

# Hypoglycemia Prevention in Hospital Patients: A Quality Improvement Project to Prevent Severe and Recurrent Hypoglycemia

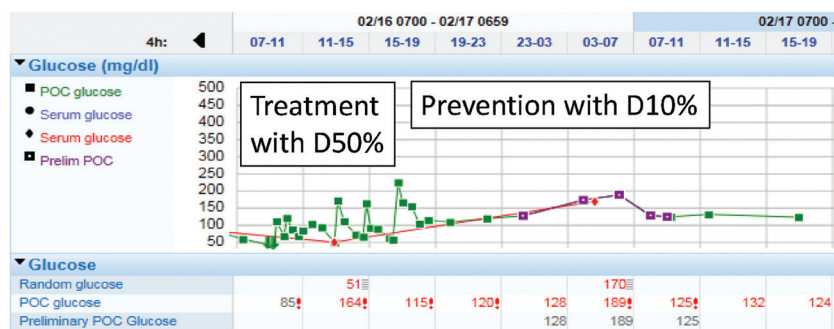
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Hypoglycemia, defined as a blood glucose level  $<70$  mg/dL (3.9 mmol/L), occurs frequently in hospitalized patients. Both inpatient and outpatient trials have shown that the risk of hypoglycemia limits the achievement of blood glucose control (1–7). In addition to causing distress for patients, severe hypoglycemia is associated with cardiac arrhythmias, cardiac ischemia, seizures, brain damage, and death (3,4,8–12). After a hypoglycemic event, the likelihood of further episodes of low blood glucose is increased (2,9,12,13).

Glycemic variability is also independently associated with risk of mortality (5–9,12,14,15) and can be an unintended consequence of reactive treatment of hypoglycemia. If dextrose is given only in response to low blood glucose levels, but the precipitating factor for hypoglycemia persists, a cycle of recurrent low glucose levels alternating with

higher post-treatment levels occurs. Fortunately, this pattern represents a modifiable risk, as illustrated in Figure 1 (14).

Recent advances in health care quality and patient safety call for a change from reactive to preventive care. When this concept is applied to hypoglycemia management, it is evident that the unevaluated assumption that reactive treatment of hypoglycemia is sufficient often underlies facility routines. Avoiding circumstances that are frequently associated with low blood glucose levels is at the core of optimal glycemic management in the inpatient setting. Recent studies show that “safe and effective glucose control” (15) can be facilitated and hypoglycemia can be prevented through tactics such as appropriate monitoring, ensuring adequate caloric intake, coordinating the timing and amount of insulin given with carbohydrate intake, and



**FIGURE 1.** Recurrent hypoglycemia: treatment versus prevention. Initially hypoglycemia was treated reactively, with at least five recurrences of low blood glucose and high glycemic variability. With initiation of proactive IV dextrose, further hypoglycemia was prevented, and glycemic variability was reduced.

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using basal-bolus insulin rather than oral antidiabetic medications in the hospital (1,5,15–17).

The occurrence of hypoglycemic events and glycemic variability can also be reduced by altering the focus from reactive treatment of each low blood glucose as if it were a separate incident to proactive measures to prevent further hypoglycemia in patients with ongoing risk (15,16). Research shows that change in routines is most likely to be successful when it is protocol driven (7).

### Intended Improvements

The goal of this performance improvement project was to improve patient safety by addressing actions that increase the risk of hypoglycemia or increase blood glucose variability. Instead of epidemiological assessment or metrics such as the percentage of patient-days with hypoglycemia, a case-based approach was used for the initial and follow-up assessments. Because hypoglycemia risk cannot be completely eliminated, this article presents a protocol that was developed to reduce the incidence of recurrent hypoglycemia in patients with ongoing risk. The objectives of the project were to 1) identify rates and frequent causes of hypoglycemia in our facility, 2) develop and implement interventions to mitigate the risk of low blood glucose, and 3) determine the impact of interventions through follow-up assessment of rates and causes of hypoglycemia.

