

Insulin Use in Hospitalized Patients With Diabetes: Navigate With Care

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“A man walks into a bar . . .” These classic words introduce countless humorous situations.

“A man enters a hospital . . .” Unfortunately, these words introduce distinctly serious situations that occur at the rate of > 35 million per year across the United States.¹ These words introduce a story in people’s lives that all too often includes mistakes, misadventures, and even preventable deaths.

The hospital is a dangerous place. Approximately one-third of all deaths in this country occur in hospitals.^{2,3} On any given day, up to 30% of all hospitalized patients have diabetes, placing almost one-third of inpatients at greater risk for complications that may adversely affect their hospital stay. The majority of these hospitalized patients with diabetes are treated with insulin, a medication that occupies a prominent place on the list of high-alert medications of the Institute for Safe Medication Practices.⁴ It is the leading medication implicated in adverse events requiring treatment in a hospital emergency department.⁵ Moreover, insulin is responsible for more drug errors during acute hospital care than other commonly used hospital medications.⁶

What is the best approach to using insulin in the hospital setting? What skills and knowledge must providers have to make the most effective use of insulin and yet minimize the danger of hypoglycemia? There are no simple answers for these questions.

As depicted in Figure 1, a single hospitalization often involves multiple transitions, each requiring a careful approach to insulin therapy.

The transitions begin when patients enter the hospital. Patients may be admitted to a ward or to the intensive care unit (ICU), proceed directly to the operating room, or undergo various invasive procedures. Patients then move within the hospital among different levels of care with overlapping or sequential interventions such as nothing-by-mouth (nil per os [NPO]) status, enteral or parenteral feeding, medications that may worsen glyce-mic control, and hemodialysis. The clinical course may be influenced by existing or newly developing clinical conditions such as renal or hepatic failure that change the metabolism of insulin. Finally, patients transition back to an outpatient setting, either directly to their home or to an intermediate setting such as a rehabilitation or skilled-nursing facility.

Thus, distinct features of every hospitalization include 1) the fluidity of the clinical situation, with changes in clinical status and need for interventions; 2) difficulty predicting or planning for when an event will occur (e.g., imaging, surgery, cancellations, NPO status, or timing of meals); and 3) numerous opportunities for breakdowns in communication among teams and various care providers at all levels.

We propose a framework in which to consider insulin therapy in the hospital setting, a basic paradigm for starting and managing insulin therapy, with special considerations for specific situations (Table 1). This brief review will focus on practical aspects of glycemic management of patients with diabetes outside of the ICU setting. It will not include inpatient management of hyperglycemia in patients without diabetes or

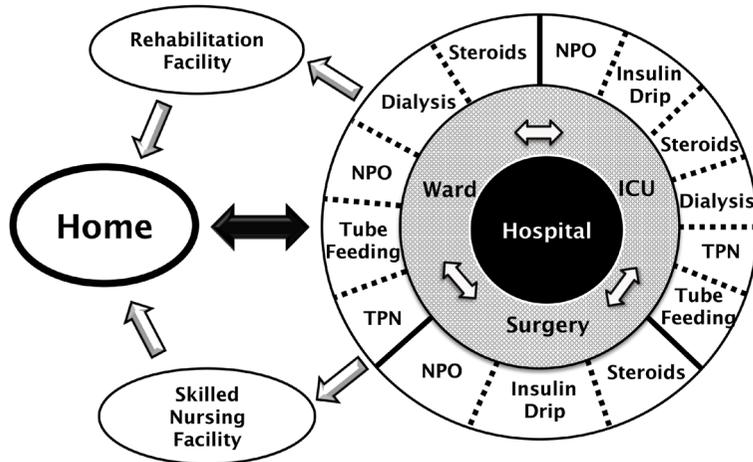


Figure 1. For patients with diabetes, a single hospitalization may involve multiple transitions. Each transition requires a careful approach to insulin therapy. Patients may be admitted to a ward or to the ICU or proceed directly to surgery. They may then receive different levels of care with overlapping or sequential interventions such as NPO status, enteral nutrition by tube feeding, or total parenteral nutrition (TPN); medications such as steroids that may worsen glycemic control; and dialysis. Patients transition back to an outpatient setting, either directly to their home or to an intermediate setting such as a rehabilitation or skilled-nursing facility. The clinical situation may shift frequently, with numerous opportunities for breakdowns in communication among teams and various care providers at all levels.

