Evaluation of Insulin Use and Hypoglycemia in Hospitalized Elderly Patients

Hospital Pharmacy
2017, Vol. 52(11) 761–765
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DOI: 10.1177/0018578717735974
journals.sagepub.com/home/hpx

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Abstract

Background: Routine administration of correctional insulin is no longer recommended as a primary strategy to treat hyperglycemia in hospitalized patients. Studies have demonstrated significant improvement in glycemic control in patients treated with basal and correctional insulin (B+C) versus correctional insulin alone (C). However, the effect of C or B+C on hypoglycemic events is not well understood. **Objective:** The objective of this study was to investigate the effect of B+C versus C on hypoglycemic events in hospitalized elderly patients. **Methods:** A single-center retrospective review of patients at least 65 years old that were admitted between April and July 2016, who were prescribed any type of insulin. Exclusion criteria included admission to the intensive care unit (ICU) on hospital admission, history of hypersensitivity to insulin, or insulin use for the management of hyperkalemia. Patients were divided based on the insulin regimen prescribed, B+C or C. The primary outcome of the study was the incidence of hypoglycemic episodes between groups. Secondary outcomes included severity of hypoglycemia, hospital length of stay (LOS), hospital mortality, and ICU transfer. Hypoglycemia was defined as a blood glucose level less than 70 mg/dL. **Results:** A total of 709 patients were included, with 144 (20.3%) prescribed B+C and 565 (79.7%) prescribed C. Incidence of hypoglycemia was greater in the B+C group than C (29.1% vs 12.6%, $p=0.012$). The average blood glucose readings during hypoglycemic episodes between B+C and C were 50 mg/dL and 52.5 mg/dL, respectively ($p<0.01$). There was no difference observed in hospital LOS. No patients required ICU admission within 24 hours of a hypoglycemic event or died during the index hospitalization. **Conclusion:** There is a higher incidence of hypoglycemia in elderly patients prescribed basal plus correctional insulin than correctional insulin alone.

Keywords

drug/medical use evaluation, gastrointestinal disorders, geriatrics, metabolic/endocrine

Introduction

Although there are several insulin management systems that have been developed, none has been as widely used as the sliding scale insulin (SSI).¹ According to the American Diabetes Association (ADA), the use of correctional or SSI alone in the inpatient hospital setting is strongly discouraged. For noncritically ill patients, basal plus correctional insulin is the preferred treatment regimen for patients with or without diabetes who are not taking anything orally or who have poor oral intake. The preferred regimen for noncritically ill patients with good nutritional intake is an insulin regimen having basal, nutritional, and correctional components.²

Guidelines and literature have specific comments about insulin management for diabetic hospitalized patients³; however, outcomes in all hospitalized patients are not as well

understood. Recommendations for blood glucose control are based on a limited number of studies, primarily in intensive care units (ICUs); results from these studies have been extrapolated for non-ICU patients.^{2–4} It has been found that SSI, which has traditionally been used in the hospital setting, is not appropriate for glucose management as it can lead to rapid changes in blood glucose concentrations. Managing blood glucose concentrations should be done by mimicking

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normal physiologic patterns and using a combination of human insulin and insulin analogues.⁵

In addition to evidence showing the ineffectiveness of SSI in controlling blood glucose concentrations, there are several problems associated with this regimen. The regimen typically results in an increase in the number of insulin injections received, allocation of resources for frequent medication administration, and insulin is given retrospectively for high blood glucose values and not given during euglycemia or before anticipated hyperglycemia attributable to concurrent or planned meals.⁶⁻¹⁰ Patients are often awakened during the night for blood glucose monitoring and insulin therapy, which may increase the incidence of nocturnal hypoglycemia. In addition, there is no standard SSI regimen, and dosages vary widely between providers and institutions.^{11,12} Furthermore, some evidence suggested that SSI regimens carry additional risk of glycemic events instead of protecting against them as studies have shown that not only has SSI been associated with an increase in hyperglycemia and hypoglycemia, but they have also been associated with an increased length of stay (LOS) for hospitalized diabetic patients.^{8,10,13,14} Similar to hyperglycemia, hypoglycemia poses significant burdens to the health care system. Numerous studies have reported the adverse effects of hypoglycemia and health-related quality of life and treatment satisfaction.¹⁵⁻¹⁹ A cohort study of more than 80,000 outpatients 66 years of age and older with and without diabetes found that hypoglycemia was associated with a 2.6-fold relative increase in mortality, a 72% increase in subsequent all-cause hospitalizations, and a 180% increase in suffering another episode of hypoglycemia requiring hospitalization.²⁰

