Randomized Controlled Trial of Insulin Supplementation for Correction of Bedtime Hyperglycemia in Hospitalized Patients With Type 2 Diabetes

OBJECTIVE
Clinical guidelines recommend point-of-care glucose testing and the use of supplemental doses of rapid-acting insulin before meals and at bedtime for correction of hyperglycemia. The efficacy and safety of this recommendation, however, have not been tested in the hospital setting.

RESEARCH DESIGN AND METHODS
In this open-label, randomized controlled trial, 206 general medicine and surgery patients with type 2 diabetes treated with a basal-bolus regimen were randomized to receive either supplemental insulin (n = 106) at bedtime for blood glucose (BG) >7.8 mmol/L or no supplemental insulin (n = 100) except for BG >19.4 mmol/L. Point-of-care testing was performed before meals, at bedtime, and at 3:00 A.M. The primary outcome was the difference in fasting BG. In addition to the intention-to-treat analysis, an as-treated analysis was performed where the primary outcome was analyzed for only the bedtime BG levels between 7.8 and 19.4 mmol/L.

RESULTS
There were no differences in mean fasting BG for the intention-to-treat (8.8 ± 2.4 vs. 8.6 ± 2.2 mmol/L, P = 0.76) and as-treated (8.9 ± 2.4 vs. 8.8 ± 2.4 mmol/L, P = 0.92) analyses. Only 66% of patients in the supplement and 8% in the no supplement groups received bedtime supplemental insulin. Hypoglycemia (BG <3.9 mmol/L) did not differ between groups for either the intention-to-treat (30% vs. 26%, P = 0.50) or the as-treated (4% vs. 8%, P = 0.37) analysis.

CONCLUSIONS
The use of insulin supplements for correction of bedtime hyperglycemia was not associated with an improvement in glycemic control. We conclude that routine use of bedtime insulin supplementation is not indicated for management of inpatients with type 2 diabetes.

Several observational and randomized controlled trials (RCTs) have shown increased risk of hospital complications, length of stay, and mortality in patients with hyperglycemia and diabetes (1–5). Randomized multicenter trials in medical and surgical patients with type 2 diabetes have shown that treatment with a basal-bolus insulin regimen results in better glycemic control and lower rates of hospital complications.
compared with treatment with supplemental regular insulin for correction of blood glucose (BG) levels (4,6–8). The basal-bolus approach requires subcutaneous administration of basal insulin given once or twice daily in combination with prandial and corrective doses of rapid-acting insulin before each meal (4,9). The use of capillary point-of-care (POC) testing is of great value in assessing glycemic control, detecting hypoglycemia, and guiding daily insulin adjustment in hospitalized patients with diabetes and hyperglycemia (4,10–12).

The Endocrine Society (10) and American Diabetes Association (12) practice guidelines recommend bedside POC testing before meals and at bedtime for most hospitalized patients with diabetes. POC testing provides insights into day-to-day excursions in BG levels, and bedtime BG testing triggers the use of insulin supplements that may result in an increased frequency of hypoglycemia (13). POC testing, however, is labor intensive and expensive, with an estimated annual hospital cost of several hundreds of millions of dollars in the U.S. (14,15). The value of POC testing and use of insulin supplements in particular at bedtime, however, has not been prospectively evaluated in insulin-treated patients with type 2 diabetes. Accordingly, we aimed to determine whether POC testing and the administration of insulin supplementation (correction doses) at bedtime results in improved glycemic control with changes in rates of hypoglycemia in nonintensive care unit (non-ICU) patients with type 2 diabetes treated with a basal-bolus insulin regimen.

**RESEARCH DESIGN AND METHODS**

This randomized controlled prospective study was conducted at Grady Memorial Hospital and Emory University Hospital in Atlanta, Georgia. The study was approved by the Institutional Review Board of Emory University School of Medicine. From May 2012 to December 2013, written informed consent was obtained from patients with acute or chronic medical illness or elective, emergency, or trauma surgeries who were eligible for the study.

