glargine 0.2 units/kg at bedtime (max dose 20 units) If NPO, consider half dose unless hyperglycemic |
| | 4. Start nutritional insulin Discrete meals: insulin aspart 0.05-0.1 units/kg per meal or home dose 0-15 minutes prior to eating |
| | Continuous tube feeds: regular insulin every 6 hours or NPH every morning and at bedtime (0.1-0.2 units/kg per day in addition to basal insulin) |
| | Hold if NPO |
| 5. Start correctional insulin |
| Scale provided based on blood glucose and daily scheduled insulin requirements |
| Daily Adjustments | 6. Adjust scheduled insulin daily |
| | • Nomogram provided based on previous day’s blood glucose trends |
| | • Premeal or bedtime glucose 140-180 mg/dL: increase corresponding basal or nutritional insulin by 10% |
| | • Premeal or bedtime glucose > 180 mg/dL: increase corresponding basal or nutritional insulin by 20% |
| | • Premeal or bedtime glucose < 80 mg/dL: decrease corresponding basal or nutritional insulin by 33-100% |
| Other Considerations | 7. Hypoglycemia management (protocols for fruit juice, glucagons, IV dextrose, and when to call physician) |
| | 8. Discharge orders (recommendations to discharge most patients on admission medication regimen, avoid sliding scale insulin, simplify dosing for patients requiring new insulin regimens, ensure adequate patient education and prompt outpatient follow-up) |

NPH: neutral protamine hagedorn, kg: kilogram; NPO: nothing by mouth
as NPH and insulin glargine), nutritional insulin (ie, scheduled regular, lispro, or aspart insulin given before each meal), daily dose adjustments under the protocol, and mean percentage of glucose readings per person greater than 180 mg/dL (hyperglycemia) and below 60 mg/dL (hypoglycemia). Comparable data from a previous cohort study of 91 GMS patients were used as baseline data for comparisons with the results of the present study.9

Other patient data collected included age, sex, weight, baseline A1C (taken at or within 6 months of admission), diabetic medications used prior to admission (none, oral agents only, or any insulin use); daily inpatient use of oral or intravenous steroids, oral diabetic medications, dextrose-containing intravenous fluids, tube feeds, total parenteral nutrition, and general nutritional intake (nothing by mouth, clear diet, low carbohydrate diet, house diet).

**Statistical Analysis**

Characteristics of the study subjects and process and outcome measures were analyzed descriptively using rates, means, and standard deviations or medians with interquartile ranges as appropriate. Comparisons between the pilot study and baseline cohorts were performed using Fisher’s exact test for dichotomous outcomes (eg, use of basal insulin). For rates of hyperglycemia (ie, fraction of readings > 180 mg/dL), we used binomial logistic regression, accounting for potential correlation among repeated events by individual patients with a dispersion parameter18 (note that we did not use the same analysis for rates of hypoglycemia because it was such a rare event; for analysis of hypoglycemia, the variables were dichotomized). We also analyzed outcomes by hospital day (through hospital day 5, the limit used in the baseline study) to determine daily trends during the course of hospitalization; for these analyses we used the Mantel-Haenszel chi-square test for dichotomous variables and binomial logistic regression with hospital day as the independent variable for rates of hyperglycemia. Two-sided P values < .05 were considered significant. SAS version 9.1 (Cary, NC) was used for all analyses.

**RESULTS**

After screening all 785 admissions to the 2 medical teams during the study period, we prospectively identified 109 patients (14%) for the pilot study. Twenty patients were subsequently excluded: 7 patients who were discharged the same day they were identified, 4 who did not have a fasting blood glucose value greater than 140 mg/dL, 4 patients who had type 1 diabetes, 2 patients who were admitted with diabetic ketoacidosis, and 3 patients whose data could not be accessed because of repeated unavailability of the medical record. Characteristics of the remaining 89 study subjects are shown in Table 2 and are compared to 91 baseline subjects. The mean age of the study subjects was 68.7 years; 45% were men. Five patients (6%) did not have a previous diagnosis of diabetes, and 51% were taking insulin prior to admission; the median A1C was 6.8%.

The medical residents agreed, at least in theory, to follow the subcutaneous insulin protocol for 50 patients (56%), partially accepted it for 8 (9%), and declined for 31 (35%). Reasons for declining the protocol included fear of hypoglycemia, severity of patient’s other disease states or overall poor health of patient, concern for the effects of renal insufficiency on insulin clearance, concern for the effect of steroid tapers on glucose levels, desire to titrate oral medications, and anticipation of patient’s imminent discharge. Other reasons such as “the glucose levels are not that bad” and “let’s watch the glucose levels for one more day” suggest that some residents did not view hyperglycemia as an acute problem requiring immediate attention.

Regarding insulin-ordering practices (Table 3), basal insulin was prescribed for 57 patients (64%) in the pilot group compared to 45 patients (49%) in the baseline group (P = .05). Nutritional insulin was prescribed to 12 patients (13%) in the pilot group compared to no patients in the baseline group (P < .001). Oral hypoglycemic agents were prescribed less often in the pilot study than at baseline (20% vs.

