ORIGINAL RESEARCH

Inpatient Management of Diabetes and Hyperglycemia Among General Medicine Patients at a Large Teaching Hospital

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BACKGROUND: Because of the relationship between inpatient hyperglycemia and adverse patient outcomes, current guidelines recommend glucose levels less than 180 mg/dL in the non-ICU inpatient setting and the use of effective insulin protocols for appropriate patients.

OBJECTIVE: To determine the current state of glucose management on an academic hospitalist service and the relationship between insulin-ordering practices and glycemic control.

DESIGN: Prospective cohort study.

SETTING: Hospitalist-run general medicine service of an academic teaching hospital.

PATIENTS: 107 consecutive patients with diabetes mellitus or inpatient hyperglycemia.

MEASUREMENTS: We collected data on up to 4 bedside glucose measurements per day, detailed clinical information, and all orders related to glucose management. The primary outcomes were rate of hyperglycemia (glucose > 180 mg/dL) per patient and mean glucose level per patient-day.

RESULTS: The mean rate of hyperglycemia was 31% of measurements per patient. Basal insulin was ordered for 43% of patients, and scheduled rapid- or short-acting insulin was ordered for 4% of patients. Sixty-five percent of patients who had at least 1 episode of hyper- or hypoglycemia had no change made to any insulin order during the first 5 days of the hospitalization. When adjusted for clinical factors, the use of sliding-scale insulin by itself was associated with a 20 mg/dL higher mean glucose level per patient-day.

CONCLUSIONS: Management of diabetes and hyperglycemia on a general medicine service showed several deficiencies in process and outcome. Possible targets for improvement include increased use of basal and nutritional insulin and daily insulin adjustment in response to hyperglycemia. *Journal of Hospital Medicine* **2006;1:145–150.** *© 2006 Society of Hospital Medicine.*

KEYWORDS: diabetes mellitus, hyperglycemia management, outcomes measurement, care standardization.

Diabetes mellitus is a common comorbidity of hospitalization; in 2003 diabetes was a secondary diagnosis in 17.8% of all adult hospital discharges.[1] When undiagnosed diabetes is included, the prevalence of inpatient diabetes or hyperglycemia may be as high as 38%.[2] Recent studies show that hyperglycemia in hospitalized patients complicates numerous illnesses and is an independent predictor of adverse outcomes.[3] Treatment of inpatient hyperglycemia improves outcomes, including mortality, for patients in surgical intensive care units[4] and possibly for those

admitted for myocardial infarction.[5,6] For these reasons, the American Diabetes Association and the American College of Endocrinology now recommend that glucose levels of all patients admitted to non-critical-care units be maintained below 180 mg/dL.[3,7]

Evidence-based recommendations for achieving these goals include "effective protocols" for subcutaneous insulin therapy for patients who do not require continuous intravenous insulin infusion. Components of these protocols include use of basal insulin and scheduled nutritional insulin, avoiding use of supplemental ("sliding-scale") insulin alone (which has been shown to be ineffective and possibly deleterious in prior studies),[8] and adjustment of insulin orders to reflect nutritional intake, insulin sensitivity, and previous response to therapy.[7]

We conducted this study to evaluate the current state of glycemic control and adherence to current recommendations on a general medicine service run by hospitalists in a busy teaching hospital. We also sought to correlate insulin-ordering practices with the quality of glycemic control in these patients.