**Inclusion/Exclusion Criteria**

Patients were enrolled if they were between the ages of 18 and 80 years, had a known history (>3 months) of type 2 diabetes treated with insulin and/or oral agents, and had an admission BG >7.8 mmol/L (140 mg/dL) but <22.2 mmol/L (400 mg/dL) without evidence of diabetic ketoacidosis (16). Patients were excluded if they were hyperglycemic without a history of diabetes, required admission or were expected to require admission to the intensive care unit (ICU), were receiving continuous insulin infusion, had clinically relevant hepatic disease, were receiving corticosteroid therapy, had a serum creatinine ≥309 μmol/L (3.5 mg/dL) and/or a glomerular filtration rate <30 mL/min/1.73 m², were pregnant, or were unable to give consent.

**Study Protocol**

Medical and surgical problems for all patients in the study were managed by the primary admitting team, and the insulin regimen was managed by the study team. After randomization, all outpatient medications for diabetes were stopped, and patients were treated with a standard basal-bolus insulin regimen with glargine once daily and aspart before meals as previously reported (6,7). In brief, patients treated with insulin at home received 80% of the outpatient total daily dose (TDD). Insulin-naive patients were started on a TDD of 0.4 units/kg/day for BG between 7.8 and 11.1 mmol/L (140–200 mg/dL) and 0.5 units/kg/day for BG between 11.2 and 22.2 mmol/L (201–400 mg/dL). The starting TDD was 0.3 units/kg/day in patients aged ≥70 years or with a serum creatinine ≥177 μmol/L (2.0 mg/dL). One-half of the TDD was given as glargine once daily and one-half as aspart divided into three equal doses before meals. Insulin doses were adjusted daily by the study team to maintain a fasting and predinner BG between 3.9 and 7.8 mmol/L (70–140 mg/dL) (6,7). All patients received supplemental aspart (rapid-acting) insulin before meals for BG >7.8 mmol/L (140 mg/dL) per standard protocol (7).

Patients were randomized either to the group that received bedtime supplemental aspart insulin (supplement) to correct BG levels >7.8 mmol/L (140 mg/dL) or to the group that did not receive bedtime supplemental insulin (no-supplement) except for severe hyperglycemia (BG >19.4 mmol/L [350 mg/dL]). Patients in the supplement group received aspart insulin at bedtime as follows: 1 unit for BG 7.8–10.0 mmol/L (141–180 mg/dL), 2 units for BG 10.0–12.2 mmol/L (181–220 mg/dL), 3 units for BG 12.3–14.4 mmol/L (221–260 mg/dL), 4 units for BG 14.5–16.6 mmol/L (261–300 mg/dL), 5 units for BG 16.7–19.4 mmol/L (301–350 mg/dL), 6 units for BG 19.5–22.2 mmol/L (351–400 mg/dL), and 7 units for BG >22.2 mmol/L (400 mg/dL). Patients in the no-supplement group received supplemental insulin at bedtime for severe hyperglycemia as follows: 6 units for BG 19.5–22.2 mmol/L (351–400 mg/dL) and 7 units for BG >22.2 mmol/L (400 mg/dL).

POC BG levels were measured before each meal, at bedtime, and at 3:00 A.M. Specifically, fasting BGs were defined as POC BG before breakfast. There was no minimum amount of fasting required. If patients were NPO and on intravenous dextrose, we did not require dextrose to be discontinued before fasting BG measurement. For the 3:00 A.M. glucose values, BGs from POC testing or chemistry panel were used in the analysis. Additional BG levels were measured if patients had symptoms of hypoglycemia or if requested by the primary treating physician. Hypoglycemia was defined as POC or serum glucose <3.9 mmol/L (70 mg/dL), and severe hypoglycemia was defined as POC or serum glucose <2.2 mmol/L (40 mg/dL) and treated per standard protocol (7). Study patients were followed for a maximum of 10 days while inpatient, even if their hospital length of stay was longer. Patients were removed from the study if they revoked consent, were discharged in <24 h, were transferred to the ICU, or were started on glucocorticoids.

