Glycemic Control in Hospitalized Patients Not in Intensive Care: Beyond Sliding-Scale Insulin

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Glycemic control in hospitalized patients who are not in intensive care remains unsatisfactory. Despite persistent expert recommendations urging its abandonment, the use of sliding-scale insulin remains pervasive in U.S. hospitals. Evidence for the effectiveness of sliding-scale insulin is lacking after more than 40 years of use. New physiologic subcutaneous insulin protocols use basal, nutritional, and correctional insulin. The initial total daily dose of subcutaneous insulin is calculated using a factor of 0.3 to 0.6 units per kg body weight, with one half given as long-acting insulin (the basal insulin dose), and the other one half divided daily over three meals as short-acting insulin doses (nutritional insulin doses). A correctional insulin dose provides a final insulin adjustment based on the preprandial glucose value. This correctional dose resembles a sliding scale, but is only a small fine-tuning of therapy, as opposed to traditional sliding-scale insulin alone. Insulin sensitivity, nutritional intake, and total daily dosing review can alter the physiologic insulin-dosing schedule. Prospective trials have demonstrated reductions in hyperglycemic measurements, hypoglycemia, and adjusted hospital length of stay when physiologic subcutaneous insulin protocols are used. Transitions in care require special considerations and attention to glycemic control medications. Changing the sliding-scale insulin culture requires a multidisciplinary effort to improve patient safety and outcomes. (*Am Fam Physician.* 2010;81(9):1130-1135. Copyright © 2010 American Academy of Family Physicians.)

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In the United States, the prevalence of diabetes mellitus is now 10.8 percent of adults 20 years and older, and 23.1 percent of adults 60 years and older.[1] An estimated one in five U.S. health care dollars is spent caring for someone with diabetes.[2] Over the past 10 years, the Agency for Healthcare Research and Quality reports a 26 percent increase in hospital discharges with a primary diagnosis of diabetes,[3] as coded in the *International Classification of Diseases, Ninth Revision*, yet glycemic control of hospitalized, non-critically ill patients with diabetes remains suboptimal in most U.S. hospitals and academic medical centers.[4] The adverse clinical consequences of poor glycemic control and its contribution to the hospitalized patient's length of stay are well documented.[5,6] Reliance on sliding-scale insulin contributes greatly to this knowledge-performance gap. Physicians caring for hospitalized patients with diabetes should adopt new strategies of subcutaneous insulin therapy to improve outcomes.

Defining Optimal Glucose Targets for Hospitalized Patients

Table 1 summarizes upper glucose limits for optimal glycemic control from guidelines developed by the American Association of Clinical Endocrinologists (AACE),[7] the American Diabetes Association (ADA),[8] and the Society of Hospital Medicine (SHM).[9] These organizations have consensus recommendations to abandon traditional sliding-scale insulin as the sole method for glycemic control. Their guidelines identify two inpatient populations—the patients in critical care who typically require admission to an intensive care unit (ICU) and intravenous insulin infusions; and the patients with diabetes who are not in an ICU and are traditionally treated with oral agents and subcutaneous insulin.

Evidence Against Sliding-Scale Insulin

The sliding scale for insulin dosage that is based on levels of glycosuria was introduced in 1934,[10] and the technique was gradually adapted to blood glucose measurements.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Traditional sliding-scale insulin should be abandoned as the sole means of controlling blood glucose levels in hospitalized patients.	B	7, 8, 9 11, 14
Physiologic subcutaneous insulin protocols with basal, nutritional, and correctional components should be used for patients with diabetes mellitus who are hospitalized (non-ICU).	B	18, 20, 21, 22
Long-acting insulin should be used for physiologic basal insulin.	B	18, 19, 20, 21, 22
Short-acting insulin should be used for physiologic nutritional and correctional insulin.	B	18, 20, 21, 22
Discontinuing outpatient oral diabetic medications should be considered upon hospitalization of patients who are not in an ICU.	C	8, 24, 26
Insulin therapy should be continued upon hospital discharge of capable patients already on two or more oral diabetic medications and with an admission A1C greater than 10 percent.	C	6, 21, 23
An A1C level should be obtained upon admission if none performed within the past 30 days.	C	7, 8, 18, 21

ICU = intensive care unit.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.xml.