METHODS
Setting and Participants
This prospective cohort study was conducted at Brigham and Women's Hospital (BWH) from August 1 through September 30, 2004. Eligible subjects were patients admitted to 3 General Medicine Service (GMS) teams with either a known diagnosis of diabetes or inpatient hyperglycemia (random glucose > 200 mg/dL). Patients admitted for diabetic ketoacidosis, hyperosmolar hyperglycemic state, or gestational diabetes were excluded. Members of the BWH/Faulkner Hospitalist Service are the teaching attendings on these 3 teams (each consisting of 2 interns and 1 junior or senior resident) and are the attendings of record for approximately 90% of the patients on these teams. A research assistant identified potential subjects each weekday from the daily computerized sign-out system used by all medical residents by searching for diabetes on the patient summary, a diabetic medication in the automatically abstracted medication list, or a laboratory glucose value greater than 200 mg/dL from automatically abstracted daily laboratory results. Eligibility criteria were confirmed by medical record review, and any question of eligibility was reviewed with the principal investigator. This study

was approved by the BWH Institutional Review Board; patient consent was not deemed necessary for this study given the relatively nonsensitive nature of the data (eg, glucose control, insulin orders), the noninvasive means of collecting it (eg, chart review), and the steps taken by research personnel to minimize any breach in patient confidentiality.

Measurements
We abstracted clinical data on each eligible subject for up to 5 days on GMS. Several data sources were used, including physician admission notes, the hospital's computerized clinical data system, nursing notes, vital sign sheets, the medication administration record, and personal communication with nurses about any missing or discrepant data. Up to 4 routine bedside blood glucose measurements were recorded each day: the measurements taken before meals and at bedtime for patients eating discrete meals or the measurements closest to 6 AM, noon, 6 PM, and midnight for patients not eating or receiving continuous nutrition. Additional measurements were not recorded to avoid ascertainment bias caused by follow-up testing of abnormal glucose values.

Study outcomes included the percentage of glucose readings below 60 mg/dL (hypoglycemia) and greater than 180 mg/dL (hyperglycemia). Use of several types of insulin ordering practices were also recorded: use of basal insulin (ie, long-acting agents such as NPH and insulin glargine), scheduled prandial insulin (eg, regular insulin, insulin lispro, and insulin aspart given before each meal), daily adjustments to insulin orders, use of different insulin sliding scales for patients with different daily insulin requirements, orders to hold or adjust insulin doses in patients not eating, and the percentage of the total daily insulin dose given as basal insulin.

Other patient variables collected were age, sex, weight; medical comorbidities (using a modified Charlson score)[9]; severity of illness (using a simplified APACHE III score)[8]; admission diagnosis; baseline HbA_{1C} (taken at or within 6 months of admission); severe complications of diabetes (blindness, dialysis, renal transplant, amputation due to peripheral vascular disease, vascular bypass surgery); diabetic medications 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, inpatient total parenteral nutrition, and

general nutritional intake (all, most, some, little, or none for each meal).

Statistical Analysis

Characteristics of the study subjects and process and outcome measures were analyzed descriptively using rates, means with standard deviations, and medians with interquartile ranges as appropriate. We also analyzed outcomes by patient-day to determine daily trends during the course of hospitalization. In these analyses, we used the Mantel-Haenszel chi-square test for the dichotomous variables (eg, daily use of any basal insulin) and univariable linear regression with general linear models clustered by patient, that is, repeated-measures analysis, for the continuous variables. We used an arcsin(square-root) transformation for those continuous outcomes that were percentages (eg, percentage of glucose readings > 180 mg/dL) and logarithmic transformation for right-tailed continuous variables (eg, total number of units of insulin administered).

To determine the effects of various insulin-ordering practices on glucose control, we also performed multivariable analysis of mean glucose levels per patient-day. We chose mean glucose rather than rates of specific glucose ranges as the outcome because of the low rate of hypoglycemia and the additional sensitivity of this method. First, univariable analysis was performed using the Student's t test, analysis of variance, or Spearman correlation as appropriate for each predictor. Multiple linear regression models were then constructed, using variables significant in the univariable testing at the $P < .10$ level. Confounding variables that changed beta coefficients by 10% or more were retained, whereas collinear terms were removed by hand; patient age and sex were also retained in the models as *a priori* selected confounding variables.

