

INPATIENT MANAGEMENT OF HYPERGLYCEMIA: THE NORTHWESTERN EXPERIENCE

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ABSTRACT

Objective: To describe a novel method of safe and effective intensive management of inpatient hyperglycemia with use of cost-effective protocols directed by a glucose management service (GMS).

Methods: An intravenous insulin protocol was designed to achieve a glycemic target of 80 to 110 mg/dL. When stable inpatients were transferred from the intravenous protocol to a subcutaneous insulin protocol, which consisted of basal long-acting and prandial and supplemental rapid-acting insulins, the blood glucose target was 80 to 150 mg/dL. Glucose levels were reviewed by the GMS at least daily for protocol adjustments, when necessary.

Results: The intravenous insulin protocol was used in 276 patients, and 4,058 capillary blood glucose levels were recorded. Glycemic target levels (80 to 110 mg/dL) were achieved, on average, 10.6 ± 5.2 hours after initiation of insulin drip therapy. The mean capillary blood glucose level during the study interval was 135.3 ± 49.9 mg/dL. Hypoglycemia (≤ 60 mg/dL) was recorded in 1.5% of glucose values, and hyperglycemia (≥ 400 mg/dL) was recorded in only 0.06%. The subcutaneous insulin protocol was used in 922 patients, and 18,067 capillary glucose levels were documented. The mean blood glucose level was 145.6 ± 55.8 mg/dL during the study period. The blood glucose target of 80 to 150 mg/dL was achieved in 58.6%, whereas 74.3% of glycemic values were in the clinically acceptable range (80 to 180 mg/dL). Hypoglycemia (≤ 60 mg/dL) occurred in 1.3% of capillary blood glucose values, and hyperglycemia (≥ 400 mg/dL) occurred in 0.4% of values.

Conclusion: Validated protocols dedicated to the achievement of strict glycemic goals were implemented by a GMS and resulted in substantial improvements in glycemic control on the surgical inpatient services, with a reduced frequency of hypoglycemia. The protocols and the GMS have been well received by the inpatient nursing and surgical staff members, and all of this has been done in a cost-effective manner. (*Endocr Pract.* 2006;12:491-505)

Abbreviations:

BMI = body mass index; **CVICU** = cardiovascular intensive care unit; **DM** = diabetes mellitus; **GMS** = glucose management service; **ICU** = intensive care unit; **SICU** = surgical intensive care unit; **TPN** = total parenteral nutrition

INTRODUCTION

Guidelines for the diagnosis and management of diabetes mellitus (DM), supported by evidence from randomized clinical trials, are well established in the outpatient setting. In contrast, corresponding guidelines for the management of DM in the inpatient arena are haphazard at best, and practice patterns differ considerably. This discrepancy is due, in part, to a lack of evidence to support the control of hyperglycemia in some inpatient populations and the belief by most health-care providers that hyperglycemia is a normal physiologic response to illness or hospital-induced stress. Recent evidence belies this belief. Hyperglycemia is common in hospitalized patients, with a prevalence of approximately 25%, and is an independent risk factor for poor clinical outcome in multiple patient populations (1,2). In addition to stress-induced hyperglycemia, contributing factors to inpatient hyperglycemia include pharmacologic agents (3), enteral and parenteral nutrition (4,5), and glucocorticoid therapy (6).

Recent clinical trials have shown clear benefits relative to morbidity and mortality from intensive management of inpatient hyperglycemia, even in patients without a prior history of DM (7-10). The medical community is

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obligated to respond to this growing literature supporting intensive treatment of inpatient hyperglycemia. The development of easy-to-follow, effective, and safe management strategies must become a priority for inpatient providers. In this report, we describe our experience at Northwestern Memorial Hospital, a 776-bed tertiary care center in Chicago, Illinois, with the development and promulgation of protocols directed by an inpatient glucose management service (GMS) to provide safe inpatient glycemic control.

METHODS

Development of Protocols to Treat Hyperglycemia

Our goal was to design a system of care for accurate identification and treatment of hyperglycemia among hospitalized patients. A retrospective review estimated that 21% of patients requiring admission to our institution in September 2003 had documented glucose levels >200 mg/dL. For our protocols, glycemic targets were set according to preexisting guidelines (11,12). In the critically ill population, a target glycemic range of 80 to 110 mg/dL was established, on the basis of evidence from other studies supporting a reduction of morbidity and mortality with achievement of similar glycemic levels (7). In the non-critically ill population, a glycemic target of 80 to 150 mg/dL was established. Blood glucose levels ranging from 80 to 150 mg/dL and from 80 to 180 mg/dL are considered clinically acceptable in the critically ill and the non-critically ill populations, respectively, as defined by a recent consensus conference (12).

Orally administered hypoglycemic agents are relatively contraindicated in the hospital setting (13). The extended duration of action and the potential for harmful drug interactions, coupled with the rapidly changing clinical scenario of hospitalized patients, make these agents less desirable for achieving strict glycemic goals. Insulin therapy can achieve strict glycemic control efficiently and predictably with the least amount of drug interactions. A literature search of extant inpatient hyperglycemia management protocols was performed (14-16). We adapted elements of these protocols to fit our patient and provider populations optimally, specifically emphasizing safety, efficacy, and ease of application. Separate protocols were designed for the delivery and management of intravenous insulin therapy and subcutaneous insulin therapy.

Intravenous Insulin Protocol

The intravenous protocol was developed to achieve a glycemic target (80 to 110 mg/dL) while minimizing the risk of hypoglycemia (Appendix 1). The efficacy of the protocol for the management of diabetic ketoacidosis has not been validated and cannot be recommended. Intravenous insulin therapy is administered as a regular insulin solution (100 U of regular insulin in 100 mL of isotonic saline). The initial insulin drip rate is determined by the initial capillary blood glucose value (Appendix 1). A loading bolus dose of regular insulin, equivalent to the

hourly drip rate, is also administered at the initiation of the infusion (see Table 1 in Appendix 1). The insulin drip is subsequently titrated on the basis of the current capillary blood glucose value and the rate of change from the preceding capillary blood glucose value. Nurses refer to the appropriate table for insulin drip adjustment, depending on whether the current glucose value had increased (see Table 2 in Appendix 1) or decreased (see Table 3 in Appendix 1) from the previous value. The degree of change from the previous blood glucose value (with a change in capillary blood glucose of 60 mg/dL as a cutoff value) determines which column within each table is referenced for insulin drip titration orders, consisting of rate changes and additional boluses as indicated (see Tables 2 and 3 in Appendix 1).