However, there are limited data showing the direct correlation between the use of SSI (correctional insulin) and incidence of hypoglycemia in hospitalized elderly patients. Therefore, the purpose of this study was to investigate the effect of the use of basal and correctional insulin (B+C) versus the use of correctional insulin alone (C) on hypoglycemic events in hospitalized elderly patients. We hypothesized that all older patients hospitalized with or without diabetes who were treated with B+C will have fewer hypoglycemic events compared with those who were treated with C.

Methods

This was a single-center retrospective cohort study performed at a 691-bed community teaching hospital. The study was approved by the institutional review board, and informed consent was waived. Adult patients who were 65 years or older, prescribed any type of insulin between April 1, 2016, and June 30, 2016, were included. Patients were excluded if they were admitted to the ICU on arrival to the hospital, if they had history of hypersensitivity to insulin, or if they received insulin only for the management of hyperkalemia. Patients were divided based on the

insulin regimen prescribed, B+C or C. The primary outcome of the study was the comparative incidence of hypoglycemic events between groups. Secondary outcomes were the comparative severity of hypoglycemia, which was defined as the average blood glucose readings during the hypoglycemic events, (1) between B+C and C groups and (2) between patients who were 65 to 79 years and patients who were 80 years and older. Other secondary outcomes included LOS, hospital mortality, and need for transfer to an ICU within 24 hours of experiencing a hypoglycemic incidence.

In this study, hypoglycemia was defined as a blood glucose level of less than 70 mg/dL as stated in our institutional hypoglycemic protocol as well as the definition used by the ADA.² Basal insulin was defined as the insulin needed to maintain good glucose control without taking into account eating any food. Correctional insulin, also called SSI, was defined as the dose of insulin given based on obtained capillary blood glucose measurements. The regimen consists of short-acting insulin given 4 to 6 times per day, or prior to meals and at bedtime.

Comparisons between the B+C group and the C group were performed using the chi-square test for categorical variables and the Student *t* test for continuous variables. A *P* value less than or equal to .05 was considered statistically significant.

Results

A total of 940 patients were identified as having orders for insulin during the study period and 231 patients were excluded. The majority of the patients who were excluded were admitted to the ICU on arrival to the hospital, while others were excluded due to insulin received for hyperkalemia management or basal insulin alone was prescribed. Seven hundred nine patients were included in primary analysis, with 144 prescribed B+C and 565 prescribed C. The patient demographics and baseline clinical characteristics are shown in Table 1. There were more patients with type II diabetes mellitus in the B+C group and more patients without diabetes in group C.

More patients in the B+C group experienced an incidence of hypoglycemia compared with those who were in the C group (20.1% vs 12.6%, *P* = .012). There was also a statistically significant difference in the average low blood glucose reading in comparison between the B+C vs the C groups (50 mg/dL vs 52.5 mg/dL, *P* = .00075). Patients in the B+C group experienced greater glucose variability than the patients in the C group (Figure 1).

There was no statistically significant difference in the average hypoglycemic readings between patients who were younger versus patients 80 years old and older (52 mg/dL vs 51.5 mg/dL, *P* = .683). The hospital LOS was also similar between group B+C and group C (7.7 days vs 7 days, *P* = .074). No mortality resulted from hypoglycemic events

Table 1. Baseline Patient Characteristics.

Characteristics	B + C (n = 144)	C (n = 565)	P value
Age, years, mean ($\pm$ SD)	72.8 ($\pm$ 6.6)	75.3 ($\pm$ 7.4)	.097
Male sex, n (%)	75 (52.1)	257 (45.5)	.079
Caucasian, n (%)	75 (52.1)	299 (52.9)	.761
African American, n (%)	68 (47.2)	258 (45.7)	
Other race, n (%)	1 (0.7)	8 (1.4)	
Weight, kg, mean ($\pm$ SD)	71 ($\pm$ 20)	84 ($\pm$ 25)	.001
Parenteral nutrition received, n (%)	4 (2.8)	6 (1.1)	.079
T1DM, n (%)	0	2 (0.4)	.635
T2DM, n (%)	123 (85.4)	371 (65.7)	.000001
Nondiabetic, n (%)	21 (14.6)	192 (34.0)	.000002
Other DM maintenance medications, n (%)	30 (20.8)	119 (21.1)	.481

Note. B + C = basal + correctional insulin; C = correctional insulin; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus; DM = diabetes mellitus.