### Methods

#### Setting

The diabetes committee chose a blood glucose value  $<50$  mg/dL (2.8 mmol/L) as the threshold for severe hypoglycemia because this level is associated with neurological changes (2) and acute cardiac events, including cardiac arrhythmia (3,8,10). The investigator examined low blood glucose values from patients  $\geq 14$  years of age, including patients both with and without known diabetes. The values assessed were those of facility

inpatients, but hypoglycemic values from the emergency department and pre-surgical area were included in the count of associated hypoglycemic events in 2014 if they were linked to an event of inpatient hypoglycemia in patients subsequently admitted to the hospital.

#### Data Sources

The data for venous and point-of-care blood glucose test results were automatically recorded in the facility's laboratory. A laboratory informatics specialist provided the investigator with a daily report summarizing data for all blood glucose values  $<70$  mg/dL (3.9 mmol/L) collected the previous day. The information included a patient identifier, location, blood glucose value, date, time, and whether the value was downloaded from a glucose meter or obtained through the laboratory.

#### Initial Retrospective Examination

The initial retrospective examination of hypoglycemic events took place in 2009. Ninety-three sequential blood glucose values  $<50$  mg/dL (2.8 mmol/L) in patients who were admitted as inpatients during a 23-day period were initially assessed. These blood glucose values were found to be associated with 59 patient events. An event was defined as an initial blood glucose value  $<50$  mg/dL (2.8 mmol/L) and all further low blood glucose values associated with it during the same time period and with the same precipitating factor. A checklist of precipitating factors that lead to hypoglycemia, derived from literature (1,6,16,18) and from experience in inpatient diabetes management, was used to document the most likely primary and contributory factors for the occurrence of hypoglycemia. The information taken into account included provider medication orders and nurse documentation of the dose and timing of administration of insulin, steroids, and other diabetes medications. Laboratory results, including assessments of renal and hepatic function, were reviewed, along with nurse

and provider notes. Assessment took into account patient age, sex, location in the hospital, admitting and managing provider group, severity and timing of hypoglycemic values, diabetes status and type, home diabetes medications, A1C if available, weight, height, BMI, and comorbidities.

#### Development and Implementation of Protocol and Education

When the diabetes committee reviewed the summary of the frequency of and precipitating factors leading to hypoglycemia, one response was to explore strategies to prevent further hypoglycemia in patients with ongoing risk, made evident by the recurrence of blood glucose values  $<70$  mg/dL (3.9 mmol/L) after treatment of an initial episode. This led to the development of a protocol that provided proactive carbohydrates by a standardized process, with appropriately scheduled re-assessment of blood glucose and nurse-driven adjustments. When intravenous (IV) dextrose was used, the instructions included a rapid, stepwise increase in the rate of dextrose-containing IV fluid to maintain blood glucose levels in the goal range of 100–150 mg/dL (5.5–8.3 mmol/L), instructions for titrating the rate down when blood glucose was above goal, and ultimately orders to discontinue treatment when 2-hour blood glucose checks remained within the goal range with no IV dextrose for 4 hours (Table 1). In addition, providers and nurses received education about management options shown to be associated with increased hypoglycemia risk and about safer alternatives.

After the protocol had been optimized and educational tools honed in the pilot, the protocol was made available throughout the hospital, again accompanied by provider and nurse education. Copies of the paper protocol were placed in all nursing units, to be initiated when hypoglycemia recurred at the routine 30-minute blood glucose recheck

**TABLE 1. Hypoglycemia Prevention Protocol for Nonpregnant Adults**

**1. Hypoglycemia Treatment:**

If blood glucose (BG) is <70 mg/dL (3.9 mmol/L):

- Give 12–15 g quick-acting carbohydrate (15 g glucose gel or 120 mL juice or 120 mL nondiet soda) or 25 mL dextrose 50% IV.
- Recheck every 15 minutes until BG is ≥70 mg/dL (3.9 mmol/L) x 2 checks. Treat any BG <70 mg/dL (3.9 mmol/L).
- When BG is ≥70 mg/dL (3.9 mmol/L) x 2, recheck BG every 30 minutes x 2 to assure patient is stable.
- Document on the diabetic record.