For example, if the previous blood glucose value was 100 mg/dL and the current blood glucose value is 170 mg/dL, the nurse would reference Table 2 in Appendix 1 because the glucose level increased. Because the degree of change in the glucose level was 70 mg/dL, the orders in the far right column of Table 2 ("Greater than 60 mg/dL") would be followed, and the insulin drip rate should be increased by 0.5 U/h with a 2-U bolus administered. The next blood glucose assessment would be in 1 hour, and further insulin drip titration would be performed.

The intravenous insulin protocol order set stipulates the frequency of capillary blood glucose monitoring. Initially, capillary blood glucose levels are monitored every hour, and then the frequency of monitoring is decreased to every 2 to 4 hours, depending on the stability of blood glucose values and the clinical situation. The protocol incorporates variables for intravenous fluid administration, including glucose and potassium repletion to minimize hypoglycemia and hypokalemia. Guidelines for the treatment of hypoglycemia are explicit (Appendix 1). Orders to notify the managing service of various clinical scenarios—specifically, persistent hypoglycemia or hyperglycemia, rapid changes in glucose values (increase or decrease >100 mg/dL), hypokalemia, or impending dietary changes—are included.

Subcutaneous Insulin Protocol

The subcutaneous insulin protocol was designed for effective and safe achievement of target blood glucose values of 80 to 150 mg/dL, with insulin delivery modeling physiologic insulin secretion (Appendix 2). Similar to previously published protocols (17), insulin needs were subdivided into basal, prandial, and supplemental requirements. Basal insulin controls hepatic glucose output and gluconeogenesis in the fasting state, prandial insulin compensates for blood glucose elevations from caloric intake, and supplemental insulin is used as a corrective factor for preprandial hyperglycemia. The GMS routinely uses the long-acting insulin analogue, glargine (Lantus), for basal insulin requirements because of its once-daily dosing and relatively flat insulin profile. Guided by the hospital formulary, the GMS generally uses the rapid-acting

insulin analogue, aspart (NovoLog), for prandial and supplemental insulin requirements.

Capillary blood glucose monitoring is ordered before every meal and at bedtime in those patients tolerating an oral diet, every 6 hours if the patient is allowed nothing orally or is receiving continuous enteral or parenteral nutrition, and with greater frequency as clinically indicated. To minimize the need to call a physician for a patient with abnormal glucose values, the nursing staff administers supplemental insulin doses according to the ordered supplemental insulin scale given concurrently with scheduled prandial insulin (if eating) or alone (if the patient is allowed nothing by mouth or is receiving enteral or parenteral therapy) (see Order 4 in Appendix 2). Daily review of bedside capillary blood glucose values is performed by the GMS so that titration of basal, prandial, or supplemental insulin doses can achieve the aforementioned glycemic goals. The subcutaneous insulin protocol provides guidelines regarding hypoglycemia management and service notification for persistent capillary blood glucose values outside the target range and if dietary changes are planned.

Development of the Glucose Management Service

The GMS was formed with a team-oriented approach to cover all aspects of hyperglycemia management. The team consists of the following health-care providers: an advanced practice nurse (or nurses) or a physician's assistant, responsible for initial patient consultation and daily management; an endocrinology attending, responsible for initial patient consultation, evaluation, and management; an endocrinology fellow, responsible for night and weekend coverage of the service; and an administrator, responsible for collection and storage of pertinent data. The team functions in coordination with ancillary health-care providers critical to comprehensive management of DM, including inpatient dietitians and diabetes educators.

Approval for use of the insulin protocols as directed by the GMS was granted by the Medication Safety, Pharmacy, and Therapeutics Subcommittee and the Quality Assurance Subcommittee at Northwestern Memorial Hospital. The initial strategy was to limit use of the insulin protocols in a select inpatient group, to monitor safety and efficacy of the protocols over a specified period and to make necessary adjustments, and then to expand the use of the service in a stepwise fashion. Initially, the insulin protocols were restricted to the GMS and available as a patient care tool only after consultation with the GMS was obtained.

The pilot groups for the GMS and insulin protocols were the surgical intensive care unit (SICU) and cardiovascular intensive care unit (CVICU) because intensive glycemic control already had been shown to provide benefit in such intensive care unit (ICU) populations (7,8). Educational sessions describing protocol rationale and use were given to the SICU and CVICU provider staffs by a member of the GMS. Data regarding efficacy to achieve glycemic targets, adherence to protocol guidelines, and

safety were collected. After 1 month of protocol use on the CVICU and SICU services, modifications were made to improve efficacy, adherence, and safety. Once safety of the protocols was demonstrated, use of the protocols was expanded to additional ICUs and the general medical and surgical hospital wards. In-service education was provided to the nursing staff of each unit before implementation of the insulin protocols.

Capillary blood glucose monitoring allows immediate point-of-care assessments with which to base clinical decisions. The SICU and CVICU nursing staffs were instructed to perform capillary blood glucose monitoring for all patients. The initiation and frequency of glucose monitoring (preoperatively, intraoperatively, or postoperatively) were based on the clinical discretion of the managing surgical and anesthesia staffs. Most commonly, capillary blood glucose monitoring was performed every 4 hours and begun in the postoperative setting. Management of hyperglycemia was considered necessary if capillary blood glucose values exceeded 110 mg/dL on 2 separate occasions or exceeded 200 mg/dL once. Once hyperglycemia was established, the GMS was consulted, and insulin administration (intravenous or subcutaneous) was determined on the basis of the clinical scenario. In most patients with hyperglycemia, intravenous insulin therapy was begun in the immediate postoperative period (24 to 72 hours), at a time when the patients had limited dietary intake, were intubated, and/or were receiving intravenously administered pressor agents. Transition to a subcutaneous insulin regimen occurred once the critical illness had resolved and dietary intake was adequate. The insulin protocols proved to be safe and effective (see the "Results" section). It became apparent after 1 month of protocol use that the SICU and CVICU nursing staffs were sufficiently qualified to use the protocols without prerequisite consultation from the GMS. Members of the GMS were available for consultation, and protocol outcomes were continually monitored.