Table 1. Upper Limits for Glycemic Control in Hospitalized Patients

Organization	*Blood glucose limits in intensive care units*	*Blood glucose limits in general care units*
American Association of Clinical Endocrinologists[7]; American Diabetes Association[8]	140 to 180 mg per dL (7.77 to 9.99 mmol per L)	Preprandial: 140 mg per dL All others: < 180 mg per dL
Society of Hospital Medicine[9]	110 to 140 mg per dL (6.11 to 7.77 mmol per L)	Preprandial: 130 mg per dL (7.21 mmol per L) All others: 180 mg per dL

Information from references 7 through 9.

Medical articles have questioned the effectiveness of sliding-scale insulin since at least 1970[11]; a Medline search of 52 trials from 1966 to 2003 showed no clinical trials demonstrating benefit from sliding-scale insulin[12]; and most experts currently question the effectiveness and safety of traditional sliding-scale insulin.[13] A retrospective observational study to determine the effectiveness of sliding-scale insulin therapy at a university hospital reported that patients had hyperglycemic glucose levels on 84 percent of measurements.[14] Although normal glucose levels were infrequently achieved, adjustment of sliding-scale insulin occurred in only 19 percent of participants.[14]

The largest prospective cohort study to date revealed that sliding-scale insulin regimens failed to adequately control hyperglycemia, resulted in high rates of hypoglycemia, and were associated with longer hospital stays.[15] Patients treated with sliding-scale insulin alone had blood glucose levels greater than 300 mg per dL (16.65 mmol per L) three times more often than patients treated with other glucose-lowering therapies. Most patients treated with sliding-scale insulin in this study never had their regimens adjusted, despite poor glycemic control. The authors concluded that although sliding-scale insulin regimens were prescribed for the majority (76 percent) of general medical inpatients with diabetes, they appeared to provide no benefit and, when used without a standing dose of long- or intermediate-acting insulin, were associated with an increased rate of hyperglycemic episodes.[15]

Traditional sliding-scale insulin regimens measure blood glucose taken preprandially and at bedtime if the patient is eating, or on a schedule of every six hours if the patient is taking nothing by mouth. The amount of regular insulin given is based on the fingerstick glucose level. Sliding-scale insulin does not take into account basal insulin needs, diet (type and amount), and personal characteristics (e.g., weight) or insulin history (e.g., previous demonstrated insulin need, insulin sensitivity or resistance). Sliding-scale insulin is a reactive approach to glucose elevation control. It is not a proactive strategy to prevent hyperglycemic states.[16,17] Using sliding-scale insulin is playing catch-up with the glucose reading, and it usually does not treat sufficiently or aggressively enough to maintain glucose levels in a normal range.

In most sliding-scale insulin regimens, the physician is only notified of extremes of hypoglycemia (i.e., blood glucose less than 60 mg per dL [3.33 mmol per L]) or hyperglycemia (i.e., blood glucose greater than 300 mg per dL). Using sliding-scale insulin creates the possibility of insulin stacking, with the pharmacokinetics of regular

insulin given every six hours.[13] The sliding-scale insulin regimen has no way to anticipate nutritional status or illness-related changes in glucose levels, further leading to insulin inadequacies. These flaws in traditional sliding-scale insulin put patients on a roller coaster of fluctuations in blood glucose, which could be harmful.[13,14] Variations in blood glucose and insulin levels create oxidative stress, endothelial dysfunction, and increased markers of inflammation, which can contribute to poor patient outcomes.[5]

Although nurses find the traditional sliding-scale insulin regimen easy to use, the entire care team must prioritize the necessity for optimal glycemic control. The time has come to challenge clinical inertia and no longer accept the poor outcomes of this regimen.[12]