**2. Hypoglycemia Prevention:**

If hypoglycemia recurs at the 30-minute BG recheck or within 6 hours, **treat** the low blood glucose and begin management to **prevent** further hypoglycemia as follows:

A. If patient is able to eat and drink:

- If BG is <100 mg/dL (5.5 mmol/L), give additional 4 oz (120 mL) of juice or a 15-g carbohydrate snack (1/2 sandwich or 240 mL milk or 180 mL yogurt), and document on the diabetic record. Recheck BG in 1 hour.
- If BG remains ≥100 mg/dL (5.5 mmol/L), recheck BG in 2 hours.
- Continue checking BG until 2-hour BG checks remain ≥100 mg/dL (5.5 mmol/L) with no interventions x 2 checks.
- When stable with no interventions x 2, restart BG checks before meals, at bedtime, and at 4:00 a.m.

B. If patient is NPO status or unwilling to take nutrition by mouth, check IV hypoglycemia prevention option below per provider instructions:

- Begin dextrose 10% IV or dextrose 50% IV per provider instructions (see options 1 and 2 below).
- Recheck BG and titrate IV dextrose per appropriate table below.
- Continue to adjust until repeated 2-hour BG checks remain ≥100 mg/dL (5.5 mmol/L) with no intervention (i.e., no IV dextrose) x 2 checks, and then initiate BG checks per section C below.

**Option 1. Dextrose 10% IV (Routine)**

- Begin dextrose 10% IV at 50 mL/hour

**Option 2. Dextrose 50% IV (Fluid or Free Water Restriction)**

- Starting bolus: 10 mL dextrose 50%

| DEXTROSE 10% MAINTAINING NORMAL BG |   |                |
|------------------------------------|---|----------------|
| BG (mg/dL [mmol/L])                | Dextrose 10% IV Titration   | Recheck BG in: |
| <70 (<3.9)                         | Give 25 mL dextrose 50%<br>and<br>↑Rate of dextrose 10% by 50 mL/hour | 15 min x 2     |
| 70–99 (3.9–5.4)                    | ↑Rate by 50 mL/hour   | 1 hour         |
| 100–150 (5.5–8.3): goal            | Continue same rate  | 2 hour         |
| 151–180 (8.4–9.9)                  | ↓Rate by 50 mL/hour   | 2 hour         |
| >180 (>9.9)                        | ↓Rate to 0 mL/hour  | 2 hour         |

| DEXTROSE 50% MAINTAINING NORMAL BG |  |                |
|------------------------------------|--|----------------|
| BG (mg/dL [mmol/L])                | Dextrose 50% IV Bolus Titration                        | Recheck BG in: |
| >70 (>3.9)                         | Give 25 mL dextrose 50%<br>and<br>↑Bolus dose by 10 mL | 15 min x 2     |
| 70–99 (3.9–5.4)                    | ↑Bolus dose by 10 mL                                   | 1 hour         |
| 100–150 (5.5–8.3): goal            | Continue same bolus dose                               | 2 hour         |
| 151–180 (8.4–9.9)                  | ↓Bolus dose by 10 mL                                   | 2 hour         |
| >180 (>9.9)                        | Hold bolus dose  | 2 hour         |

C. Discontinue dextrose 10% or dextrose 50% when 2-hour BG is stable with no intervention x 2. Begin fingerstick BG checks before meals, at bedtime, and at 4:00 a.m. or  every 4 hours  every 6 hours  other: \_\_\_\_\_

D. For patients with type 1 diabetes:

To prevent diabetic ketoacidosis once hypoglycemia has resolved, contact physician to:

- Continue basal insulin (at reduced dose) **or**
- Begin insulin infusion

Physician Signature

Date

Time

Patient Identification/Label

Hypoglycemia Prevention Protocol  
(for Nonpregnant Adults)