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Patient Characteristics*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
<td>Baseline (n = 91)</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>66.0 (14.5)</td>
</tr>
<tr>
<td>Male</td>
<td>53/91 (58%)</td>
</tr>
<tr>
<td>No diagnosis of diabetes at admission</td>
<td>7/91 (8%)</td>
</tr>
<tr>
<td>Prediabetes regimen</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>15/91 (16%)</td>
</tr>
<tr>
<td>Oral medications only</td>
<td>32/91 (35%)</td>
</tr>
<tr>
<td>Insulin</td>
<td>44/91 (48%)</td>
</tr>
<tr>
<td>A1C (IQR)</td>
<td>7.0 (6.0, 8.0)</td>
</tr>
<tr>
<td>Hospital length of stay (days), median (IQR)</td>
<td>5 (3, 7)</td>
</tr>
</tbody>
</table>

*Values in parentheses are percentages of patients, except where noted. SD, standard deviation; IQR, interquartile range.
38%, \( P = .01 \)). The use of a standard default sliding scale from the hospital computer order set was high and was not significantly different in the pilot study compared with that at baseline (93% vs. 90%, \( P = .78 \)). Twenty-four of the 83 patients in the pilot group (29%) received sliding-scale insulin without ever receiving basal or nutritional insulin during hospitalization compared to 45 of 91 patients in the baseline group (49%; \( P = .01 \) for comparison).

Among patients started on basal insulin, 42% (24 of 57) were started after the first full hospital day. The initial basal insulin dose was appropriate according to the protocol (within 20%) in 38 of 57 patients (67%). Only 20 of 61 patients (33%) who had any hypo- or hyperglycemia had any change to their insulin regimen made during days 2 through 7 of their hospitalization on GMS, similar to the rate noted at baseline (36%).

Regarding glucose control (Table 3), the mean percentage of glucose readings per patient greater than 180 mg/dL (SD) was not significantly different in the pilot study compared to baseline (31.6% vs. 29.6%, \( P = .85 \)). Only 20 of 61 patients (33%) who had any hypo- or hyperglycemia had any change to their insulin regimen made during days 2 through 7 of their hospitalization on GMS, similar to the rate noted at baseline (36%).

Patients for whom the resident accepted or partially accepted the protocol had higher use of basal insulin (91% vs. 13%, \( P < .0001 \)), higher use of nutritional insulin (21% vs. 0%, \( P = .01 \)), and more frequent dose adjustments (47% vs. 7%, \( P = .01 \)) compared with patients for whom the resident declined the protocol. However, the rate of hyperglycemia was higher in patients for whom the protocol was accepted or partially accepted than in patients for whom the protocol was declined (37% vs. 20%, \( P = .02 \)).
DISCUSSION

Our subcutaneous insulin protocol focused on increasing the use of basal and nutritional insulin, avoiding the use of sliding-scale insulin by itself, and performing daily insulin adjustments in response to the hypo- or hyperglycemia of general medical inpatients with diabetes or hyperglycemia.

The most notable finding of our pilot study was that residents were resistant to using the protocol, both in general and in its specific recommendations. Despite receiving education about inpatient diabetes control and protocol recommendations from the team pharmacist, and despite being on a hospitalist-run medical service, the residents accepted use of the protocol for only half the eligible patients. Patients who were started on basal insulin were often underdosed or started after the first day of hospitalization, and daily dose adjustments were not consistently made despite persistent hypo- or hyperglycemia. Although the use of nutritional insulin was greater compared with that in the baseline group, it was still only prescribed for 13% of patients. Use of a standard sliding scale from the hospital computer order set was common in the pilot study and similar to that in the baseline group. These results suggest significant resistance to changing the current standard of practice.

Despite this lack of adherence to the protocol, some modest improvements in processes of care were seen. Basal insulin was ordered more often during the pilot study than at baseline, especially over the course of a hospital stay. Nutritional insulin was also ordered more often during the pilot study than at baseline, but was still infrequent. Oral antihyperglycemic agents were ordered less often during the pilot study than at baseline. This demonstrates that use of the protocol may be able to improve process outcomes. However, the modest improvements in process outcomes could have simply been a result of increased awareness and education, not the protocol itself.

Regarding patient outcomes, the overall hyperglycemia rate did not improve in the pilot study.
relative to that at baseline. Importantly, hypoglycemia rates did not increase significantly compared with those at baseline. However, because of the small number of hypoglycemia events, the sample size may not have been sufficient to detect a true difference between groups.