other important aspects of optimal diabetes care in the hospital such as patient and staff education or dietary considerations.⁷

Transitioning from Home to Hospital

A key aspect of the basic paradigm of insulin use in the hospital is an evaluation of patients' glycemic regimen with a current or recent A1C and review of hypo- and hyperglycemia before hospitalization. Higher A1C levels are associated with a greater risk for hospitalization.⁸ Thus, patients with diabetes who are admitted to the hospital are likely to have poorer glycemic control.

In a majority of patients, the first steps in planning for diabetes care in the hospital are the discontinuation of oral glucose-lowering agents and initiation of insulin therapy.⁹ Patients may be unable to take oral medications, or they may have contraindications to the use of non-insulin glucose-lowering agents while hospitalized. The use of glucagon-like peptide-1 (GLP-1) agonists or dipeptidyl peptidase-4 (DPP-4) inhibitors may prove to be beneficial in select inpatient populations, but

there are insufficient data at this time to support continuing these medications in the hospital setting.

In addition, all patients with diabetes admitted to the hospital should have 1) blood glucose monitoring at least before meals and at bedtime,

2) clear parameters and instructions for institution of a hypoglycemia protocol, and 3) the diagnosis of diabetes clearly indicated in hospital documentation. Clinicians should also have patients' inpatient glycemic goals in mind. For patients admitted to a general medical ward, the glycemic goal range may be 110–140 mg/dl preprandially and 140–180 mg/dl postprandially.⁹

Selecting initial insulin doses in the hospital. Overall, we highly recommend the use of scheduled doses of insulin rather than “sliding-scale” insulin. The scheduled-dose insulin regimen is divided into three components: basal, nutritional, and correctional (supplemental) doses.

Selecting an initial basal insulin dose

For patients treated with insulin before hospitalization, the daily insulin dose adjusted for the level of pre-hospitalization glycemic control would be a reasonable starting dose. If patients who are treated with a basal-bolus regimen have nutrition withheld on admission to the hospital (NPO status), only the basal component should be used. Importantly, patients with type 1 diabetes must never be left without basal insulin.

For patients whose diabetes is managed by diet and lifestyle only

Table 1. Basic Paradigm for Insulin Therapy in Hospitalized Patients With Diabetes

Home to Hospital

- Evaluate patient's outpatient glycemic control; quick review of glucose patterns and current or recent A1C
- Decide on patient's inpatient glycemic goals
- Write orders:
 - Discontinue most, if not all, noninsulin glucose-lowering medications
 - Schedule point-of-care glucose monitoring
 - Provide clear instructions and parameters for management of hypoglycemia
 - Schedule insulin dosing

In the Hospital

- Evaluate blood glucose records (both point-of-care and in laboratory test results) daily
- Adjust insulin daily, if needed
- Consider planned discharge regimen

Hospital to Outpatient Setting

- Consider key factors that may limit feasibility and complexity of the outpatient regimen
- Modify previous outpatient regimen in many cases
- Schedule timely outpatient follow-up

Table 2. Suggested Initial Insulin Doses in Hospitalized Patients With Diabetes

Scheduled insulin doses, rather than “sliding-scale” insulin, are highly recommended and should consist of basal, nutritional, and correctional doses.