TABLE 2. Precipitating Factors for Hypoglycemia &lt;50 mg/dL (2.8 mmol/L) in 2009 and 2014

| Precipitating Factor  | Blood Glucose Values <50 mg/dL (<2.8 mmol/L) in 2009 (%) | Blood Glucose Values <50 mg/dL (<2.8 mmol/L) in 2014 (%) | Blood Glucose Values <50 mg/dL (<2.8 mmol/L) per 1,000 Patient Days in 2009 (n)* | Blood Glucose Values <50 mg/dL (<2.8 mmol/L) per 1,000 Patient Days in 2014 (n)* |
|---|--|--|--|--|
| Long-acting or mixed insulin  | 44.1   | 37.6   | 5.02   | 1.96   |
| IV regular insulin to treat high potassium  | 0  | 18.3   | 0  | 0.89   |
| Rapid-acting analog insulin, nutritional or corrective                                | 2.2  | 11.8   | 0.24   | 0.61   |
| Sulfonylurea  | 31.2   | 12.9   | 3.55   | 0.67   |
| Organ failure and/or sepsis   | 4.3  | 9.7  | 0.49   | 0.50   |
| Titratable IV insulin, set rate IV insulin for diabetic ketoacidosis, or insulin pump | 14   | 8.6  | 1.59   | 0.45   |
| Other, no exogenous agent   | 4.3  | 2.2  | 0.49   | 0.22   |
| Total   | 100  | 100  | 11.38  | 5.20   |

\*In 2009, there were 8,174 adult inpatient days between 16 January and 7 February; in 2014, there were 17,878 adult inpatient days between 28 March and 16 May.

or within 6 hours of a blood glucose level <70 mg/dL (3.9 mmol/L). Provision of oral carbohydrates and follow-up blood glucose checks were within the nurses' scope of practice. If IV dextrose was necessary, it was initiated after a call to the provider. The rate of IV dextrose 10% was modified according to titration instructions dependent on the blood glucose level, with the goal range of the protocol set at 100–150 mg/dL (5.5–8.3 mmol/L). It was found that patients on IV dextrose generally required 5–15 g/hour. Ten percent dextrose was chosen as the default fluid because the volume load would have been unacceptably high using 5% dextrose.

#### Follow-Up Retrospective Examination

In 2014, a follow-up retrospective examination of blood glucose values was initiated by the same investigator. Ninety-three sequential values in 55 patient events during 50 days were assessed using criteria equivalent to those used in 2009. In examining the collected values, an approach similar to that used in the 2009 evaluation was maintained so that the results could be numerically compared. The

greatest difference between the two retrospective examinations was that, in 2014, the investigator collected additional information on blood glucose values of 50–69 mg/dL (2.8–3.9 mmol/L) that occurred in conjunction with hypoglycemic values <50 mg/dL (2.8 mmol/L).

#### Results

##### Initial Retrospective Examination

As seen in Table 2, 44.1% of hypoglycemic values were related to the use of long-acting or mixed insulin in 2009. A second category, sulfonylureas used before or during hospitalization, was linked to 31.2% of hypoglycemic values. Assessment of precipitating factors for hypoglycemia in 2009, summarized in Table 3, led to awareness that most factors associated with low blood glucose lasted many hours to days. When each low blood glucose was treated reactively as an isolated event, recurrent hypoglycemia often resulted. This cycle was broken when proactive steps were taken to compensate for the effects of long-acting insulin, sulfonylureas, and organ failure.

##### Follow-Up Retrospective Examination

The 2014 follow-up retrospective examination included 50 days' data. As shown in Table 2, the greatest proportion of hypoglycemic events, 37%, once again was associated with the use of long-acting insulin. The second most common factor, linked to 18.3% of hypoglycemic events, was the use of IV regular insulin given to treat high potassium, which had not contributed to any hypoglycemic events in 2009. The third most common factor in 2014, linked to 12.9% of hypoglycemic events, was the use of sulfonylureas. Organ failure or sepsis were present in 9.5% of hypoglycemic events. Table 4 also demonstrates that many of the initial hypoglycemic values recorded for each precipitating factor were followed by additional episodes of blood glucose values <50 mg/dL (2.8 mmol/L) or 50–69 mg/dL (2.8–3.8 mmol/L) that were associated with the same factor.