Evidence for Physiologic Subcutaneous Insulin Regimens

Research shows that subcutaneous insulin administration in the non-ICU hospitalized patient should include three components to be effective: basal insulin (to inhibit hepatic gluconeogenesis), nutritional insulin (to facilitate mealtime glucose metabolism), and correctional insulin (to provide real-time adjustment of insulin dosing based on the patient's insulin sensitivity).[18] The importance of a long-acting basal insulin is illustrated by a randomized controlled trial of insulin glargine (Lantus) compared with sliding-scale insulin in patients who had bariatric surgery.[19] Insulin glargine treatment resulted in superior glycemic control, with only three episodes of hypoglycemia in 926 measurements.[19] The addition of short-acting nutritional and correctional insulin to a basal long-acting insulin are current best-practice recommendations. Prospective observational studies have documented superior glycemic control with this three-pronged physiologic approach.[20]

The University of California-San Diego has a structured insulin protocol that produced significantly fewer hyperglycemic and hypoglycemic patient-days compared with sliding-scale insulin.[18] Results from the Brigham and Women's Hospital protocol showed increased days of euglycemia (i.e., blood glucose of 60 to 180 mg per dL [3.33 to 9.99 mmol per L]) and reduced adjusted length of stay in non-ICU hospitalized patients treated with the protocol compared with patients treated with sliding-scale insulin.[21]

The Randomized Study of Basal Bolus Insulin Therapy in the Inpatient Management of Patients with Type 2 Diabetes trial is the only prospective randomized controlled study that compared traditional sliding-scale insulin with a new basal-bolus subcutaneous insulin glargine (for long-acting insulin) and insulin glulisine (Apidra; for nutritional and supplemental doses).[20] Participants who received the basal-bolus insulin achieved blood glucose averages of 27 mg per dL (1.50 mmol per L) less than the participants who received sliding-scale insulin, with significantly more participants in the basal-bolus group who had levels below the target blood glucose level of 140 mg per dL (7.77 mmol per L), and no significant difference in hypoglycemia.

Physiologic Subcutaneous Insulin Protocols

Practical guidelines for implementing physiologic subcutaneous insulin have been published.[18,21,22] These regimens are designed for patients with type 1 or 2 diabetes who are not in diabetic ketoacidosis, and for patients with newly discovered hyperglycemia during a hospital stay (i.e., those with random blood glucose levels greater than 180 mg per dL or two or more fasting blood glucose values greater than 130 mg per dL [7.21 mmol per L]). Implementing quality protocols is neither simple nor accomplishable in a single week because it involves a change in the medical culture. This multidisciplinary change includes detailed education of physicians, nurses, and dietary and pharmacy professionals to ensure that all are working to replace sliding-scale insulin with more effective strategies. *Table 2* summarizes the key concepts of any protocol promoting the use of physiologic subcutaneous insulin.[18,21]

Subcutaneous insulin administration in the non–intensive-care hospitalized patient should include basal, nutritional, and correctional insulin doses.

Physiologic insulin regimens that used the basal, nutritional, and correctional insulin approach were thoroughly reviewed for best practices by the 2007 to 2008 SHM Glycemic Control Task Force. These results and best practices are available at SHM's online glycemic control resource room (http://www.hospitalmedicine.org/ResourceRoomRedesign/GlycemicControl.cfm). The ADA, AACE, and SHM published the University of California-San Diego protocol in their task force document as the highlighted best practice,[7,18] but other institutional protocols might better fit individual needs and hospital resources (for more information, visit http://www.hospitalmedicine.org/ResourceRoomRedesign/html/12Clinical_Tools/00_Clinical_Landing.cfm).

Although most patients use different regimens in the hospital than at home, the benefit will be uniform, and coordinated implementation from the entire care team