**Outcomes**

The primary outcome was the difference in mean fasting glucose levels by POC testing before breakfast between the supplement and no-supplement groups. Secondary outcomes were differences between supplement and no-supplement groups in mean BG before lunch, dinner, bedtime, and 3:00 A.M.; mean daily BG and number of patients with BG within target (70–140 mg/dL); number of patients with mild hypoglycemia (BG <3.9 mmol/L [70 mg/dL]), severe hypoglycemia (BG <2.2 mmol/L [40 mg/dL]), and severe hyperglycemia (BG >16.6 mmol/L [300 mg/dL]); total daily dose of insulin; length of hospital stay; mortality; and hospital complications.
(nosocomial infections, pneumonia, bacteremia, respiratory failure, cardiovascular events, and acute renal failure [rise >50% of baseline or creatinine >221 \( \mu \text{mol/L} \) (2.5 mg/dL)]).

**Statistical Analysis**

The primary end point was to assess for differences in mean fasting BG concentration between groups. We set the equivalence margin in our noninferiority hypothesis for comparing treatment effect as 1 mmol/L (18 mg/dL). A BG difference of such magnitude has been reported as nonclinically significant and is typically smaller than significant treatment effects detected in other superiority trials (6,7). Based on previous studies (6,7), we anticipated an SD of mean fasting BG of ~2.8 mmol/L (50 mg/dL). Based on two-sample \( t \) tests or Wilcoxon tests, 100 subjects would be required in each group to achieve a power of 80%. All glycemic end points, such as mean fasting, premeal, and daily BG; basal and rapid-acting insulin doses; and hypoglycemic episodes were calculated starting the day after randomization.

For comparison of the primary outcome, we performed an intention-to-treat and as-treated analysis. The intention-to-treat analysis included all patients randomized to either the supplement or the no-supplement group irrespective of the need for bedtime supplemental insulin. The as-treated analysis was performed because only 66% of the patients randomized to the supplement group received bedtime supplemental insulin. The as-treated analysis compared fasting and 3:00 a.m. BG levels after every episode of bedtime BG between 7.8 and 19.4 mmol/L (140–350 mg/dL) between the supplement and no-supplement groups. We also compared for fasting, 3:00 a.m., bedtime BG levels, hypoglycemia rates between the supplement and no-supplement groups by bedtime BG levels stratified by 5.5 mmol/L (100 mg/dL) intervals starting at >7.8 mmol/L (140 mg/dL). In the no-supplement group, we also compared differences in fasting and 3:00 a.m. BG levels between patients who received bedtime supplemental insulin and those who did not. Additionally, we examined the number of hypoglycemic episodes in each group after bedtime supplemental insulin was given.

Five patients in the no-supplement group deviated from protocol and received supplemental insulin for a bedtime BG <19.4 mmol/L (350 mg/dL). The subset analyses excluding these five patients did not show differences in outcome data from the intention-to-treat analysis; therefore, we reported the intention-to-treat and as-treated analyses without the exclusion of these five patients. Continuous variables were compared by nonparametric Kruskal-Wallis tests. Categorical variables were compared using \( \chi^2 \) or Fisher exact tests. Data are presented as mean ± SD unless otherwise indicated. A two-tailed \( P \) value of 0.05 was considered significant. All statistical analyses were performed using SAS version 9.2 software (SAS Institute Inc., Cary, NC).

**RESULTS**

A total of 250 patient admissions were consented for the study. Fifteen patients did not pass the screening because they were found to have a history of type 1 diabetes (6), had increasing creatinine (1), were discharged in <24 h (6), or revoked consent for any reason (7) before randomization. A total of 235 patients were randomized to the supplement (6) and no-supplement (6) groups. After randomization, 16 patients in the supplement group (revoked consent, 6; discharged <24 h, 10; transferred to the ICU, 6; started total parenteral nutrition, 6) and 13 patients from the no-supplement group (revoked consent, 6; discharged <24 h, 7; started on glucocorticoids, 4) were excluded. A total of 106 patient admissions in the supplement and 100 patient admissions in the no-supplement groups were included in the final intention-to-treat analysis.