Basal Insulin

Pre-hospital glucose control, as measured by A1C (%)	Initial Basal Insulin Dose (units/kg body weight/day)	
	BMI < 28 kg/m ²	BMI ≥ 28 kg/m ²
< 8	0.2	0.3–0.4
8–9	0.3–0.4	0.4–0.5
> 9	0.5–0.6	0.6–0.8

- Precautions regarding using the home dose of basal insulin for patients on basal insulin pre-hospitalization:
 - If the patient’s A1C is < 7.5–8%, use a dose lower than the outpatient basal insulin dose
 - Because some patients’ outpatient basal insulin covers nutritional needs in addition to basal needs, the basal insulin dose ordered for hospitalization should be lower than the outpatient basal insulin dose. Clues that this may be the case:
 - Basal insulin dose much > 50% of the total daily insulin dose for patients on a basal-bolus insulin regimen
 - Patient has a total basal insulin dose > 1 unit/kg body weight/day

Nutritional Insulin

Nutritional Status	Suggested Dosing
NPO	No nutritional insulin ordered
Taking food by mouth	
Consumes < 25% of meal	Do not administer nutritional insulin
Consumes ≥ 25% of meal	Full nutritional insulin dose before each meal

Correctional Insulin

Patient Circumstances	Suggested Dosing
Patients with a BMI < 28 kg/m ² or other factors decreasing insulin requirements (e.g., decreased clearance of insulin from renal insufficiency) and those with prior multiple episodes hypoglycemia	
Pre-meal	1 unit for every 50 mg/dl that blood glucose is elevated above target (e.g., 150 mg/dl)
Bedtime	1 unit for every 50 mg/dl that blood glucose is elevated above target (e.g., 200 mg/dl)
Patient with a BMI ≥ 28 kg/m ² or other factors increasing insulin resistance (e.g., previous poor glycemic control)	
Pre-meal	1 unit for every 25 mg/dl that blood glucose is elevated above target (e.g., 150 mg/dl)
Bedtime	1 unit for every 25 mg/dl that blood glucose is elevated above target (e.g., 200 mg/dl)

or who are on noninsulin glucose-lowering agents and have relatively well-controlled diabetes (arbitrarily defined as an A1C < 8%), a good starting point would be to institute a daily basal dose of subcutaneous insulin at 0.2 units/kg body weight/day, along with rapid-acting insulin at a set dose before meals (see below). For overweight or obese patients who are likely to be more insulin resistant and for those with less well-controlled glycemia as an outpatient (an A1C of 8–9%), the starting dose of basal insulin could be higher,

ranging from 0.3 to 0.5 units/kg body weight/day. For patients with very poorly controlled diabetes as an outpatient (an A1C > 9%), an even higher basal dose of insulin may be instituted, ranging from 0.5 to 0.8 units/kg body weight/day. Conversely, for patients with an A1C ≤ 7.5% or frequent hypoglycemia, the initial starting basal dose of insulin in the hospital should be reduced accordingly.

If the home dose of basal insulin is to be used, some precautions must be taken into consideration. For

patients with an A1C < 7.5–8%, a dose lower than the outpatient basal insulin dose should be considered. In addition, because some patients’ outpatient basal insulin covers nutritional needs in addition to basal needs, the basal insulin dose ordered for hospitalization should be lower than the outpatient basal insulin dose. Clues that this may be the case include 1) a basal insulin dose much > 50% of the total daily insulin dose for patients on a basal-bolus insulin regimen or 2) a total basal insulin dose > 1 unit/kg body weight/day.

These recommendations are summarized in Table 2.

Selecting initial nutritional and correctional insulin doses

Having selected a basal dose of insulin, attention should be shifted to nutritional-correctional doses of rapid-acting insulin, also known as “mealtime insulin.” The rapid-acting insulin protocol should include a safety measure such as a “no carbohydrates” scale with correction dose insulin only for patients who are NPO or consume < 25% of the calories on their meal tray (Table 2). The rapid-acting insulin modification scale used at our institution also includes a separate correction factor for bedtime that is more conservative than the “no carbohydrates” scale to minimize the risk of nocturnal hypoglycemia.