Table 2. Physiologic Subcutaneous Insulin Guidelines

Step	*Action*	*Comment*
1	Measure blood glucose before meals and at bedtime, or every six hours if nothing by mouth; stop oral agents; order A1C if none obtained in past 30 days	Initiate protocol for patients with known diabetes mellitus and anyone with two or more random blood glucose readings > 180 mg per dL (9.99 mmol per L) or fasting glucose > 126 mg per dL (6.99 mmol per L)
2	Calculate initial total daily dose of insulin	0.3 units per kg: underweight; older age; hemodialysis 0.4 units per kg: normal weight 0.5 units per kg: overweight ≥ 0.6 units per kg: obese; glucocorticoids; insulin resistance
3	Order 50 percent of the total daily dose as long-acting basal insulin	Insulin glargine (Lantus) every 24 hours, or insulin isophane (NPH) or detemir (Levemir) every 12 hours
4	Order 50 percent of the total daily dose as short-acting nutritional insulin given in three divided doses zero to 15 minutes before meals (if eating) or before bolus tube feeds	If continuous tube or parenteral feeds, consider every six hour dosing of short-acting or regular insulin; hold if nothing by mouth
5	Select a scale of short-acting correctional insulin given zero to 15 minutes before meals	Use patient's insulin sensitivity as a guide for initial scale selection
6	Subsequent daily adjustment of total daily dose based on previous day's total units given	—

EXAMPLE: A 50-year-old man with diabetes who is 180 cm (71 in) tall and weighs 90 kg (198 lb) is admitted for pneumonia treatment with a random blood glucose level of 300 mg per dL (16.65 mmol per L) and an A1C level of 10.8 percent; oral diabetic agents are discontinued, and blood glucose testing is ordered before meals and at bedtime.

Calculated total daily dose of insulin: 0.5 units per kg × 90 kg = 45 units

Ordered: 23 units of insulin glargine taken once daily (50 percent of total daily dose) and 7 units of insulin aspart (Novolog) taken zero to 15 minutes before meals (50 percent of total daily dose, in three divided doses); based on glucose readings, give additional aspart per standard correctional insulin schedule in Table 4.

Information from references 18 and 21.

ensures better outcomes. It is recommended that hospital teams establish a target glucose range *(Table 1)*.[7-9] Higher targets may be preferable when initiating a hospital-wide change, for patients who are in palliative care, and for patients with multiple hypoglycemia risk factors (e.g., advanced age, hemodialysis, low body weight). Success in lowering target glucose levels from 200 mg per dL (11.10 mmol per L) to 110 mg per dL (6.11 mmol per L) has been demonstrated over several years for patients receiving intravenous insulin by building upon physician and nursing staff education, encouraging acceptance, and rewarding good performance.[23]

Most protocols strongly advocate the use of the basal insulins glargine or detemir (Levemir), except in pregnant patients because these insulins are class C.[16,18,21] Isophane insulin (NPH) historically has been used safely in pregnancy. Nutritional insulin in patients who are eating requires coordination with nursing and dietary staff for timing the doses zero to 15 minutes before each meal. *Table 3* outlines the types of insulin used for physiologic subcutaneous insulin protocols.[16]

In situations where the patient may not be sure about eating, the insulin should be withheld until after the meal. Special situations (e.g., nothing by mouth, continuous tube feeding, total parenteral nutrition, glucocorticoid therapy) are reviewed in detail on SHM's online glycemic control resource room. Correctional insulin dosing *(Table 4*[21]*)* should not be confused with traditional sliding-scale insulin. Correctional dosing of insulin fine tunes suboptimal glycemic control by offering

Table 3. Subcutaneous Insulins Used for Physiologic Protocols in Hospitalized Patients

Type of insulin	*Time of onset*	*Duration of action*
Basal insulin		
Glargine (Lantus)	1 to 2 hours	24 hours
Detemir (Levemir)	1 to 2 hours	18 to 24 hours
Isophane (NPH)*	1 to 2 hours	10 to 20 hours
Nutritional and correctional insulin		
Lispro (Humalog), aspart (Novolog), glulisine (Apidra)†	5 to 15 minutes	3 to 6 hours
Regular human insulin‡	1 to 2 hours	6 to 10 hours

**—Dose every 12 hours.*

†—If patient is eating, dose zero to 15 minutes before meals.

‡—Consider dosing for every six hours only if patient is taking nothing by mouth or is on continuous parenteral or tube feeding.

Adapted with permission from Michota F. What are the disadvantages of sliding-scale insulin? J Hosp Med. *2007;2(suppl 1):22.*

the flexibility of adding insulin beyond the calculated nutritional dose.