Eventually, approval for the use of the insulin protocols was granted hospitalwide by the various hospital care committees. Consultation with the GMS was no longer mandatory for insulin protocol implementation. The most common scenario for postsurgical hyperglycemia identification, insulin protocol initiation, and GMS consultation at our institution is schematically represented in Figure 1.

Hyperglycemia Management Strategies

Postoperative capillary blood glucose monitoring has now become routine in the ICUs and as clinically indicated on the general surgical nursing units. In the SICU and CVICU, a blood glucose level is determined within an hour after transfer from the recovery room. SICU and CVICU protocol indicates initiation of an insulin drip if blood glucose values exceed 200 mg/dL once or 110 mg/dL on 2 occasions independent of the GMS. In the non-ICU areas, the GMS is consulted for assistance with glycemic control in patients with hyperglycemia at the dis-

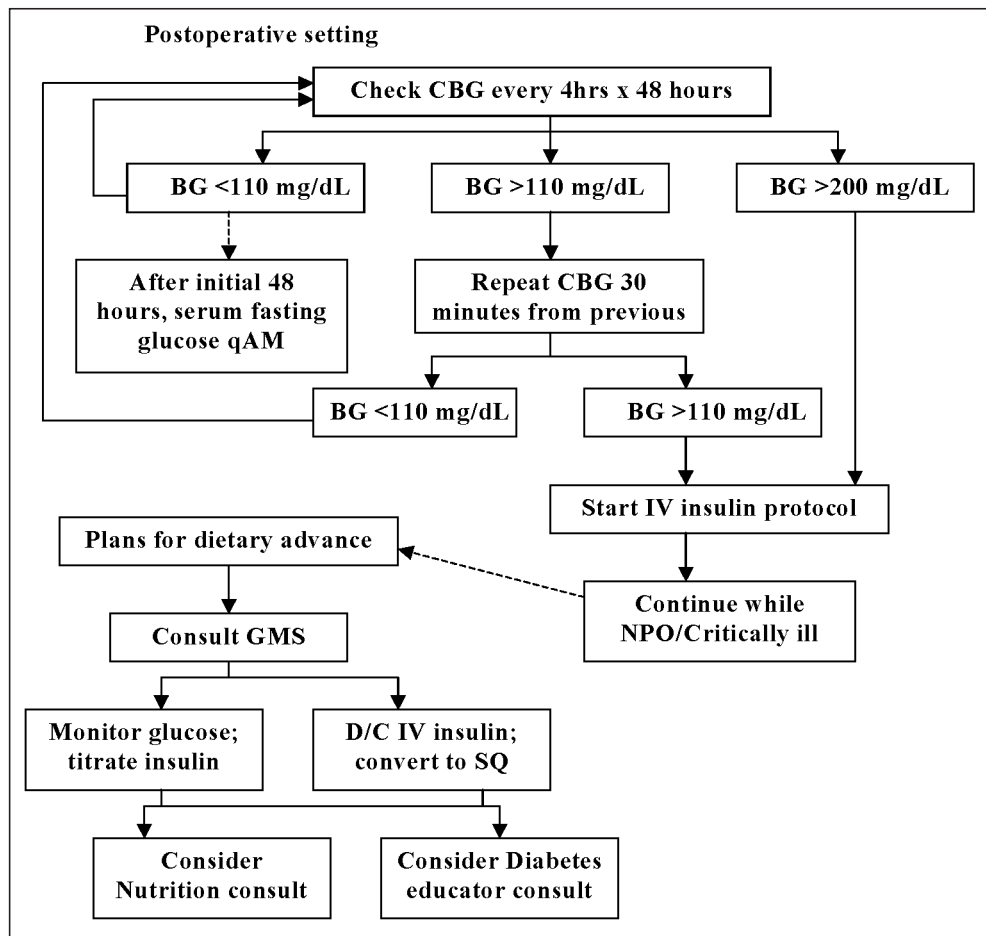


Fig. 1. Algorithm for identification and treatment of inpatients with hyperglycemia. *BG* = blood glucose; *CBG* = capillary blood glucose; *D/C* = discontinue; *GMS* = glucose management service; *IV* = intravenous; *NPO* = nothing allowed by mouth; *qAM* = every morning; *SQ* = subcutaneous.

cretion of the managing service. The initial hyperglycemia treatment strategy is dependent on the clinical scenario and multiple variables.

Intravenously administered insulin is most appropriate, but not exclusively, for critically ill patients with blood glucose values exceeding 110 mg/dL, those with a history of DM unable to receive oral caloric support, and patients with severe hyperglycemia (glucocorticoids, sepsis, pressor agents). In the postoperative critical care setting, the patient is often intubated, and dietary intake is restricted. Nursing personnel initiate the intravenous insulin protocols and titrate infusion rates accordingly for those patients identified as having hyperglycemia. The insulin infusions are maintained while the patient is receiving nothing orally. The GMS is consulted if the target glycemic range is not achieved within 8 hours after insulin drip initiation or for assistance with conversion to subcutaneous insulin therapy after the critical illness resolves and the decision to advance diet is made by the managing service. The GMS continues insulin management throughout the rest of the hospitalization.

A subcutaneous insulin treatment strategy is optimal for inpatients with hyperglycemia who are receiving a stable caloric source or in whom orally administered hypoglycemic agents are contraindicated. Many clinical variables are taken into account by the GMS to determine the basal, prandial, and supplemental insulin requirements to be met by a subcutaneous insulin strategy. Patients receiving total parenteral nutrition (TPN) will commonly have regular insulin added to their TPN after GMS consultation with the TPN nurse. Patients with hyperglycemia receiving continuous enteral nutrition are usually treated with a long-acting basal insulin. Supplemental insulin is administered as needed on the basis of capillary blood glucose monitoring every 6 hours.