To facilitate comparison over time or with data from other facilities, the number of adult inpatient-days for each time period of assessment was taken into account. There were 8,174 patient-days during the initial assess-

**TABLE 3. 2009 Precipitating Factors for Hypoglycemia <50 mg/dL (2.8 mmol/L) and Subsequent Low Blood Glucose Values Associated With the Same Initial Episode**

| Precipitating Factor   | Initial Blood Glucose Values <50 mg/dL (2.8 mmol/L) (n) | Subsequent Blood Glucose Values <50 mg/dL (2.8 mmol/L) (n) | Total Blood Glucose Values <50 mg/dL (2.8 mmol/L) (n) |
|--|---|--|---|
| Long-acting or mixed insulin   | 29  | 12   | 41  |
| IV regular insulin to treat high potassium   | 0   | 0  | 0   |
| Rapid-acting analog insulin, nutritional or corrective                                 | 2   | 0  | 2   |
| Sulfonylurea   | 17  | 12   | 29  |
| Organ failure and/or sepsis  | 3   | 1  | 4   |
| Titrateable IV insulin, set rate IV insulin for diabetic ketoacidosis, or insulin pump | 6   | 7  | 13  |
| Other, no exogenous agent*   | 2   | 2  | 4   |
| Total  | 59  | 34   | 93  |

\*Levofloxacin in one instance, hydrocortisone discontinued in a patient with adrenal insufficiency in the other.

ment from 16 January to 7 February 2009; the second assessment included data from 28 March to 16 May, encompassing 17,878 patient-days. Inclusion of this information allowed comparison of the number of events per 1,000 patient-days and is summarized in columns 4 and 5 of Table 2.

### Discussion

Overall, the rate of severe hypoglycemia <50 mg/dL (2.8 mmol/L) was reduced by >50% in 2014 compared to 2009 (5.20 vs. 11.38 events per 1,000 patient-days in 2014 and 2009, respectively). In particular, data from the 2014 follow-up showed a decrease in hypoglycemic events related to the use of long-acting insulin and the use of sulfonylureas, which were specifically targeted by the protocol and accompanying education.

In 2014, the association of blood glucose values <50 mg/dL (2.8 mmol/L) with further hypoglycemic episodes was explored in greater detail than in 2009. Less than one-third of blood glucose values <50 mg/dL (2.8 mmol/L) were isolated incidents. Review of the primary precipitating factor for low blood glucose clarified the reason for recurrence; the precipitating factors for

most severe hypoglycemic episodes were the use of long-acting insulin in excess of basal need, the use of sulfonylureas, or the presence of organ failure. The impact of these factors can be expected to persist for hours to days, resulting in ongoing risk of hypoglycemia.

Self-reported and observed dietary intake is often lower in the hospital than at home, adding to hypoglycemia risk. Within the context of this performance improvement project, education addressed the risks of sulfonylureas in the hospital and the need for revision of home doses of basal or mixed insulin, and orders for basal, nutritional, and corrective insulin were facilitated in the insulin order sets. Furthermore, when the risk for hypoglycemia was already established, provision of proactive carbohydrates to prevent recurrent hypoglycemia was facilitated by a nurse-driven protocol. Figure 1 shows the difference in the blood glucose patterns of a patient who initially received only reactive treatment for recurrent hypoglycemia and was then started on proactive IV dextrose. The figure illustrates how, with proactive provision of carbohydrates (in this case, IV dextrose), the recurrence of

hypoglycemia was prevented and glycemic variability was reduced.