Table 1 shows the baseline characteristics of patients in both treatment groups. No significant differences existed among sex, racial distribution, age, BMI, duration of diabetes, length of hospital stay, and duration of study period between the supplement and no-supplement groups. Significantly more patients were admitted to the medicine than to the surgery service in both groups. Diabetes treatment before admission, mean serum creatinine, and glomerular filtration rate were similar in both groups.

Differences in glycemic control, insulin therapy, and clinical outcome for the

| Table 1—Baseline characteristics of study patients |
|-----------------|-----------------|-----------------|
|                | Supplement group \( (n = 106) \) | No-supplement group \( (n = 100) \) | \( P \) value |
| Sex             |                              |                              |              |
| Male            | 60 (57)                     | 54 (54)                      | 0.71         |
| Female          | 46 (43)                     | 46 (46)                      |              |
| Age (years)     | 58 ± 10                     | 57 ± 11                      | 0.53         |
| Race            |                              |                              | 0.38         |
| Black           | 88 (83)                     | 79 (79)                      |              |
| White           | 17 (16)                     | 17 (17)                      |              |
| Other           | 1 (1)                       | 4 (4)                        |              |
| BMI \((\text{kg/m}^2)\) | 33.7 ± 9.0                  | 33.0 ± 8.8                   | 0.60         |
| Body weight \((\text{kg})\) | 99.9 ± 29.1                 | 97.4 ± 25.6                  | 0.73         |
| Diabetes duration \((\text{years})\) | 12 ± 9                     | 10 ± 8                       | 0.12         |
| Admission service |                             |                              | 0.02         |
| Medicine        | 63 (59)                     | 75 (75)                      |              |
| Surgery         | 43 (41)                     | 25 (25)                      |              |
| Hospital length of stay \((\text{days})\) | 7 (4–13)                  | 6 (5–9)                      | 0.50         |
| eGFR \((\text{mL/min/1.73 m}^2)\) | 80 ± 29                    | 82 ± 27                      | 0.55         |
| Serum creatinine \((\mu\text{mol/L} \ [\text{mg/dL}])\) | 106 ± 35 [1.2 ± 0.4]       | 97 ± 35 [1.1 ± 0.4]          | 0.53         |
| Diabetes admission therapy |          |                              | 0.95         |
| Diet alone      | 13 (12)                     | 13 (13)                      |              |
| Oral agents     | 34 (32)                     | 33 (33)                      |              |
| Insulin         | 40 (38)                     | 39 (39)                      |              |
| Insulin and oral agents | 18 (17)         | 14 (14)                      |              |

Data are \( n \)\%, mean ± SD, or median (25th–75th interquartile range). eGFR, estimated glomerular filtration rate.
intention-to-treat analysis are shown in Table 2. There were no differences in hemoglobin A1c, admission BG, and randomization BG between groups (Table 2). We found no differences in mean fasting BG (primary outcome) between patients in the supplement group (8.8 ± 2.4 mmol/L [159 ± 44 mg/dL]) and no-supplement group (8.6 ± 2.2 mmol/L [155 ± 40 mg/dL], P = 0.76) (Table 2). There were no differences in the overall mean daily BG during the study, premeal BG levels, BG before each bedtime BG between groups (Table 2). We found no differences in mean fasting BG between 3.9 and 7.8 mmol/L (70–140 mg/dL) (72% vs. 74%, P = 0.71) or had severe hyperglycemia (BG > 16.6 mmol/L [300 mg/dL]) (Table 2). Mean fasting daily BG levels also did not differ during the study between groups (Fig. 1).