Conversion From Intravenous Insulin Therapy

When the patient's therapy is being converted from an intravenous insulin drip, the drip rate is used as a guide to determine total daily insulin requirements. The insulin drip rate for the preceding 6 hours is averaged to obtain a stable hourly rate. The average rate is multiplied by 24

hours to calculate the total daily insulin requirement. The basal insulin dose ordered is 80% of the total daily insulin requirement and usually administered as a once-daily subcutaneous injection of glargine insulin. Most commonly, the prandial insulin dose for each meal is 10% of the glargine dose, usually given as insulin aspart per hospital formulary. The prandial insulin dose is adjusted accordingly as the patient's appetite improves postoperatively. The proportion of insulin given for prandial dosing is substantially less than that recommended by others because these patients are generally consuming only a clear liquid diet initially with a reduced caloric content. The dose is maintained the next day because the overall insulin requirement is generally decreasing substantially as the stress of the surgical procedure or acute illness abates. The initial doses of basal and prandial insulin are given at separate injection sites concomitant with the discontinuation of the intravenous insulin drip and ingestion of the first postoperative meal (see Example 1 in Table 1). During the first few months of using the protocols, it was mandated that the insulin infusion be continued for at least 2 hours after the injection of glargine to maintain adequate serum

insulin levels. Data analysis revealed inadequate glycemic control 6 hours after the glargine injection despite the overlap period with the insulin drip. In addition, it became apparent that practical necessities outweighed this physiologic reasoning, in that transfer of the patient from intravenous to subcutaneous insulin therapy often coincided with transfer of the patient out of the ICU, with the result that the insulin infusion was simply stopped without an overlap period. Therefore, we changed our protocol to include a conversion dose of aspart insulin that was 10% of the glargine dose given simultaneously to discontinuing the intravenous infusion and the first administration of glargine to maintain adequate glycemic control.

Initiation of Subcutaneous Insulin Protocol When No Intravenous Insulin Therapy Has Been Given

In the non-critical care surgical population, the GMS is consulted for management of hyperglycemia in patients with known DM or those in whom postoperative hyperglycemia develops. Often these patients are receiving a stable caloric source and have not received insulin intravenously during the current hospitalization. A subcuta-

Table 1
Calculation of Subcutaneous Insulin Need

Example 1. Conversion From Intravenous Insulin Therapy

- Step 1. Intravenous insulin drip rate averaged 1.8 U/h with final glucose level 98 mg/dL
- Step 2. Calculate average insulin infusion rate for last 6 h = 2.1 U/h and multiply $\times 24$ to get total daily insulin requirement ($2.1 \times 24 = 50$ U/24 h)
- Step 3. Multiply this 24-h dose (50 U) $\times 80\%$ to obtain glargine dose = 40 U, which is given and the infusion is stopped
- Step 4. Multiply the glargine dose by 10% to give as a rapid-acting insulin (e.g., aspart, lispro, or glulisine) at the time the glargine is given and the infusion is stopped
- Step 5. Give 10% of the glargine dose as prandial doses before each meal

Example 2. Estimating Insulin Doses When No Intravenous Insulin Therapy Has Been Given

- Step 1. Calculate estimated total daily dose of insulin as follows:
 - Type 2 diabetes (known): 0.5 to 0.7 U/kg
 - Type 1 diabetes (known): 0.3 to 0.5 U/kg
 - Unknown: 0.3 to 0.5 U/kg
- Step 2. Divide total daily dose of insulin into 50% basal as glargine and 50% prandial as aspart, lispro, or glulisine
- Step 3. Divide prandial insulin into 3 equal doses to be given with meals

neous insulin strategy is developed by the GMS. The total daily insulin requirement is influenced by multiple clinical variables (for example, prior history of DM, type of DM, body mass index [BMI], outpatient hypoglycemia regimen, surgical stress, concomitant medications, caloric intake) that affect insulin sensitivity and secretion. Body weight can be used as a guideline to calculate initial insulin dosing requirements (0.5 U/kg for patients with type 2 DM and 0.3 U/kg for those with type 1 DM or without a prior history of DM). Half of the calculated daily insulin requirement is given as a daily subcutaneous injection of glargine insulin to meet basal insulin coverage. The remainder is divided into 3 equal doses administered as aspart insulin with meals to fulfill prandial insulin needs (see Example 2 in Table 1).

A supplemental insulin scale is determined on the basis of multiple clinical factors (for example, type and severity of hyperglycemia, BMI, insulin requirements, medical stress, concomitant medications) and is delivered in addition to the standing prandial insulin dose in the form of aspart insulin to correct preprandial hyperglycemia. Capillary blood glucose is monitored at meals and at bedtime. Daily adjustment of basal or bolus insulin doses on the basis of individual glycemic results is a critical function of the GMS.

ANALYSES

The major efficacy end points for the intravenous insulin protocol were the time from initiation of drip insulin therapy to target glycemia (80 to 110 mg/dL) and the mean blood glucose level during the infusion. The incidences of hypoglycemia (≤ 60 mg/dL) and hyperglycemia (≥ 400 mg/dL) were tallied. Adherence to the protocol was also monitored.

The efficacy of the subcutaneous insulin protocol was determined by percentages of capillary blood glucose measurements in the target glycemic range (80 to 150 mg/dL) and the clinically acceptable range (80 to 180 mg/dL). The incidences of hypoglycemia (≤ 60 mg/dL) and hyperglycemia (≥ 400 mg/dL) were recorded as well. Approval to publish data was granted by the Institutional Review Board of the Northwestern University, Feinberg School of Medicine.

Adherence to the protocol was defined as a function of accuracy of insulin dosing and accuracy of service notification, as outlined by the protocol order sets. Adherence of the nursing staff to the intravenous insulin protocol was monitored retrospectively.