As with the repeated-measures analysis, we used general linear models, accounting for within-patient clustering, with an exchangeable correlation structure. In addition, standard regression techniques could not be applied to the basal insulin variable because use of basal insulin is a mediator of subsequently lower glucose levels but often is the result of previously elevated glucose levels. Instead, we used a marginal structural model,[10,11] weighting the usual regression analysis to statistically remove the effect of confounding by indication. The weights for this analysis were based on the inverse probability of use of basal insulin, given previous

TABLE 1
Patient Characteristics*

Characteristic	
Age, mean (SD), y	65.2 (14.5)
Male	59/107 (55)
No diagnosis of diabetes at admission	9/107 (8)
Preadmission diabetes medication regimen:	
None	24/106 (22)
Oral medications only	36/106 (34)
Insulin	46/106 (43)
HbA$_{1C}$, median (IQR)	7 (6, 8)
Diabetic complications†	15/107 (14)
Hospital length of stay, median (IQR), d	5 (3, 7)
Charlson score,‡ mean (SD)	5.3 (3.0)
APACHE III score, mean (SD)	36.9 (15.6)

*Values in parentheses are percentage of patients, except where noted. †Blindness, end-stage renal disease, amputation, or vascular bypass surgery. ‡Upper estimate of modified Charlson comorbidity score, on a 0-25 scale.[8] Abbreviations: SD, standard deviation; IQR, interquartile range.

glucose levels and prior use of basal insulin and were estimated from a separate logistic regression analysis. Results were considered significant at $P < .05$ except as noted above. SAS version 8.1 (Cary, NC) was used for all analyses.

RESULTS

We prospectively identified 123 patients for the study. Subsequently, 16 patients were excluded, 11 who did not have diabetes or inpatient hyperglycemia (most of whom had been placed on insulin prophylactically to avoid steroid-induced hyperglycemia), 2 who were admitted for diabetic ketoacidosis, 2 who were not on GMS teams 1-3, and 1 whose data could not be accessed. Characteristics of the remaining 107 study subjects are shown in Table 1. The mean age of the subjects was 65.2 years; 55% were men. Nine patients had no previous diagnosis of diabetes, 43% were taking insulin prior to admission, 14% had severe diabetic complications, and the median HbA$_{1C}$ was 7.

Regarding insulin-ordering practices (Table 2), 47 patients (43%) had basal insulin prescribed, while 4% of patients had an order for scheduled mealtime short- or rapid-acting insulin. Of the 89 patients on sliding-scale insulin, 80 (90%) had orders written for the default sliding scale built into the computerized physician order entry system at BWH. There was no correlation between intensity of the sliding scale and the patient's total daily insulin dose (data not shown). Of the patients on sliding-scale insulin, 47% were prescribed basal in-

TABLE 2
Diabetes Management by Patient*

Measure	
Process	
Any basal insulin during hospitalization	47/107 (43)
Separate nutritional insulin order	4/107 (3.7)
Change in dose to any insulin order during hospitalization if any hyper- or hypoglycemia	26/75 (35)
Standard sliding scale from hospital computer order set	80/89 (90)
Any oral diabetic agents during hospitalization	39/107 (36)
Outcomes	
Any hyperglycemia (glucose > 180 mg/dL)	74/98 (76)
0%-20% of readings	20/98 (20)
20%-40%	19/98 (19)
40%-60%	19/98 (19)
60%-80%	6/98 (6.1)
Greater than 80%	10/98 (10)
Any hypoglycemia (glucose < 60 mg/dL)	11/98 (11)
0%-20% of readings	9/98 (9.2)
20%-40%	2/98 (2.0)

*Values in parentheses are percentages of patients.

sulin, 39% were prescribed oral agents, and 23% were prescribed neither.

Regarding glucose control, 317 of 1022 glucose meter readings (31%) were greater than 180 mg/dL, and the mean rate of glucose readings greater than 180 mg/dL per patient was also 31%. Approximately three quarters of all patients had at least one routine glucose reading greater than 180 mg/dL, and 35% of patients had at least 40% of their routine glucose readings greater than 180 mg/dL (Table 2). Twelve of 1022 readings (1.2%) were less than 60 mg/dL, and 11% of patients had at least one glucose reading less than 60 mg/dL (Table 2).