For patients on a sophisticated intensive insulin regimen at home, there is the option of ordering a customized rapid-acting insulin modification scale that includes an insulin-to-carbohydrate ratio and a correction/sensitivity factor determined by the provider.

However, for most patients consuming meals in the hospital, the total daily dose of rapid-acting insulin should be roughly equal to the total basal insulin dose and divided among three meals. A reasonable correction/sensitivity factor could be either 1 unit for every 25 mg/dl that blood glucose is elevated above goal or 1 unit for every 50 mg/dl that blood glucose is elevated above goal, with a preprandial blood glucose goal of 110–140 mg/dl (Table 2).

A crucial component of successful insulin therapy in the hospital is synchrony between meals and insulin administration. In many hospitals, meal-time insulin is administered immediately after meals to minimize the risk of hypoglycemia. This is done to avoid situations in which patients do not eat after receiving insulin. If the policy of administering insulin after meals is instituted, a great deal of effort should be directed at providing insulin as soon after meal consumption as possible.

The daily evaluation of blood glucose monitoring records is also of paramount importance. Clinicians

must review point-of-care glucose records and plasma glucose on chemistry panels for episodes of hyper- and hypoglycemia and make adjustments daily as needed. If correction doses of rapid-acting insulin were used, these must be incorporated into the total daily insulin dose, as additional basal insulin and/or nutritional insulin.

If there has been an episode of hypoglycemia (glucose < 70–80 mg/dl), the precipitating cause should be determined. Was it because of mistimed insulin administration and a delayed meal? Was insulin given in the setting of a missed meal? Did the patient consume less of a meal than expected? Was there overestimation of the carbohydrate content of the meal? Was there stacking of correction dose insulin, with corrections given too frequently?

If any of these factors contributed to the hypoglycemia, a problem-solving approach should be used. If not, then the total daily dose of insulin should be reduced, possibly by 10–20% or more, depending on the specific glucose levels observed. Which dose(s) of insulin should be reduced would depend on what time of day the hypoglycemia occurred.

Transitions Within the Hospital

There is often confusion about the optimal way to dose insulin when patients with diabetes are NPO for a radiological procedure, a surgery, or because the clinical condition necessitates it. Often, basal insulin may be continued and the “no calories” rapid-acting insulin modification scale used. Continuing basal insulin and point-of-care glucose monitoring is particularly important for patients with type 1 diabetes or severe long-standing type 2 diabetes because a lack of insulin therapy may lead to very severe hyperglycemia and even to diabetic ketoacidosis (DKA).

The transition from an intravenous insulin infusion to a subcutaneous regimen while patients are in the ICU or when transitioning from the ICU to a ward may also cause problems. This is addressed in the next section.

Special Considerations

Transitioning from intravenous insulin infusion

There are various ways to transition patients with diabetes who are on an intravenous insulin infusion to subcutaneous insulin.^{10–14} Most patients on an insulin infusion are not eating because of the severity of their critical illness or other factors. In patients who are on a continuous insulin infusion for DKA, assuming that they have not yet started eating while on the insulin infusion, the total daily basal insulin requirement may be estimated by extrapolating from infused insulin received at a stable rate for at least 6–8 hours. The insulin infusion is discontinued 1–2 hours after the first dose of basal insulin is administered. If the next day’s scheduled basal dose of insulin is < 18 hours from the time of discontinuing the insulin infusion, we adjust the initial dose of basal insulin accordingly.

As above, scheduled doses of nutritional rapid-acting insulin are calculated by dividing the total daily basal dose by three and distributing the insulin across three meals.