RESULTS

Intravenous Insulin Protocol

Two hundred seventy-six patients were managed with the intravenous insulin protocol after consultation with the GMS between June 2004 and June 2005 (excluding

September 2004, for which no data are available). Demographic data for these patients are shown in Table 2. Most patients were men (63%), and cardiovascular surgery was the managing service most frequently requesting consultation (47%). The majority of patients were in the CVICU or SICU while receiving intravenous insulin therapy. The mean age was 59.6 years, and the mean BMI was 29.1 kg/m². The majority of patients had no prior history of diabetes (64%), whereas 32% had a history of type 2 DM and only 4% a history of type 1 DM (Table 2). It bears repeating that the intravenous insulin protocol was not intended for use in the treatment of diabetic ketoacidosis, and any use of the protocol outside the postoperative setting should be done with caution.

Glycemic target levels (80 to 110 mg/dL) were achieved, on average, 10.6 \pm 5.2 hours after initiation of insulin drip therapy. The mean capillary blood glucose concentration for the study interval was 135.3 \pm 49.9 mg/dL. In these 276 patients, 4,058 capillary blood glucose levels were recorded. Hypoglycemia (≤ 60 mg/dL) was recorded in 1.5% of capillary blood glucose values, and hyperglycemia (≥ 400 mg/dL) was recorded in only 0.06%.

Glycemic control in the CVICU and SICU from September 1 through September 30, 2003, before the development of the GMS and implementation of the intravenous insulin protocol, was used as a historic control for comparative purposes. The mean blood glucose level in patients in the CVICU and SICU during that period was 169.0 \pm 69.0 mg/dL, with 0.6% and 0.4% of capillary blood glucose values (N = 526) ≤ 60 mg/dL and ≥ 400 mg/dL, respectively.

With respect to protocol adherence, insulin drip rates were appropriately initiated in accordance with the protocol 84% of the time. Insulin drip rates were titrated in

Table 2
Demographic Data
for 276 Patients Managed
With the Intravenous Insulin Protocol

| Factor | Data |
|---------------------------------|----------------|
| Mean age (yr) | 59.6 \pm 6.8 |
| Male patients | 63% |
| Admitting service, no. (%) | |
| Cardiovascular surgery | 129 (46.7) |
| Transplantation surgery | 51 (18.5) |
| General surgery | 12 (4.3) |
| Surgical oncology | 17 (6.2) |
| Other | 67 (24.3) |
| History of diabetes, no. (%) | |
| Known type 1 diabetes | 10 (3.6) |
| Known type 2 diabetes | 88 (31.9) |
| No previous history of diabetes | 178 (64.5) |

Table 3
Demographic Data
for 922 Patients Managed
With the Subcutaneous Insulin Protocol

| Factor | Data |
|---------------------------------|-------------|
| Mean age (yr) | 60.5 ± 13.5 |
| Male patients | 61% |
| Admitting service, no. (%) | |
| Cardiovascular surgery | 388 (42.1) |
| Transplantation surgery | 161 (17.5) |
| General surgery | 62 (6.7) |
| Surgical oncology | 101 (11.0) |
| Other | 210 (22.8) |
| History of diabetes, no. (%) | |
| Known type 1 diabetes | 60 (6.5) |
| Known type 2 diabetes | 390 (42.3) |
| No previous history of diabetes | 472 (51.2) |

accordance with the protocol 58% of the time, with the most common error (22%) being underdosing of insulin.

Subcutaneous Insulin Protocol

A total of 922 patients received subcutaneous insulin management in consultation with the GMS from June 2004 through June 2005 (excluding September 2004, for which no data are available). Similar to those receiving the intravenous insulin protocol, the majority were male patients (61%), and the most frequent service requesting GMS consultation was cardiovascular surgery (42%). Demographic data for these patients are summarized in

Table 3. The mean age at the time of GMS consultation was 60.5 years, and the mean BMI was 29.2 kg/m². The majority of patients with hyperglycemia had no prior history of diabetes (51.2%); 42.3% and 6.5% had a history of type 2 DM and type 1 DM, respectively.

In these 922 patients, 18,067 capillary blood glucose levels were obtained. The mean blood glucose concentration was 145.6 ± 55.8 mg/dL during the study period. The majority of capillary blood glucose measurements (58.6%) were in the target range of 80 to 150 mg/dL, and 74.3% were in the clinically acceptable range (80 to 180 mg/dL). Hypoglycemia (≤60 mg/dL) was documented in 1.3% of capillary blood glucose values, with an incidence of 0.25 episode per patient. Hyperglycemia (≥400 mg/dL) was less frequent; it was documented in 0.4% of capillary blood glucose measurements and occurred with a frequency of 0.09 episode per patient (Fig. 2).

A historical comparison of glycemic control on the same surgical services from September 1 through September 30, 2003, a period before the development of the GMS and implementation of the subcutaneous insulin protocol, was made. During that period, 2,379 capillary blood glucose levels were determined. The mean blood glucose level was 163.5 ± 68.3 mg/dL, with the glycemic target range (80 to 150 mg/dL) being achieved in 48.4% of capillary blood glucose values and the clinically acceptable range (80 to 180 mg/dL) being achieved in 67%. Hypoglycemia (≤60 mg/dL) occurred in 1.4%, and hyperglycemia (≥400 mg/dL) occurred in 0.88% of these values.