Figure 1. Box plot of the individual serum glucose readings.

Note. B + C = basal + correctional insulin; C = correctional insulin.

and no patients were transferred to the ICU within 24 hours of a hypoglycemic event.

Discussion

Spontaneous and insulin-related hypoglycemia are common among diabetic and nondiabetic hospitalized patients. The prevalence of hypoglycemia based on a blood glucose value of <70 mg/dL varies between 3.5% and 11% among noncritically ill patients.^{15,16,21,22} The ADA recommends initiating insulin therapy for treatment of persistent hyperglycemia starting at a threshold of 180 mg/dL and higher, aiming at a target glucose range of 140 to 180 mg/dL for critically and noncritically ill patients.² However, in-hospital insulin therapy is associated with an increased risk of hypoglycemia. Hypoglycemia is associated with several complications, including neurologic and ischemic events, longer hospital stay, and an increased mortality risk.¹⁵⁻¹⁹ It is reported that patients with any blood glucose value of <70 mg/dL had 7% higher odds of in-hospital mortality compared with patients

without hypoglycemia.¹⁸ In our present study, we attempted to determine the relationship between patients who were ordered B+C or C and the incidence of hypoglycemia in elderly patients.

For our primary objective, patients in the C group had a lower overall incidence of hypoglycemic events and also had a less severe hypoglycemic reading. For our secondary objectives, the difference in the severity of hypoglycemia was not clinically relevant as it was merely a 2.5 mg/dL difference. The prescription of B+C did not affect patients differently as compared with the prescription of C alone with regard to the average hypoglycemic readings, hospital mortality rate, need for transfer to an ICU, and hospital LOS. These findings could be explained by the fact that the number of patients without any history of diabetes is more than double in the C group in comparison with the B+C group (34% vs 15%, respectively). Those patients with history of diabetes could have been accustomed to the insulin administration and have a better response overall. This study also did not take into account other factors that could have

impacted the incidence of hypoglycemia, such as nutritional status and other concurrent medication administration. In accordance with previous studies, in our cohort, 14.1% of the noncritically ill patients treated with any type of insulin had at least one episode of hypoglycemia. Umpierrez et al. reported that 23% of surgical patients with diabetes mellitus who received a basal-bolus insulin regimen developed hypoglycemia.²³ Furthermore, Farrokhi et al. reported that 19% of noncritically ill medical patients with diabetes mellitus developed mild hypoglycemia (<70 mg/dL) overall while receiving either basal-bolus regimen or SSI regimen.²⁴

This study has several limitations. First, the retrospective design has inherent limitations including the assumption that documentation in the medical record was complete and accurate. Another limitation is that we did not have information about the temporal relation between insulin injection and hypoglycemic event. A further limitation is that other noninsulin antidiabetic medications were not specifically analyzed although they possess different risks for hypoglycemia. In addition, it was unclear whether these patients were controlled on insulin prior to indexed hospitalization. Data regarding patient's nutritional status, for example, whether patients were kept "nothing by mouth" or received tube feeding, were not assessed. Data on patients received parenteral nutrition were reported; however, information on whether insulin was added to the formulation was not available. Moreover, patients were included in the study as long as they had insulin orders that met the inclusion criteria; we did not further evaluate whether they actually received the insulin order. Although this was a significant limitation of our study, it is a reflection of real world practice and represents a common issue with inpatient SSI orders. Depending on the glycemic threshold for SSI initiation, some patients may not receive any insulin for prolonged periods, while nursing is also allowed to make clinical judgment to withhold insulin administration. The number of times when correctional insulin was given was also not collected between the 2 groups. The blood glucose readings collected were not distinguished between point of care fingerstick result and from a laboratory result. Last, the inclusion of patients with and without diabetes could confound our findings. However, the authors feel this better represents standard practice and improves the generalizability of the results.

Conclusion

Hypoglycemic events were more common in hospitalized elderly patients ordered B+C than those ordered C. Although the combination of basal and correctional insulin is preferred by several guidelines in the management of hyperglycemia, the use of C continues to be a common practice in hospitalized patients.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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