The most likely reason that the protocol did not show an effect on glycemic control was that its recommendations were not adhered to. In turn, this may have been a result of incomplete education, training, and implementation measures and/or inherent problems with the protocol that made its recommendations difficult to follow. Another possibility is that the protocol itself may not have been capable of improving glucose control, even when properly used. However, we do know that resident agreement to use the protocol did lead to higher rates of recommended best practices being carried out, such as basal insulin use and daily insulin dose adjustments, and that use of the protocol was associated with improvements in glucose control over the hospital stay. A larger study with a higher degree of protocol adherence would be better able to evaluate the merits of the protocol itself, as would a randomized controlled trial using instrumental variables to measure treatment efficacy. Another possibility explanation for the lack of effect is that glucose control on admission happened to be worse in the pilot group than in the control group: rates of hyperglycemia on day 1 were 48% in the pilot group compared with 37% in the baseline group (Fig. 1). Also, the decreased use of oral agents in the pilot group, a purposeful change to decrease the risk of hypoglycemia, may have counteracted the beneficial effects of more appropriate insulin use. Finally, there were few patients with poorly controlled diabetes at baseline (18 patients with A1C ≥ 8.0 in the baseline group and 12 such patients in the pilot group), arguably those most likely to benefit.

There is a pressing need to identify protocols that can improve glucose control in the non-ICU inpatient setting and successfully implement these protocols with a minimum of resources and effort. To date, most studies that have improved glucose control in the non-ICU setting have relied on frequent input from diabetologists or nurse-practitioners.¹⁴,¹⁵

The results of this study should be viewed in light of its limitations, including its relatively small sample size (thus limiting our ability to detect possible significant differences between groups) and that it was conducted at a single institution (thus limiting its generalizability). Patients were enrolled on weekdays, so patients admitted and discharged over a weekend or on a holiday may have been missed. Also, because of the nonrandomized design of the study, we cannot exclude the possibility that the improvements noted in the pilot study were a result of the increased education provided or of increased awareness and general improvement in diabetes management over the course of the study. Finally, implementation of the protocol was somewhat labor intensive and required staff support that could be difficult to replicate in other institutions. However, most of the study staff’s effort was necessary either to implement the protocol in the absence of an order set or to evaluate barriers to implementation. Widespread implementation of a protocol with an order set, education, and the use of highly reliable tools should be possible with much less effort and resources. The strengths of this study include its prospective data collection methods, which included rigorous inclusion criteria and collection of detailed clinical data.

Our study findings suggest several approaches to improve care in the future. To combat resistance to change, the American Association of Clinical Endocrinologists strongly recommends that each institution ensure that all its clinicians involved agree about general philosophies of diabetes management.¹⁹ A more expansive, hospital-wide educational and promotional plan may increase the initial acceptance of the protocol. Interviews with residents also indicated there was unfamiliarity with diabetes management and significant concerns about the harmful affects of tight glucose control (ie, risk of hypoglycemia), especially in certain patient subgroups. These results confirmed the need for more practical individualized training and sparked the implementation of small-group, case-based educational sessions on inpatient diabetes management for all house officers, with a particular focus on patients with multiple comorbidities, on steroid tapers, and/or with renal failure.

The lack of nutritional insulin orders, delays in ordering basal insulin, and use of inadequate doses of insulin may be counteracted by the use of an order set, in our case built into our computer physician order entry (CPOE) system. The
use of CPOE also allows reminders to be automatically sent to clinicians if eligible patients are not started on these orders. Clinical inertia (e.g., failure to adjust the insulin doses of specific patients despite hyperglycemia) is more difficult to combat but may be addressed through better organization of clinical data, individualized, case-based education, and CPOE reminders and eventually through culture change.

As a result of our pilot study, additional revisions were made to the protocol in hopes of increasing protocol adherence. For example, for patients eating discrete meals who are not taking insulin at home, the pilot protocol had suggested a starting insulin dose range for basal and nutritional insulin that required 2 separate calculations. The revised protocol was simplified to recommend a total daily insulin dose to be split evenly between basal and nutritional insulin. The daily adjustment instructions were also simplified. The pilot protocol had included a complicated table of adjustment recommendations based on bedside glucose trends. The revised protocol recommends adjusting the new daily dose by adding the total units of insulin given the previous day (including supplemental doses), making minor adjustments for hyper- or hypoglycemia and other clinical factors (like renal failure), and splitting this dose evenly between scheduled basal and nutritional insulin. In addition, 3 order sets were built into our computerized physician order entry system to facilitate early and appropriate insulin orders for patients with different diets (discrete meals, continuous tube feeds, and nothing by mouth); 3 different insulin sliding scales were created for patients with different degrees of insulin resistance; a diabetes management page for our electronic medication administration record is being developed to better organize clinical data; and hospital-wide education and individualized training are ongoing.

In conclusion, the adherence to an inpatient glycemic management protocol that focused on increasing use of basal insulin and performing daily insulin adjustments was only fair. Barriers to successful implementation included clinical inertia regarding individual patients, unfamiliarity with inpatient diabetes management strategies, fear of hypoglycemia, and resistance to changing the current standard of practice. Targeted education, standard order sets, better organization of clinical data, protocol simplification, and institutional culture changes may be necessary for successful protocol implementation and improved inpatient glucose control.

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