Improvement With Protocol Use Over Time

A basic tenet of the GMS is to conduct periodic review of outcomes and to adjust protocols and management strategies as needed for improvement. A comparison of outcomes for both the intravenous insulin protocol and

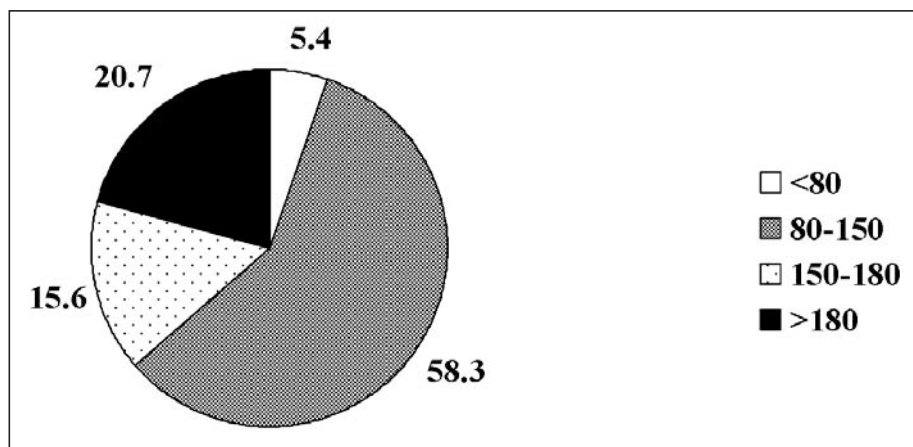


Fig. 2. Glycemic ranges in hospitalized patients treated with the subcutaneous insulin protocol between June 2004 and June 2005 (excluding September 2004). The results consist of 18,067 capillary glucose measurements performed in 922 patients. The percentages of glucose values in the ranges of <80 mg/dL, 80 to 150 mg/dL, 150 to 180 mg/dL, and >180 mg/dL are shown. Overall, 74% of values were in the clinically acceptable range of 80 to 180 mg/dL. It should be noted that only 1.3% of values were ≤60 mg/dL and only 0.4% of values were ≥400 mg/dL.

Table 4
Comparison of Glucose Values in the Initial Quarter*
and the Latest Quarter† for the
Intravenous and Subcutaneous Insulin Protocols

| Protocol | Initial quarter | Latest quarter |
|--------------------------------------|-----------------|----------------|
| <i>Intravenous</i> | | |
| Total number of patients | 34 | 114 |
| Total number of glucose measurements | 674 | 1,543 |
| Time to glucose goal (h) | 18.2 | 8.3 |
| Mean glucose level (mg/dL) | 148.4 | 133.2 |
| Glucose levels (mg/dL) | | |
| 80-110 (%) | 24.1 | 27.6 |
| 80-150 (%) | 57.3 | 65.8 |
| ≤60 (%) | 3.1 | 1.0 |
| ≥400 (%) | 0.2 | 0.3 |
| <i>Subcutaneous</i> | | |
| Total number of patients | 120 | 331 |
| Total number of glucose measurements | 2,337 | 6,524 |
| Mean glucose level (mg/dL) | 153.6 | 139.7 |
| Glucose levels (mg/dL) | | |
| 80-110 (%) | 47.0 | 66.2 |
| 80-150 (%) | 65.5 | 79.8 |
| ≤60 (%) | 1.6 | 1.1 |
| ≥400 (%) | 0.5 | 0.3 |
| *June 1, 2004 to August 31, 2004. | | |
| †April 1, 2005 to June 30, 2005. | | |

the subcutaneous insulin protocol for the first quarter (June 1, 2004 to August 31, 2004) and the most recent quarter (April 1, 2005 to June 30, 2005) analyzed is outlined in Table 4. An improvement in glycemic end points is seen, despite an increase in the number of consultations.

DISCUSSION

The number of hospitalizations for DM or DM-related complications in the United States was estimated at 4.6 million in 2001, with an estimated cost of \$40 billion (18). In the hospital setting, however, DM is often unrecognized, and treatment is seldom standardized. A retrospective review of patients admitted to a Philadelphia hospital revealed that 31% met the American Diabetes Association criteria for DM, 41% of whom were unrecognized as having DM at the time of dismissal from the hospital (19). A retrospective analysis of blood glucose measurements (N = 3,092) on the medicine services at Northwestern Memorial Hospital from September 1 through September 30, 2003, revealed a mean blood glucose level of 182.6 ± 87.8 mg/dL, with only 53.1% of the capillary blood glucose levels measured being in the clinically acceptable range of 80 to 180 mg/dL.

Hyperglycemia has been shown to be an independent risk factor for a poor clinical outcome in multiple inpatient settings. In patients who have undergone a cardiac surgical procedure, DM is an independent predictor of prolonged ICU stay, sternal wound infection, postoperative delirium, perioperative stroke, renal dysfunction, and need for postoperative reintubation (20). Patients with a mean blood glucose level >150 mg/dL during the 3 days after a cardiovascular surgical procedure have double the infection rate and up to 13 times the mortality of their normoglycemic counterparts (8). Hyperglycemia is associated with a 9-fold and a 2-fold increase in mortality during hospitalization among those with new-onset hyperglycemia and those with a known history of diabetes, respectively (1). The results of these studies emphasize the importance of recognition of hyperglycemia in all inpatients, even those without a prior history of DM. As noted previously, less than half of the patients with hyperglycemia treated by us had a prior diagnosis of DM.

Treatment of hyperglycemia with insulin has been shown to reduce mortality, sepsis, ICU stay, need for dialysis, need for transfusion, and duration of ventilation in the postoperative setting (7). Furthermore, postoperative glycemic control has been shown to decrease postopera-

tive wound infections (8). On the basis of these studies, the American Diabetes Association and the American Association of Clinical Endocrinologists have put forward recommendations for inpatient management of hyperglycemia (11,12).

In this report, we describe a practical approach to identify and treat inpatient hyperglycemia. We have shown a substantial improvement in mean blood glucose level and percentage of blood glucose values reported in the target glucose range (80 to 150 mg/dL) and in what has been termed the clinically acceptable range (80 to 180 mg/dL) (12) at our institution with the use of easy-to-follow insulin protocols guided by a formal management service. This change has been accomplished safely with no increase in hypoglycemia in comparison with historical methods of glycemetic management.

The limited number of patients treated thus far has not allowed us to evaluate the effect of this service on morbidity and mortality outcomes. On the basis of the results of other studies, however, we would expect similar clinical benefits. Our results are limited to the inpatient surgical services, and extrapolation to other inpatient populations may not be appropriate. Nevertheless, one could argue that the complicated clinical environment characteristic of the current inpatient experience necessitates a focused specialized approach to hyperglycemia in all such patients. Hyperglycemia has been associated with a poor clinical outcome in a variety of other patient populations, including those admitted to the hospital with a diagnosis of congestive heart failure (21), stroke (2), and acute myocardial infarction (22), and improved glycemetic control has been shown to benefit the last-mentioned group of patients.