Despite a relatively constant percentage of glucose readings greater than 180 mg/dL per patient over the first 5 days of hospitalization (25%-36% each day), we found no evidence of change in the percentage of patients prescribed basal insulin or the percentage of insulin given as basal insulin, and there was a small but significant increase in the total amount of insulin prescribed (Table 3). Of the 75 patients with at least one episode of hypo- or hyperglycemia, 43 (57%) were ever prescribed basal insulin, 29 (39%) were prescribed oral diabetes agents, and only 26 (35%) had any change to their insulin regimen during the first 5 days of their hospitalization on GMS. Of the 47 patients prescribed basal insulin in the hospital, 41 had been taking insulin prior to admission.

In a multivariable analysis of the mean glucose reading per patient-day, we found several predictors of lower glucose readings, including diet-controlled diabetes prior to admission and prescription of oral hypoglycemic medications in the hospital. We also found several predictors of higher glucose readings, including severe diabetic complications and higher glucose level at admission. Finally, we noted variation both by medical team (each composed of 1 medical attending, 1 resident, and 2 interns) and by floor of the hospital (each staffed by a different cadre of nurses). Adjusting for these factors (as well as for the daily use of dextrose-containing intravenous fluids and steroids, sex, age, Charlson comorbidity score, APACHE 3 score, prior diagnosis of diabetes, HbA_{1C} level, and length of hospital stay) use of sliding-scale insulin alone (eg, without scheduled basal or nutritional insulin) was associated with a daily average glucose reading that was 20 mg/dL higher than that for those prescribed scheduled insulin or those not prescribed a sliding scale at all (95% confidence interval, 5.0-35 mg/dL; Table 4). In a separate analysis, adjusting for the same clinical factors, we could find no relationship between change in daily dose of basal insulin and change in daily average glucose level (data not shown).

DISCUSSION

In this observational study, we found several deficiencies in the management of diabetes and hyperglycemia among hospitalized patients on a hospitalist-run general medical service. These deficiencies were both in processes of care (eg, limited use of basal and especially nutritional insulin) and in outcomes (ie, glycemic control) compared with national guidelines. We also found evidence of clinical inertia when comparing outpatient to inpatient regimens, when evaluating daily changes in management, and when evaluating responses to previous hyperglycemia. Finally, we demonstrated that use of an insulin sliding scale by itself was associated with worse glycemic control after extensive adjustment for a variety of clinical factors.

Of note, other than the use of sliding-scale insulin by itself, we could not find a relationship between specific daily adjustments to insulin orders and daily glycemic control in this study. However, we did find differences in glycemic control by medical team and by floor (the latter a proxy for nursing staff). This suggests that glycemic control

TABLE 3
Diabetes Management by Hospital Day

	Hospital day					P value for Trend
	1	2	3	4	5	
Number of patients	107	105	85	66	48	
Mean adjusted total daily insulin units*	17	22	23	20	27	0.03
Patients prescribed any basal insulin (%)	29/79 (37)	41/93 (44)	33/74 (45)	27/57 (47)	20/43 (47)	0.18
Mean % of total insulin dose consisting of basal insulin	35	42	38	39	33	0.80
Mean % glucose readings < 60 mg/dL	2	1	1	0	1	0.13
Mean % glucose readings> 180 mg/dL	36	34	29	25	32	0.13

*Adjusted for fraction of day spent in hospital.

Numbers in parentheses are percentages.