Insulin and glucocorticoids

Administration of glucocorticoids worsens glycemic control in diabetes,^{15–17} presenting a significant challenge for inpatient management. The doses and frequency of glucocorticoid administration vary widely, and steroids may be tapered or stopped abruptly. Acute or short-term administration of methylprednisolone causes predominantly postprandial hyperglycemia that lasts 6–12 hours. Prednisone is similar to methylprednisolone, with hyperglycemic effects occurring 6–12 hours after administration, but dexamethasone has an even longer duration of action. In our experience, the effect of dexamethasone to increase insulin resistance and thus increase insulin requirements may last as long as 48–52 hours.

Because NPH insulin usually has an onset of action at 2–4 hours, a peak of action occurring at 6–8 hours, and a duration of action of 10–14 hours, it may be used at the time of methylprednisolone or pred-

nisone administration to counteract the hyperglycemic effect of these forms of glucocorticoid.^{18,19} NPH insulin can then be discontinued as soon as the glucocorticoid is discontinued, providing a safer option than having residual insulin action from high doses of long-acting insulin lasting for hours after discontinuation of steroids. The NPH insulin may be added to patients' existing insulin regimen and administered only as long as the patient is on glucocorticoids. Our rule of thumb is to use 0.5 units of NPH insulin/mg of prednisone or methylprednisolone, ranging between 0.25 and 1 unit of insulin/mg of glucocorticoid (Table 3).

Unfortunately, no systematic research has been published in patients receiving either multiple daily doses of glucocorticoids or in those receiving dexamethasone. We use at least twice-daily dosing of NPH or daily long-acting basal insulin in these patients.

An alternative to adding NPH insulin to patients' regimen is to increase the basal and bolus insulin doses by 30–50% across the board (Table 3). Anecdotal evidence sug-

gests that GLP-1 agonists or DPP-4 inhibitors may be useful in treating steroid-induced hyperglycemia. This is an important area for future research.

Insulin and dialysis

Glycemic management in patients on hemodialysis may be fraught with difficulties in the inpatient setting. Patients with renal failure are at higher risk of hyperglycemia because of uremia-induced insulin resistance. The risk for hypoglycemia is also quite high because of decreased insulin clearance, decreased renal contribution to gluconeogenesis, and decreased oral nutrient intake. However, good glycemic control is especially important in patients with end-stage renal disease (ESRD) because of this population's increased risk for sepsis.

The data for optimal outpatient regimens for ESRD patients on dialysis are sparse; there are even fewer data for inpatient regimens. Hemodialysis clears uremia and improves insulin resistance, so individuals with diabetes often have significantly lower blood glucose levels in the time period following

dialysis.^{20,21} Therefore, patients may require different insulin regimens before and after hemodialysis. There is some evidence to support reduction of the basal insulin dose by ~ 25% the day after a hemodialysis session.²² Close monitoring of blood glucose levels is imperative.

Patients with diabetes who are on peritoneal dialysis become hyperglycemic in the post-dialysis period because of high concentrations of glucose in the dialysate, which is absorbed from the peritoneal cavity.^{23,24} One might consider using extra NPH insulin at the beginning of peritoneal dialysis in these situations.

Insulin and parenteral and enteral nutrition

Enteral and parenteral nutrition pose major challenges for glucose management in the hospital. These nutritional approaches frequently result in hyperglycemia, even in patients without a history of diabetes, and have been associated with poor outcomes in the setting of resultant hyperglycemia.^{25–27} Scheduled subcutaneous insulin may be difficult to implement safely because of

Table 3. Special Considerations for Insulin Therapy in Hospitalized Patients With Diabetes