### Innovations of the Protocol

In terms of action steps, the aim was to develop a protocol that 1) defined triggers for initiation, 2) treated all blood glucose values <70 mg/dL (3.9 mmol/L) in a standardized manner, 3) rapidly up-titrated the proactive IV dextrose to a rate that kept blood glucose in the goal range (100–150 mg/dL [5.5–8.3 mmol/L]), and 4) titrated down and discontinued use of the IV dextrose when it was no longer needed. These strategies addressed glycemic variability by breaking the cycle of hypoglycemia followed by blood glucose elevation with treatment and then by recurrent low blood glucose 1–2 hours later that requires further reactive treatment (16).

### Recommendations and Conclusions

#### Recommendations

This report highlights the importance of further research in this area. Further study is necessary to refine the orders for titration of IV dextrose and timing of the follow-up blood glucose checks proposed in this arti-

**TABLE 4. 2014 Precipitating Factors for Hypoglycemia <50 mg/dL (2.8 mmol/L) and Subsequent Low Blood Glucose Values Associated with the Same Initial Episode**

| Precipitating Factor  | Initial Blood Glucose Values <50 mg/dL (2.8 mmol/L) (n) | Subsequent Blood Glucose Values <50 mg/dL (2.8 mmol/L) <1 Hour After Initial Event (n) | Subsequent Blood Glucose Values <50 mg/dL (2.8 mmol/L) ≥1 Hour After Initial Event (n) | Total Blood Glucose Values <50 mg/dL (2.8 mmol/L) as Part of the Same Event (n) | Subsequent Blood Glucose Values 50–69 mg/dL (2.8–3.8 mmol/L) as Part of the Same Event (n) | Total Blood Glucose Values <70 mg/dL (3.9 mmol/L) Associated With the Event (n) |
|---|---|--|--|---|--|---|
| Long-acting or mixed insulin  | 22  | 7  | 6  | 35  | 36   | 71  |
| IV regular insulin to treat high potassium  | 8   | 4  | 4  | 16  | 8  | 24  |
| Rapid-acting analog insulin, nutritional or corrective                                | 8   | 3  | 0  | 11  | 5  | 16  |
| Sulfonylurea  | 4   | 2  | 6  | 12  | 22   | 34  |
| Organ failure and/or sepsis   | 6   | 1  | 2  | 9   | 8  | 17  |
| Titratable IV insulin, set rate IV insulin for diabetic ketoacidosis, or insulin pump | 5   | 3  | 0  | 8   | 8  | 16  |
| Other, no exogenous agent*  | 2   | 0  | 0  | 2   | 0  | 2   |
| Total   | 55  | 20   | 18   | 93  | 87   | 180   |

\*Nesidioblastosis and dumping syndrome.

cle. A major challenge is to maintain order simplicity while addressing the importance of individualized treatment. Further studies are also needed to confirm or revise observations about the amount of glucose required to maintain blood glucose at goal (generally 5–15 g/hour) and the appropriateness of the goal range of 100–150 mg/dL (5.5–8.3 mmol/L). Frequency of blood glucose monitoring and timing of the most recent blood glucose check before the initial hypoglycemic value, not assessed in our study, should be included in future research. Finally, it is important to test the impact of proactive hypoglycemia prevention on mortality and morbidity, with a special focus on critically ill patients and on deaths related to cardiac arrhythmias.

### Limitations

This analysis was retrospective and performed at a single facility. In addition, multiple factors contribute to hypoglycemia risk in many cases, and assignment of the primary precipitating factor in this study was necessarily subjective. Additional limitations are related to the nature of the assessment as part of a performance improvement project. Factors important for optimal data assessment became apparent over time through the insights gained in this preliminary assessment.

### Conclusion

The approach to hypoglycemia proposed in this article reflects a paradigm shift from reactive treatment to proactive prevention of hypoglycemia, similar to the change from reactive sliding-scale treatment of high glucose to the use of proactive basal-bolus insulin. Moving from reactive treatment to prevention represents a cultural change for hospital staff, with an opportunity for improved patient care.

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### Duality of Interest

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

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