TABLE 4
Multivariable Predictors of Mean Glucose per Patient-Day

Characteristic	Effect size (95% CI)*	P value
Sliding scale insulin alone	20 (5.0-35)	0.01
Oral diabetes regimen during hospitalization	− 22 (−41-−3.0)	0.02
Diet-controlled diabetes prior to admission	− 32 (−57-−7.6)	0.01
No prior diagnosis of diabetes	28 (−3.2-60)	0.08
Complications of diabetes[†]	44 (21-67)	< 0.001
HbA$_{1C}$[‡]	−6.1 (−12-0.0073)	0.05
Admission glucose[§]	0.19 (0.067-0.31)	0.002
Medical Team [|]	− 47 (−67-−27)	< 0.001
Hospital Floor[¶]	− 46 (−68-−24)	< 0.001

*Change in mean glucose level per patient-day (in mg/dL).

[†]Any complication vs. no complications.

[‡]Per point (percent) HbA$_{1C}$.

[§]Per milligram per deciliter.

[|] General medicine service (GMS) team 1 vs. GMS team 3 (see text for explanation).

[¶]Floor 14CD vs. not on floor 14 (see text for explanation). Also adjusted for daily use of dextrose-containing intravenous fluids and steroids, sex, age, Charlson comorbidity score, APACHE 3 score, and hospital length of stay.

depends on the exact details of how insulin is managed, rather than on crude measures of insulin adjustment such as change in dose in response to hyperglycemia. These findings also suggest that interventions focused on medical and nursing staff may be able to improve inpatient glycemic control.

The association between the use of oral diabetic agents and improved glucose control was notable and could represent an actual benefit of these agents (especially when added to sliding-scale insulin by itself) and/or the result of uncontrolled confounding (ie, as a marker of well-controlled di-

abetes). Further study is needed to distinguish among these possibilities.

Previous studies have shown evidence of poor inpatient glycemic control as well as the deleterious effects of sliding-scale insulin by itself.[8] This study is perhaps most notable for the suggestion that little, if anything, has changed over the previous decade in this area, despite recent well-done observational and randomized controlled trials demonstrating the hazards of inpatient hyperglycemia and the publication of expert consensus statements on inpatient glucose management. Strategies to improve glucose control have been investigated to a greater extent in intensive care units[12,13] than on general medical wards,[14] perhaps because the strength of evidence is strongest in this setting. Without such strong evidence for general medical patients, factors such as clinician fear of hypoglycemia, clinical inertia, and resistance to institutional change may play predominant roles.

Clinical inertia (ie, recognition of the problem but failure to act)[15] has been demonstrated previously in the outpatient management of diabetes[16,17]; this study provides evidence of the phenomenon in the inpatient setting. Work by Phillips and colleagues[15] has shown that clinical inertia results from at least 3 problems: overestimation of care provided; use of "soft reasons" to avoid intensification of therapy; and lack of education, training, and practice organization aimed at achieving specific goals. All 3 problems likely contribute to clinical inertia in inpatient diabetes management. Revised educational programs; systems for improving care such as reminders, flow sheets, and order

sets; and performance feedback can help address clinical inertia and improve care.[15]

This study should be viewed in light of its limitations, including relatively small sample size, thus limiting our ability to detect other possible significant predictors of glycemic control, and the use of a single institution, thus limiting generalizability. However, recent data from the University Health-System Consortium revealed that our institution was typical of the 37 participating academic medical centers in that study.[18] In addition, only 9 patients were identified without a prior diagnosis of diabetes, raising the possibility that some patients with undiagnosed diabetes were missed in our study. However, our search strategy included a daily review of automatically abstracted laboratory values, making this possibility less likely. Strengths of this study include its prospective data collection methods with rigorous inclusion criteria, collection of detailed clinical data, and use of a novel statistical technique to more accurately assess the complex relationship between insulin use and glycemic control, appropriately adjusting for confounding by indication caused by prior glucose measurements.

Future research should focus on patient, clinician, and system barriers to improving inpatient glycemic management, using the clinical inertia framework as a starting point, and on the creation of insulin protocols that can be used and proven effective in the non-ICU inpatient setting. Also needed are improved measures of the quality of glycemic control, insulin orders, and daily insulin adjustment.

