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BRIEF REPORT

Delay in Blood Glucose Monitoring During an Insulin Infusion Protocol Is Associated with Increased Risk of Hypoglycemia in Intensive Care Units

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Disclosure: Nothing to report.

BACKGROUND: Hypoglycemia during insulin infusion therapy is a major problem. We investigated whether a delay in blood glucose (BG) monitoring during an insulin infusion protocol (IIP) in the intensive care unit (ICU) is associated with hypoglycemia.

METHODS: Data were collected for 50 consecutive patients treated with Brigham and Women's Hospital's IIP. Point-of-care BG values were obtained from the bedside paper flow sheets and the exact times of individual measurements were ascertained from an internet-based glucose meter download program. Data were carefully studied for protocol time violations, defined as a delay of >10 minutes after the recommended time for BG measurement.

RESULTS: A total of 2309 BG values were evaluated for time violation. A total of 1474 (63.9%) measurements had been obtained at the recommended time or earlier; 835 (36.1%) measurements had been obtained >10 minutes after the recommended time for measurement. There were a significantly higher proportion of BG values <80 mg/dL following the time violation as compared to no time violation (17.8% versus 11.6%; $P < 0.001$).

CONCLUSION: We conclude that the risk of hypoglycemia during insulin infusion therapy is higher after a delay in BG measurement. ***Journal of Hospital Medicine*** **2009;4:E5–E7.** © *2009 Society of Hospital Medicine.*

KEYWORDS: hypoglycemia, ICU, insulin infusion.

Since publication of the first randomized controlled trial of insulin infusion therapy in surgical intensive care unit (ICU) patients,[1] most institutions have implemented insulin infusion protocols (IIP) for tight glycemic control in their ICUs.[2–9] The major problem with tight glycemic control is the risk of hypoglycemia. In the randomized controlled trial involving medical ICU patients, 18.7% patients experienced at least 1 episode of blood glucose (BG) <40 mg/dL.[10] Recently, a major insulin infusion trial involving patients with severe sepsis was stopped due to unacceptably high risk of hypoglycemia.[11] Potential benefits of BG control may be offset by potential risks of hypoglycemia. While there can be multiple factors that could contribute to the risk of hypoglycemia, suboptimal protocol implementation is relatively amenable to correction.

Most IIPs are nurse driven. Nurses monitor BG levels every 30 to 60 minutes and make adjustments in insulin infusion rates. Each point of care testing and insulin dose adjustment takes about 5 minutes of nursing time.[12] Given the numerous other nursing responsibilities for monitoring and documentation in very sick patients, nurses may not always be able check BGs at the recommended times. We investigated whether a delay in BG monitoring during insulin infusion therapy is associated with higher risk of hypoglycemia.

Methods

Data were collected for 50 consecutive patients treated with Brigham and Women's Hospital's insulin infusion protocol (BHIP) between September 27, 2006 and October 13, 2006. The investigation was part of the hospital's ongoing diabetes quality improvement program. Partners-Health Human Research Committee approved the study. Patient demographics, history of diabetes mellitus, and glycosylated hemoglobin (A1C) were obtained from paper and electronic medical records. Point-of-care BG values were obtained from the bedside paper flow sheets. The exact times of individual BG measurements were ascertained from Point of Care Precision Web (QCM3.0; Abbott, Inc.).

Target BG range with BHIP is 80 to 110 mg/dL. BHIP requires BG testing every 60 minutes unless a BG value of <60 mg/dL is obtained; in which case, testing is required every 30 minutes. A time violation was assumed to have occurred if the BG was measured >70 minutes after a previous value of ≥60 mg/dL or >40 minutes after a previous BG value of <60 mg/dL (ie, >10 minutes after the recommended time for measurement). Although the choice of 10 minutes was arbitrary, we think it is a reasonable and practical time frame for getting a BG measurement. If a measurement was obtained earlier than the recommended time, it was not considered a time violation. However, measurements obtained within 30 minutes of a previous BG value (overwhelmingly drawn for confirmation of a previous BG value) were excluded from analysis.

BG values were divided into 2 categories: values following time violation and values following no time violation. The

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TABLE 1. Time Violations and Blood Glucose Values during BHIP

	Time Violation [n = 835 (100%)]	No Time Violation [n = 1,474 (100%)]	*P* Value
BG values <80 mg/dL	149 (17.8)	171 (11.6)	<0.001
BG values 80–110 mg/dL	316 (37.8)	596 (40.4)	NS
BG values >110 mg/dL	370 (44.3)	708 (47.8)	NS

Abbreviation: NS, statistically nonsignificant.

TABLE 2. Patient Characteristics and Frequency of Time Violation

Characteristic	Number of Patients	% of BG Values Associated with Time Violations	*P* Value
Gender			NS
Male	27	36	
Female	23	36	
Diabetes status			NS
Known diabetes	18	37	
No known diabetes	32	35	
Type of ICU			NS
Medical	20	38	
Surgical	30	35	
Admission diagnosis			
Cardiovascular disease	7	35	
Gastrointestinal disease	4	43	
Malignant disorder	8	32	
Neurological disease	7	36	
Orthopedic problem	2	51	
Respiratory disease	13	33	
Renal failure	3	46	
Sepsis	6	36	

Abbreviation: NS, statistically nonsignificant.

numbers of values in different BG ranges (<80, 80–110, >110 mg/dL) were compared in the 2 categories using a chi square test. Data are presented as mean ± standard deviation (SD), median and numbers with percentage. Statistical significance was set at $P < 0.05$.