In the as-treated analysis, 96 patients in the supplement group had 302 bedtime BG levels between 7.8 and 19.4 mmol/L (140–350 mg/dL), whereas 93 patients in the no-supplement group had 303 bedtime BG levels between 7.8 and 19.4 mmol/L (140–350 mg/dL). There were no differences between groups for overall fasting BG levels (8.9 ± 2.4 mmol/L [160 ± 43 mg/dL] vs. 8.8 ± 2.2 mmol/L [155 ± 44 mg/dL]) for the supplement vs. no-supplement group, respectively; P = 0.92). 3:00 A.M. BG levels (8.9 ± 2.4 mmol/L [160 ± 44 mg/dL] vs. 9.3 ± 2.8 mmol/L [168 ± 50 mg/dL], respectively; P = 0.19), and bedtime BGs (10.7 ± 1.9 mmol/L [192 ± 34 mg/dL] vs. 10.8 ± 1.7 mmol/L [195 ± 31 mg/dL], respectively; P = 0.41) (Table 3). There were no differences in fasting and 3:00 A.M. BG levels after each bedtime BG between 7.8 and 19.4 mmol/L (140–350 mg/dL) (Table 3).

The average total daily insulin use was 0.4 ± 0.2 units/kg/day in the supplement group and 0.5 ± 0.3 units/kg/day in the no-supplement group (P = 0.31). The daily dose of glargine (P = 0.30) and aspart (P = 0.61) did not differ between groups (Table 2). As expected, significantly more patients in the supplement group received bedtime supplemental insulin than those in the no-supplement group (P < 0.001) (Table 2). However, patients in the no-supplement group received significantly higher doses of supplemental insulin per day at bedtime than those in the supplement group (P = 0.003), as expected (Table 2). Some patients in the supplement group received bedtime supplemental insulin every evening, whereas some patients in the no-supplement group received bedtime supplemental insulin for only 6 days of the study (Supplementary

| Table 2—Glycemic control, insulin therapy, and hospital complications in patients treated with a basal-bolus insulin regimen with and without bedtime insulin supplementation |
|-----------------------------------------------|-----------------|-----------------|-----------------|
| Supplement group (n = 106) | No-supplement group (n = 100) |  |
| Glycemic control | |  |
| Hemoglobin A1c (mmol/mol [%]) | 75 ± 26 [9.0 ± 2.4] | 75 ± 27 [9.0 ± 2.5] | 0.92  |
| Admission BG (mmol/L [mg/dL]) | 11.5 ± 4.2 [207 ± 76] | 11.9 ± 4.2 [215 ± 76] | 0.38  |
| Randomization BG (mmol/L [mg/dL]) | 11.9 ± 3.1 [214 ± 56] | 11.9 ± 3.0 [214 ± 54] | 0.88  |
| Fasting BG (mmol/L [mg/dL]) | 8.8 ± 2.4 [159 ± 44] | 8.6 ± 2.2 [155 ± 40] | 0.76  |
| Prelunch BG (mmol/L [mg/dL]) | 8.8 ± 2.1 [159 ± 38] | 9.2 ± 2.2 [166 ± 40] | 0.36  |
| Predinner BG (mmol/L [mg/dL]) | 7.9 ± 4.2 [142 ± 40] | 8.1 ± 1.7 [146 ± 30] | 0.12  |
| Bedtime BG (mmol/L [mg/dL]) | 9.0 ± 2.2 [163 ± 39] | 9.3 ± 2.2 [167 ± 40] | 0.19  |
| 3:00 A.M. BG (mmol/L [mg/dL]) | 8.7 ± 2.5 [156 ± 45] | 8.8 ± 2.6 [158 ± 46] | 0.69  |
| Daily BG (mmol/L [mg/dL]) | 8.7 ± 1.8 [157 ± 32] | 8.8 ± 1.7 [159 ± 31] | 0.35  |
| Target fasting BG 3.9–7.8 mmol/L | 76 (72) | 74 (74) | 0.71  |
| BG > 16.6 mmol/L | 13 (12) | 19 (19) | 0.49  |
| | |  |
| Insulin therapy | |  |
| Insulin TDD (units/day) | 39 ± 23 | 44 ± 33 | 0.46  |
| Glargine dose (units/kg/day) | 0.3 ± 0.1 | 0.3 ± 0.2 | 0.30  |
| Aspart dose (units/kg/day) | 0.2 ± 0.1 | 0.2 ± 0.2 | 0.61  |
| Supplemental insulin dose (units/day) | 6 ± 3 | 6 ± 4 | 0.79  |
| Received bedtime supplement | 70 (66) | 8 (8) | <0.001  |
| Bedtime supplemental insulin dose (units/day) | 2 ± 1 | 4 ± 3 | 0.003  |
| | |  |
| Hospital complications | |  |
| Pneumonia | 1 (1) | 0 (0) | 1.00  |
| Acute kidney injury | 4 (4) | 4 (4) | 1.00  |
| Cardiovascular event | 3 (3) | 1 (1) | 0.62  |
| Respiratory failure | 1 (1) | 0 (0) | 1.00  |
| Nosocomial infection | 0 (0) | 0 (0) | N/A  |
| Other complications | 4 (4) | 4 (4) | 1.00  |
| | |  |
| Hypoglycemic events | |  |
| Any BG < 2.2 mmol/L | 0 (0) | 1 (1) | 0.49  |
| Any BG < 3.9 mmol/L | 32 (30) | 26 (26) | 0.50  |
| Fasting BG < 3.9 mmol/L | 9 (8) | 11 (11) | 0.64  |
| 3:00 A.M. BG < 3.9 mmol/L | 7 (7) | 3 (3) | 0.33  |
| Bedtime BG < 3.9 mmol/L | 9 (8) | 7 (7) | 0.80  |