The use of advanced practice nurses as the cornerstone of inpatient hyperglycemia management, in conjunction with supervision by a board-certified endocrinologist, has proved effective and financially viable. Revenue generated by the GMS consultation activity at the current census has been able to provide salary support for 2 full-time advanced practice nurses, an administrator, and 25% of a supervising physician's salary.

CONCLUSION

In summary, we have developed strategies to identify inpatient hyperglycemia and validated protocols dedicated to the achievement of strict glycemetic goals. With use of these interventions, we have made substantial improvements in glycemetic control on our surgical inpatient services. These efforts have been undertaken without jeopardizing patient safety and have, in fact, reduced the frequency of hypoglycemia. The protocols and GMS have been well received by the inpatient nursing and surgical staff members, and all of this has been done in a cost-effective manner. Analyses of long-term health outcome

data in patients managed with use of these protocols are now in progress.

DISCLOSURE

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APPENDIX 1

INTRAVENOUS INSULIN INFUSION ORDERS

1. Start the insulin infusion when blood glucose is greater than 110 mg/dL
2. If the initial blood glucose is greater than 300 mg/dL, draw a STAT Basic Chemistry Panel and notify the managing service with results.
3. Blood Glucose
 - A. Check values hourly until the value is in goal range (80-110 mg/dL) for 2 hours
 - B. If within goal range, decrease checks to every
 - 2 hours (in ICU) 4 hours (in General Care areas)
 - Other _____
 - C. If glucose meter reading is greater than 400 mg/dL, obtain a blood glucose sample for chemistry laboratory confirmation and quantification. Do not wait for laboratory results, adjust treatment.
4. Check serum potassium every _____ hours
5. When the blood glucose concentration is less than 180 mg/dL and if the patient is not on enteral or parenteral nutrition, discontinue the current IV fluids. Start IV glucose.
 - Dextrose 10% in water at _____ mL/hour
 - Dextrose 5% in water at _____ mL/hour
 - Dextrose 5%/sodium chloride 0.9% at _____ mL/hour
 - Dextrose 5%/sodium chloride 0.45% at _____ mL/hour
 - Dextrose _____ % in _____ at _____ mL/hour
6. Prime tubing with 20 mL of the insulin infusion solution. Repeat this process with any tubing changes.
7. Bolus and initiate insulin as per Table I.

TABLE 1. INITIAL INSULIN DOSE AND INFUSION RATES

| INITIAL BLOOD GLUCOSE VALUE | INITIAL BOLUS DOSE (UNITS) | INFUSION RATES (UNITS/HOUR) |
|-----------------------------|----------------------------|-----------------------------|
| 110 - 180 | 2 | 2 |
| 181 - 240 | 3 | 3 |
| 241 - 300 | 4 | 4 |
| 301 - 360 | 5 | 5 |
| 361 - 420 | 6 | 6 |
| 421 - 480 | 7 | 7 |

8. Titrate the infusion based on current blood glucose and rate of blood glucose change according to Table 2 or Table 3 on page 3.
9. RN to document each insulin infusion rate change in the orders according to protocol

APN Signature _____
OR

INTRAVENOUS INSULIN INFUSION ORDERS

10. For blood glucose less than 60 mg/dL
 - A. Stop insulin infusion
 - B. If patient can take orally, give 15 g of fast-acting carbohydrate (4 oz. fruit juice/non-diet soda, 8 oz nonfat milk, or 3-4 glucose tablets).
 - C. If patient cannot take orally, give 50% dextrose IV
 - If patient awake and appropriately responsive: administer 25 mL
 - If patient not appropriately responsive: administer 50 mL
 - D. Recheck blood glucose every 20 minutes and repeat 25 mL of 50% dextrose IV if less than 60 mg/dL (notify service if less than 40 mg/dL after first dose of dextrose)
 - E. Restart insulin infusion at 50% of the previous setting once blood glucose is greater than 110 mg/dL on 2 consecutive checks 20 minutes apart.
11. Notify service for:
 - A. Blood glucose change (increase or decrease) of greater than 100 mg/dL in one hour.
 - B. Blood glucose greater than 400 mg/dL on two consecutive readings
 - C. Hypoglycemia requiring more than one dose of IV dextrose (per protocol in step 10)
 - D. For serum potassium less than 3.5 mEq/L or greater than 5.5 mEq/L
 - E. If blood glucose not within target range within 8 hours after starting the insulin infusion
12. Consults:
 - Diabetes Education Service (extension 6-4710)
 - Clinical Nutrition
 - Endocrine Diabetes Management Service (page 5-4385)
 - Other: _____

APN Signature _____
OR

INTRAVENOUS INSULIN INFUSION ORDERS

TABLE 2. INCREASING Blood Glucose

| CURRENT BLOOD GLUCOSE | BOLUS REGULAR INSULIN | CHANGE FROM PREVIOUS BLOOD GLUCOSE | |
|-----------------------|-----------------------|------------------------------------|-----------------------------------|
| | | INCREASE | |
| | | Less than 60 mg/dL | Greater than 60 mg/dL |
| 80 - 110 mg/dL | No Bolus | No change | No change |
| 111-180 mg/dL | 2 units | INCREASE infusion by 0.3 units/hr | INCREASE infusion by 0.5 units/hr |
| 181-240 mg/dL | 3 units | INCREASE infusion by 0.8 units/hr | INCREASE infusion by 1 unit/hr |
| 241-300 mg/dL | 4 units | INCREASE infusion by 1 unit/hr | INCREASE infusion by 1.2 units/hr |
| 301-360 mg/dL | 5 units | INCREASE infusion by 1.5 units/hr | INCREASE infusion by 1.8 units/hr |
| 361-420 mg/dL | 6 units | INCREASE infusion by 2 units/hr | INCREASE infusion by 2.5 units/hr |
| 421-480 mg/dL | 8 units | INCREASE infusion by 3 units/hr | INCREASE infusion by 4 units/hr |