	Frequency	Insulin dosing
Glucocorticoids		
Prednisone or methylprednisolone	Every day	<ul style="list-style-type: none"> NPH 0.5 units/mg glucocorticoid (range 0.25–1.0 units) daily administered at the time of the glucocorticoid dose
	≥ 2 times per day	<ul style="list-style-type: none"> NPH 0.5 units/mg glucocorticoid (range 0.25–1.0 units) in divided doses twice daily OR Use 130–140% of basal and bolus insulin doses
Dexamethasone		<ul style="list-style-type: none"> NPH 3 units/mg glucocorticoid equivalent (range 2–5 units) in divided doses twice daily OR Use 140–150% of basal and bolus insulin doses
Dialysis		
Hemodialysis		Consider reducing basal insulin by 15% the day after a dialysis session
Peritoneal dialysis		NPH insulin dose at start of dialysis session
Parenteral and Enteral Nutrition		
TPN		1 unit of regular insulin per 12–15 g of carbohydrate in TPN bag
Enteral nutrition (tube feeding)		<ul style="list-style-type: none"> 70/30 insulin every 8 hours Rapid-acting insulin correction doses every 4 hours Check blood glucose every 4 hours If enteral nutrition is stopped, start 10% dextrose infusion

both planned and unplanned interruptions, as well as titration of the nutritional source.

In the case of enteral nutrition, a small, randomized clinical study demonstrated that subcutaneous basal insulin is more effective than correction dosing alone.²⁸ Another study suggested that using pre-mixed 70/30 insulin twice or three times daily (Table 3) may be safer than using long-acting insulin in patients on continuous tube feeding.²⁹ Other approaches such as scheduled short-acting insulin may be equally safe and efficacious, but studies are not available.

In the case of TPN, no randomized controlled trials comparing various approaches to insulin therapy are available, although retrospective data suggest that the addition of insulin in the TPN bag provides good control with less hypoglycemia than the use of intravenous or subcutaneous insulin alone.³⁰ This study suggested that an initial insulin-to-dextrose ratio of 1 unit for every 12–15 g of carbohydrate in the TPN bag is both safe and efficacious (Table 3). This ratio is then adjusted daily to achieve a glycemic target of 140–180 mg/dl.

Because patients on TPN and continuous enteral nutrition remain in a postprandial state, more aggressive glucose lowering is not recommended and could lead to severe hypoglycemia. We include orders for initiation of a 10% dextrose infusion if tube feeding is interrupted or discontinued abruptly. For both enteral and parenteral nutritional approaches, a computerized intravenous insulin algorithm may provide safer or more effective alternatives, but very few data are available.

Transitioning From Hospital to Outpatient Settings

Transitioning from hospital to home
For patients with diabetes who are being discharged from the hospital to home, an immediate issue is timely outpatient follow-up. Another concern is how and when changes to pre-admission medication regimens should be implemented. Conditions in the hospital may cause dramatic differences in glucose handling that

may not return to baseline just before and after discharge. Doses of insulin recommended at discharge may be significantly higher or lower than those actually needed at home.

Hospitalizations, planning for discharge, and designing a diabetes medication regimen for hospital discharge may represent opportunities to modify previous outpatient diabetes care.³¹ Unfortunately, this may be a missed opportunity.³²

We take into account both patient factors and external factors when recommending a glucose-lowering regimen for discharge. Patient factors include patients' ability and motivation to handle different levels of complexity in a glucose-lowering regimen and are affected by physical limitations, comorbid conditions, and understanding of diabetes self-care. External factors include patients' support system, resources, and financial considerations. We try to determine these factors early in the hospitalization so that the inpatient regimen can be designed to mimic the proposed outpatient regimen as much as possible.

Transitioning to a rehabilitation or skilled nursing facility

The diabetes regimen recommended for discharge to a rehabilitation or skilled nursing facility might differ from one recommended for use after discharge to home if there is concern about patients' ability or preferred level of involvement in self-care in instituting a complex glucose-lowering regimen. These factors, as well as the level of nursing care available at the discharge facility, should be taken into consideration when planning a diabetes regimen for discharge to an intermediate level of care.

Conclusion

The basic paradigm for effective management of glucose levels in the hospital setting takes into consideration the many factors that may come into play. The use of scheduled insulin regimens, close glucose monitoring, daily adjustments, and awareness of the obstacles for glycemic control allow for better and safer control of glucose levels in hospitalized patients with diabetes.

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