Data are mean ± SD or n (%). All data are calculated beginning the day after randomization. BG SI unit conversion from mmol/L to mg/dL: 2.2 mmol/L = 40 mg/dL, 3.9 mmol/L = 70 mg/dL, 7.8 mmol/L = 140 mg/dL, 16.6 mmol/L = 300 mg/dL. N/A, not applicable; randomization BG, glucose level at the time of obtaining consent and inclusion in the study.
In the subset analyses where bedtime BG levels were stratified by 5.5 mmol/L (100 mg/dL) intervals starting at >7.8 mmol/L (140 mg/dL), there were no differences in glycemic control, hypoglycemia rates, or insulin dose requirements between the supplement and no-supplement groups (data not shown). In the no-supplement group, there were no differences in fasting (P = 0.56) or 3:00 a.m. BG (P = 0.27) in patients who received bedtime insulin supplementation compared with those who did not. Protocol violations were reported in five patients in the no-supplement group. They received 2–4 units of bedtime supplemental insulin for BG ≤ 19.4 mmol/L (350 mg/dL). An analysis excluding these five patients also did not show differences between the groups in glycemic control, hypoglycemia rates, or insulin dose requirements (data not shown), indicating that the lack of difference in insulin doses and in glycemic control in the intention-to-treat analysis was not confounded by the five patients with protocol violations.

CONCLUSIONS

This prospective RCT compared the clinical efficacy and safety of POC testing and insulin supplementation at bedtime in non-ICU medical and surgical patients with type 2 diabetes. The results indicate that administration of bedtime insulin supplementation to correct mild to moderate hyperglycemia in patients treated with a basal-bolus regimen was not associated with significant improvement in glycemic control. Furthermore, no differences were found between groups in the frequency of hypoglycemic episodes, length of hospital stay, or hospital complications. These results do not support current guidelines for treatment of BG >140 mg/dL at bedtime with supplemental insulin (10–12).

The study highlights the importance of performing POC testing in the recognition of hypoglycemia before meals and at bedtime. In agreement with previous studies (6,7,17), we showed that the use of a basal-bolus insulin regimen is associated with a 20%–30% rate of mild hypoglycemia. In the intention-to-treat analysis, 30% of patients receiving supplemental insulin and 26% receiving no supplement experienced a BG <3.9 mmol/L (70 mg/dL) (P = 0.50), and only one patient experienced a BG <2.2 mmol/L (40 mg/dL). Of interest, ~75% of patients with hypoglycemia in both groups experienced hypoglycemic episodes between dinner time and early morning, irrespective of receiving a bedtime supplement. These results are slightly higher than the those from POC testing at other institutions, where ~60%–70% of hypoglycemic episodes occurred between 9:00 p.m. and 9:00 a.m. (18–20). Although the current study was not powered to detect differences in hypoglycemia, the results show that POC testing at bedtime is a useful tool to identify patients with hypoglycemia. Minimizing the rate of hypoglycemic events is of major importance in hospitalized patients because it has been shown to be an independent risk factor of poor outcome (17,21).