Results

Mean age of the 50 patients treated with BHIP was 64.0 ± 13.6 years. There were 27 men and 23 women. Eighteen patients had preexisting diabetes (1 had type 1 and 17 had type 2 diabetes, mean A1C 7.1 ± 1.7%) and 32 patients had no previous history of diabetes (mean A1C 5.9 ± 0.9%). Mean serum creatinine was 1.34 ± 1.0 mg/dL. Mean BG at the start of BHIP was 173 ± 69.6 mg/dL; median 167.5 mg/dL. Mean BG during insulin infusion was 117.3 ± 43.1 mg/dL; median 107 mg/dL. Mean BG during insulin infusion was higher in diabetic patients compared to nondiabetic patients (125.2 ± 57.8 versus 113.4 ± 38.8 mg/dL; $P < 0.01$).

TABLE 3. Patient Characteristic and Relation of Time Violation to Hypoglycemia

	% BG Values <80		
Characteristic	Time Violation	No Time Violation	*P* Value
Male	19.1	11.9	<0.001
Female	16.1	11.2	0.03
Known diabetes	13.3	11.1	NS
No diabetes	20	11.9	<0.001
Medical ICU	19.2	11.9	0.002
Surgical ICU	16.8	11.3	0.004
Cardiovascular diseases	21.1	14.1	
Gastrointestinal diseases	22.1	14.8	
Malignant disorders	22.0	11.7	
Neurological diseases	7.5	5.0	
Orthopedic problems	6.2	6.6	
Respiratory diseases	11.9	10.4	
Renal failure	35.7	15.6	
Sepsis	19.7	13.5	

Abbreviation: NS, statistically nonsignificant.

Monitoring for BGs was done with similar frequency in all patients. Overall, 40.2% of the total 2,605 BG values were in a range of 80 to 110 mg/dL. A total of 1.5% of values were below 60 mg/dL; only 4 values were <40 mg/dL.

A total of 2,309 values could be studied for time violations. The remaining 296 values were either obtained within 30 minutes of the previous test or the exact time of measurement could not be ascertained. A total of 1,474 (63.9%) measurements had been obtained at the recommended time or earlier than the recommended time; 835 (36.1%) measurements had been obtained >10 minutes after the recommended time for measurement (time violation). The proportion of BG values below the target (<80 mg/dL) was significantly higher following the time violation as compared to no time violation (Table 1). On the other hand, values >110 mg/dL were not more common following a time violation, compared to instances when no time violation occurred.

Frequency of time violation was similar in subgroups of patients divided according to gender, presence of diabetes and the type of ICU (Table 2). Comparison among subgroups of admission diagnoses was not possible due to the small number of patients. Overall, the proportion of low BG values was lower in diabetic patients compared to nondiabetic patients (11.9% versus 15.0%, $P = 0.03$). An increased rate of hypoglycemia following time violations was present in all subgroups except for the diabetic subgroup (Table 3).

Discussion

Our study shows that a delay in BG testing during BHIP is associated with higher chances of a low BG value. This effect was consistent in multiple subgroups. However, the effect was nonsignificant in diabetic patients, probably due to higher mean BG levels and less frequent low BG values.

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Over one-third of all BG measurements were obtained after a time violation. Protocol violations in our study are no different from those reported by others.[7,13,14] Our patient characteristics of severe hypoglycemic episodes and the overall BG control achieved with BHIP were also similar to those reported by others with similar protocols.[5,7,15–17] While the results of this study may still be specific to BHIP, we think they are applicable to other similar protocols.

Because a delay in testing by itself is unlikely to cause hypoglycemia, a more likely explanation for these results is that hypoglycemia occurred when insulin infusion adjustments were not made in a timely fashion due to prolonged BG monitoring intervals. Insulin infusions are the preferred treatment in rapidly changing clinical settings because changes in insulin doses can be made frequently. Most IIPs are designed with the assumption that insulin dose adjustments will be made regularly and frequently, based on BG measurements. Although there is no gold standard for the optimal BG test frequency, in most protocols BG testing is performed every hour in order to ensure safety as well as efficacy. Our results are consistent with the intuitive assumption that a timely measurement of the BG is important for successful implementation of an IIP.

It was somewhat surprising that high BG values were not more frequent following a time violation. We can only speculate as to the reason for this. It is possible that critically ill patients are near maximally insulin resistant and, once an effective insulin infusion rate is achieved, further increases are not as frequently required. On the other hand, insulin requirements may decrease rapidly as contributors to insulin resistance resolve. Another possibility is that there may be a limit to hepatic glucose production during acute illness making patients more prone to hypoglycemia. It is also possible that the nurses tend to test more promptly when the BG levels are running high. Thus, the insulin doses may be increased at proper times until BG levels are in the target range. However, when BG levels are in the target range, nurses may become less vigilant, leading to a delay in testing. As a result a decrease in insulin dose, when required, does not happen as promptly as an increase in dose.

In our study the absolute risk of hypoglycemia associated with time violation was 6%. Avoiding this hypoglycemia may have an impact on glycemic control in the ICU and may change clinical outcomes. Moreover, this is 1 of the few factors that are potentially amenable to correction. Therefore, measures to improve adherence to protocols, eg, prompts for BG testing and better nurse training regarding importance of timely testing, may reduce the risk of hypoglycemia.

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