In conclusion, inpatient glycemic management was shown to be in need of improvement. Institutionwide quality improvement efforts should probably target both physician and nursing behavior and should focus on increasing use of basal and nutritional insulin, as proposed in recent guidelines, avoiding use of sliding-scale insulin by itself, and performing daily insulin adjustment in response to previous hypo- or hyperglycemia. Hospitalists can play a major role in these institutionwide quality improvement efforts.

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REFERENCES

1. Agency for Healthcare Research and Quality. HCUPnet, Healthcare Cost and Utilization Project. 8/17/2005. Available at: http://www.ahrq.gov/HCUPnet/. Accessed November 29, 2005.
2. Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab.* 2002;87:978-982.
3. Clement S, Braithwaite SS, Magee MF, et al. Management of diabetes and hyperglycemia in hospitals. *Diabetes Care.* 2004;27:553-597.
4. van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in the critically ill patients. *N Engl J Med.* 2001;345:1359-1367.
5. Malmberg K. Prospective randomised study of intensive insulin treatment on long term survival after acute myocardial infarction in patients with diabetes mellitus. DIGAMI (Diabetes Mellitus, Insulin Glucose Infusion in Acute Myocardial Infarction) Study Group. *Br Med J.* 1997;314:1512-1515.
6. Malmberg K, Ryden L, Wedel H, et al. Intense metabolic control by means of insulin in patients with diabetes mellitus and acute myocardial infarction (DIGAMI 2): effects on mortality and morbidity. *Eur Heart J* 2005;26:650-661.
7. Garber AJ, Moghissi ES, Bransome ED, Jr., et al. American College of Endocrinology position statement on inpatient diabetes and metabolic control. *Endocr Pract.* 2004;10(Suppl2):4-9.
8. Queale WS, Seidler AJ, Brancati FL. Glycemic control and sliding scale insulin use in medical inpatients with diabetes mellitus. *Arch Intern Med.* 1997;157:545-552.
9. Katz JN, Chang LC, Sangha O, Fossel AH, Bates DW. Can comorbidity be measured by questionnaire rather than medical record review? *Med Care.* 1996;34:73-84.
10. Hernan MA, Brumback B, Robins JM. Marginal structural models to estimate the joint causal effect of nonrandomized treatments. *J Am Stat Assoc—App Case Stud.* 2001;96:440-448.
11. Robins JM. Correction for non-compliance in equivalence trials. *Stat Med.* 1998;17:269-302; discussion 87-89.
12. Goldberg PA, Siegel MD, Sherwin RS, et al. Implementation of a safe and effective insulin infusion protocol in a medical intensive care unit. *Diabetes Care.* 2004;27:461-7.
13. Krinsley JS. Effect of an intensive glucose management protocol on the mortality of critically ill adult patients. *Mayo Clin Proc.* 2004;79:992-1000.
14. Baldwin D, Villanueva G, McNutt R, Bhatnagar S. Eliminating inpatient sliding-scale insulin: a reeducation project with medical house staff. *Diabetes Care.* 2005;28:1008-1011.
15. Phillips LS, Branch WT, Cook CB, et al. Clinical inertia. *Ann Intern Med.* 2001;135:825-834.
16. el-Kebbi IM, Ziemer DC, Gallina DL, Dunbar V, Phillips LS. Diabetes in urban African-Americans. XV. Identification of barriers to provider adherence to management protocols. *Diabetes Care.* 1999;22:1617-1620.
17. Grant RW, Cagliero E, Dubey AK, et al. Clinical inertia in the management of type 2 diabetes metabolic risk factors. *Diabet Med.* 2004;21:150-155.
18. University HealthSystem Consortium. Glycemic control 2005 findings and conclusions. Paper presented at Glycemic Control 2005 Knowledge Transfer Meeting. August 19, 2005, Chicago, IL.