The administration of supplements or correction doses of insulin before meals represents the standard of care in the basal-bolus regimen (4,9). This recommendation comes from an expert consensus panel, and no previous RCTs have evaluated the safety and efficacy of correcting mild hyperglycemia before meals and bedtime. The total dose of insulin supplements is small, ranging from 6 to 12 units/day in previous RCTs in non-ICU settings (6,7,22,23). In the current study, the total daily supplemental insulin dose in patients with hyperglycemia was 6 ± 3 units/day with ~2 units at bedtime. Because there were no differences in any of the glycemic outcomes, it is likely that such small amounts of insulin supplementation at bedtime did not influence glucose control or clinical outcomes. Future RCTs should study the safety and efficacy of the use of supplements before each meal for patients with mild-moderate hyperglycemia. It is possible that avoiding insulin supplements to correct mild-moderate hyperglycemia may reduce the risk of hypoglycemic events, number of insulin injections, nursing labor, and risk of medication errors.

We recognize several limitations in the study, including a relatively small number of patients recruited and the fact that the study was conducted in a single academic institution, albeit in two separate hospitals. We excluded patients with clinically relevant hepatic disease or with serum creatinine ≥309 µmol/L (3.5 mg/dL), patients with severe hyperglycemia, and patients requiring ICU care. We treated all patients with a
Data are mean ± SD. The 3 A.M. and fasting BG levels reflect those after receiving a bedtime supplement in response to bedtime BG levels the previous day of the study. N/A, not applicable.

| Group | Day 4 BG (mmol/L [mg/dL]) | Day 3 BG (mmol/L [mg/dL]) | Day 2 BG (mmol/L [mg/dL]) | Day 1 BG (mmol/L [mg/dL]) | Average BG (mmol/L [mg/dL]) |
|-------|---------------------------|---------------------------|---------------------------|---------------------------|-----------------------------|
| No-supplement | 8.8 ± 0.9 | 9.0 ± 0.8 | 8.8 ± 0.8 | 11.3 ± 0.8 | 9.1 ± 0.9 |
| Supplement | 9.1 ± 0.8 | 9.1 ± 0.9 | 9.2 ± 0.9 | 11.4 ± 0.9 | 9.5 ± 1.0 |

Table 3: Fasting and 3:00 a.m. BG levels in patients with bedtime BG levels between 7.8 and 19.4 mmol/L (140-350 mg/dL).
basal-bolus regimen; thus, the results may not be generalizable to patients treated with other regimens. Only 66% in the supplement group received any bedtime supplemental insulin, which may have affected the comparison of fasting BG levels. However, when we analyzed the primary outcome for only when bedtime BG levels were between 7.8 and 19.4 mmol/L (140–350 mg/dL), there were no differences in fasting or 3:00 A.M. levels. In addition, the study was not powered to determine differences in hospital complications or to detect differences in hypoglycemia across treatment groups. We also did not require a minimum number of hours of fasting or discontinuation of intravenous dextrose or note whether patients had a bedtime snack before measurement of fasting BG; therefore, these may have affected the rates of hypoglycemia and fasting BG levels.

In summary, this study challenges current clinical guidelines for the management of inpatient hyperglycemia in non-ICU settings, which recommend bedtime insulin supplementation to correct mild-moderate hyperglycemia (10,11). The study indicates that in general medicine and surgery patients with type 2 diabetes placed on a basal-bolus insulin regimen, the routine use of bedtime insulin supplementation for treatment of mild-moderate hyperglycemia may not be necessary. POC testing at bedtime, 3:00 A.M., and breakfast, however, is necessary to identify patients with hypoglycemia. Eliminating the routine use of bedtime insulin supplementation may have the potential to simplify glycemic control for patients with mild-moderate bedtime hyperglycemia in the inpatient setting.

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