TABLE 3. DECREASING Blood Glucose

| CURRENT BLOOD GLUCOSE | CHANGE FROM PREVIOUS BLOOD GLUCOSE | | |
|-----------------------------------|------------------------------------|-----------------------|--|
| | DECREASE | | |
| | Less than 60 mg/dL | Bolus Regular Insulin | Greater than 60 mg/dL |
| Less than 60 mg/dL (Hypoglycemia) | <i>(follow step #10 on page 2)</i> | | |
| 61-80 mg/dL | STOP Infusion* | NO BOLUS | STOP Infusion* |
| 81-110 mg/dL | No change | NO BOLUS | DECREASE infusion by 50% of current rate |
| 111-180 mg/dL | INCREASE infusion by 0.3 units/hr | NO BOLUS | DECREASE infusion by 30% of current rate |
| 181-240 mg/dL | INCREASE infusion by 0.5 units/hr | 2 units | NO change, NO BOLUS |
| 241-300 mg/dL | INCREASE infusion by 1 unit/hr | 3 units | NO change, NO BOLUS |
| 301-360 mg/dL | INCREASE infusion by 1.2 units/hr | 4 units | NO change, NO BOLUS |
| 361-420 mg/dL | INCREASE infusion by 1.5 units/hr | 5 units | NO change, NO BOLUS |
| 421-480 mg/dL | INCREASE infusion by 2 units/hr | 6 units | NO change, NO BOLUS |

***Recheck blood glucose in one hour, restart infusion when blood glucose is greater than 110 mg/dL on 2 consecutive 20 minute checks. Restart infusion at 50% of the previous setting.**

APN Signature _____
OR

APPENDIX 2

PRINT ALL ORDERS

IMPRINT

PRESS VERY FIRMLY
USE BALL POINT PEN ONLY

ENDOCRINE SERVICE: Subcutaneous Insulin Orders

1. Check capillary blood glucose values QID (before meals and before bedtime snack)

2. Basal Insulin (Choose one):

Insulin glargine (Lantus) _____ units subcutaneously daily (at bedtime)

NPH Insulin _____ units subcutaneously at _____
_____ units subcutaneously at _____

3. Prandial Insulin (Choose one):

Insulin Lispro (Humalog) Insulin Aspart (NovoLog) Insulin Regular Insulin 70/30
_____ Units subcutaneously at breakfast
_____ Units subcutaneously at lunch
_____ Units subcutaneously at supper

4. Supplemental Insulin (Choose one insulin and one algorithm): to be administered **in addition** to scheduled prandial insulin dose and at bedtime

Insulin Lispro (Humalog) Insulin Aspart (NovoLog) Insulin Regular

Low Dose

| Capillary Blood Glucose | Supplemental Dose |
|-------------------------|-------------------|
| Less than 150 mg/dL | +0 |
| 150-199 mg/dL | +1 unit |
| 200-249 mg/dL | +2 units |
| 250-299mg/dL | +3 units |
| 300-349 mg/dL | +4 units |
| 350-400 mg/dL | +5 units |
| Greater than 400 mg/dL | Call service |

Medium Dose

| Capillary Blood Glucose | Supplemental Dose |
|-------------------------|-------------------|
| Less than 150 mg/dL | +0 |
| 150-199 mg/dL | +1 unit |
| 200-249 mg/dL | +3 units |
| 250-299mg/dL | +5 units |
| 300-349 mg/dL | +7 units |
| 350-400 mg/dL | +9 units |
| Greater than 400 mg/dL | Call service |

High Dose

| Capillary Blood Glucose | Supplemental Dose |
|-------------------------|-------------------|
| Less than 150 mg/dL | +0 |
| 150-199 mg/dL | +2 units |
| 200-249 mg/dL | +4 units |
| 250-299mg/dL | +7 units |
| 300-349 mg/dL | +10 units |
| 350-400 mg/dL | +13 units |
| Greater than 400 mg/dL | Call service |

Individualized Dose

| Capillary Blood Glucose | Supplemental Dose |
|-------------------------|-------------------|
| Less than 150 mg/dL | |
| 150-199 mg/dL | |
| 200-249 mg/dL | |
| 250-299mg/dL | |
| 300-349 mg/dL | |
| 350-400 mg/dL | |
| Greater than 400 mg/dL | Call service |

PHYSICIAN'S ORDERS

APN Signature _____

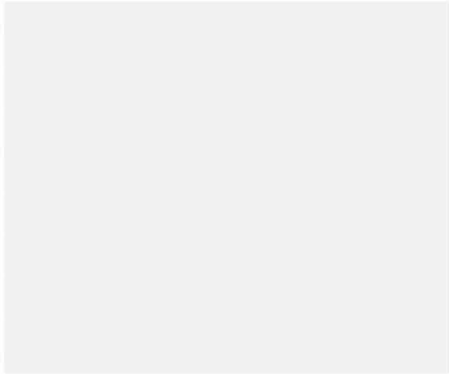
PRINT ALL ORDERS

IMPRINT

ENDOCRINE SERVICE: Subcutaneous Insulin Orders

PRESS VERY FIRMLY
USE BALL POINT PEN ONLY

- 5. For blood glucose less than 60 mg/dL
 - A. If patient can take by mouth give 15 grams of fast-acting carbohydrate (4 oz. fruit juice/non-diet soda, 8 oz. non-fat milk, or 3-4 glucose tablets).
 - B. If patient cannot take orally, give 50% dextrose, 25 mL
 - C. Check capillary blood glucose every 20 minutes until greater than 60 mg/dL. Repeat above if less than 60 mg/dL.



- 6. Notify service for:
 - A. Capillary blood values less than 40 or greater than 400 mg/dL
 - B. Change in dietary orders

- 7. Consults:
 - Diabetes Education Service (extension 6-4710)
 - Clinical Nutrition
 - Other _____

PHYSICIAN'S ORDERS

APN Signature _____