Transitions of Care

It is a challenge to transition patients with hyperglycemia across various care settings. Variables affecting glycemic control include the previous level of control (as represented by A1C level), current dietary intake, and the severity of illness and associated hyperglycemia.[24] Oral medications prove difficult to use and present their own concerns during inpatient use. Changing renal function and potential use of contrast dye are contraindications to metformin (Glucophage) use.[25] Changes in diet and caloric intake can lead to an increase in hypoglycemic episodes when sulfonylureas are used. In general, oral medications should be stopped on hospital admission and insulin protocols should be initiated.[24,26] Patients who were using an insulin regimen as outpatients can be converted to the hospital protocol initially on a unit-for-unit ratio before making individualized adjustments for patient variables. Outpatient regimens with a high ratio of basal insulin should be modified so that only 50 to 60 percent of long-acting insulin is used.[24]

Transitioning patients from insulin infusions used in critical care settings to the subcutaneous regimens used on general hospital wards requires adjustment of the hyperglycemic regimen. The insulin dose given to the patient during the previous six hours should be extrapolated to a 24-hour dose, and then reduced by 20 percent as a safety factor to calculate the new total daily dose.[27] The total daily dose is then divided according to the guidelines in *Table 2*.[18,21] It is important to give the basal insulin injection at least one to two hours before discontinuation of the insulin infusion to prevent rebound hyperglycemia. If a faster discontinuation of the infusion is required, a portion of basal insulin is given with a more rapid analog to cover until the basal insulin can take effect or preferred administration time is reached.[26] If the patient is starting to eat and the infusion can be continued, bolus insulin injections are added in addition to the drip to cover these new requirements.[24]

The final transition of care occurs with patient discharge to home. Considerations include the discharge location, the patient's ability to comply with therapy, and, perhaps most importantly, the level of glycemic control at admission.[24] For patients who were adequately controlled before admission (i.e., A1C level was below target goal), discharge on their home therapy is appropriate.[28] However, for patients who were admitted with an elevated A1C level, the addition of another oral agent or basal insulin should be considered.[28] Insulin is preferred if the patient was admitted while taking two or more oral medications. For patients with poor glycemic control (i.e., A1C level greater than 10 percent), the physician should consider continuing a basal-bolus regimen as long as the patient will monitor blood glucose aggressively and has been educated on the new regimen.[24] In this circumstance, the basal insulin requirements can often be maintained, but less bolus insulin prescribed to account for less acute stress. For patients who were not treated by their primary care physician during hospitalization, it is important to communicate treatment changes to their primary care physician.[19]

Table 4. Correctional Insulin Dosing

Blood glucose level	*Insulin-sensitive dosing (units of insulin)**	*Standard dosing (units of insulin)†*	*Insulin-resistant dosing (units of insulin)‡*
150 to 199 mg per dL (8.32 to 11.04 mmol per L)	1	1	2
200 to 249 mg per dL (11.10 to 13.82 mmol per L)	2	3	4
250 to 299 mg per dL (13.88 to 16.59 mmol per L)	3	5	7
300 to 349 mg per dL (16.65 to 19.37 mmol per L)	4	7	10
> 349 mg per dL	5 + call	8 + call	12 + call

**—Total daily dose: less than 40 units.*

†—Total daily dose: 40 to 80 units.

‡—Total daily dose: greater than 80 units.

Adapted with permission from Schnipper JL, Ndumele CD, Liang CL, Pendergrass ML. Effects of a subcutaneous insulin protocol, clinical education, and computerized order set on the quality of inpatient management of hyperglycemia: results of a clinical trial. J Hosp Med. *2009;4(1):25.*

Glycemic "Never Ever" Events

In October 2008, Medicare announced that hospitals would no longer be paid for hospital-acquired diabetic ketoacidosis, hyperglycemic coma, or hypoglycemic coma.[29] This is further incentive for hospitals to adopt physiologic subcutaneous insulin protocols. To avoid hypoglycemia, insulin regimens should be modified if the patient's blood glucose level is less than 70 mg per dL (3.89 mmol per L).[7]

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