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Achieve better glucose control for your hospitalized patients

Forget sliding-scale insulin. A basal/bolus regimen yields better results with no additional risk

Practice recommendations

- Use the basal/bolus insulin regimen for inpatients with diabetes. It follows normal physiological insulin rhythm and is associated with significantly better glycemic control than the sliding-scale regimen. (**B**)
- If a patient on a basal/bolus regimen consistently requires supplemental insulin, reevaluate baseline dosing and make adjustments as needed. (**B**)
- Whenever possible, switch hospitalized patients to their outpatient diabetes control regimen ≥24 hours prior to discharge. (**C**)

Strength of recommendation (SOR)
A Good-quality patient-oriented evidence
B Inconsistent or limited-quality patient-oriented evidence
C Consensus, usual practice, opinion, disease-oriented evidence, case series

Mr. H, a 62-year-old with type 2 diabetes, hypertension, and hypercholesterolemia, arrives at the emergency department complaining of acute onset chest pain. An EKG shows no ischemic changes and his initial cardiac enzymes are normal, but Mr. H is admitted to telemetry for further monitoring and to rule out myocardial infarction. Mr. H normally takes metformin and glipizide to manage his diabetes; his most recent glycosylated hemoglobin (HbA1c) was 8.2. After admission, he is placed on a diabetic diet and switched to insulin.

As primary care physicians, we all care for patients like Mr. H, who are hospitalized because of cardiovascular or other symptoms and have diabetes—a comorbidity that affects an estimated 12% to 25% of inpatients.[1] We are also well aware of the elevated risks such patients face—for bacterial infection, impaired wound healing, and reduced tissue and organ perfusion,[2] among others. In one study, a single blood glucose reading >220 mg/dL was associated with a nearly 6-fold increase in nosocomial infection.[2] A number of recent studies have also found hyperglycemia to be an independent marker of overall inpatient mortality.[1,3-5]

American Diabetes Association goals. In 2008, the ADA issued new glycemic control goals for inpatients with diabetes. For critically ill patients, the association recommends that blood glucose levels be maintained at <140 mg/dL—and as close to 110 mg/dL as possible. For patients who are hospitalized but are not critically ill, the ADA recommends fasting blood glucose levels of 90 to 130 mg/dL and postprandial levels <180 mg/dL.[6]

As the ADA recommendations make clear, it is imperative that we do everything possible to lower the blood glucose

levels of our hospitalized patients. Ironically, though, fear of hypoglycemia has prevented many physicians from putting patients with diabetes on a basal/bolus insulin protocol[1]—a dosing regimen that, according to at least one recent report, is more effective than the traditional sliding-scale insulin regimen.[7] (See "No heightened hypoglycemia risk with basal/bolus regimen" on page 785.) To help you achieve glycemic targets safely and confidently using the basal/bolus regimen, we've assembled this review of the latest evidence, complete with strategies for success.

Oral agents are no match for the hospital routine

The hospital environment interferes with the patterns and schedules that people with diabetes rely on to manage their condition. Thus, it is not unusual even for patients whose glucose levels were very well-controlled at home to have poor glycemic control as inpatients. Dietary change is one of the primary reasons.

Mealtimes typically deviate from the patient's at-home schedule. In addition, patients are often put on a calorie-restricted, carefully enforced diabetic diet, which is quite different from their usual eating pattern. NPO orders are also common in preparation for diagnostic testing or other procedures. And some medications—particularly high doses of steroids—affect glucose levels. It is difficult to adjust oral hypoglycemic agents to accommodate such variations.

A look at Mr. H's regimen. Mr. H's physician knew that continuation of his oral medications—particularly glipizide—in combination with the hospital's strict diabetic diet could result in hypoglycemia. Continuing to take metformin was also a concern, given that Mr. H was at risk for new cardiac symptoms—a contraindication to metformin use. So his physician switched him over to insulin, a safer alternative.

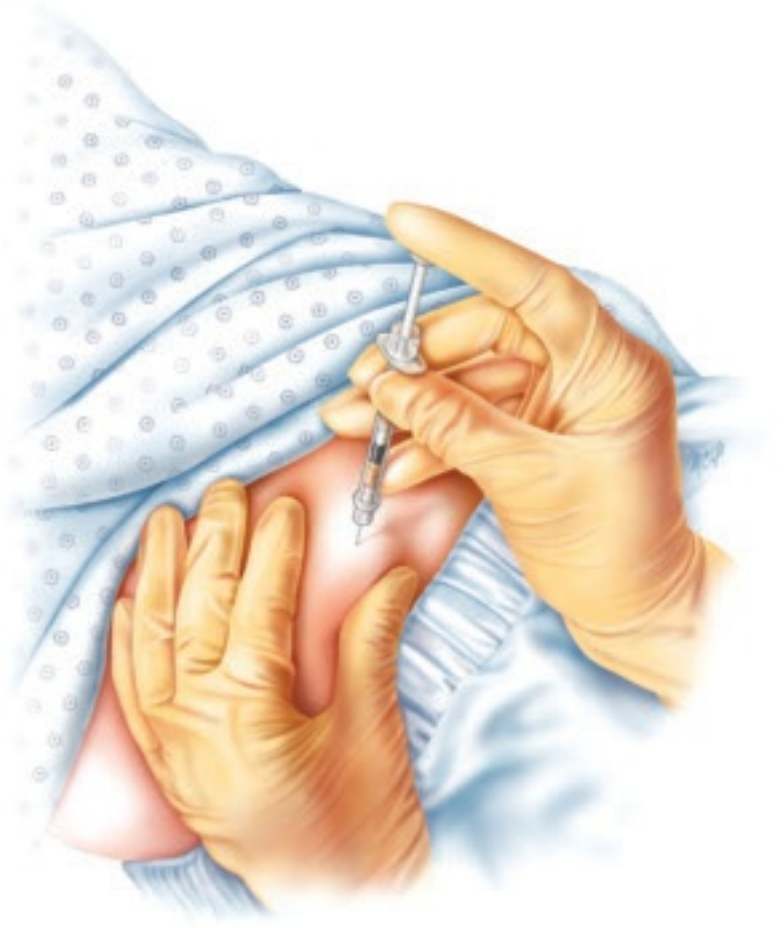

IMAGE © MAURA FLYNN

Finding the right insulin regimen

For years, a sliding-scale regimen was the most common approach to glycemic management of inpatients with diabetes. This concept, developed in 1934, originally used urine glucose testing to determine dosing, and its convenience and ease of treatment initiation led to widespread use. Although many variations have been introduced over the years, traditional sliding-scale regimens use short-acting analog or regular insulin in predetermined doses based on blood glucose readings at mealtimes and bedtime.

Despite the popularity of this method, however, there is little evidence to support it. Sliding-scale insulin as monotherapy has not been associated with effective glycemic control or improved outcomes.[8,9] By design, this traditional regimen makes hyperglycemia the

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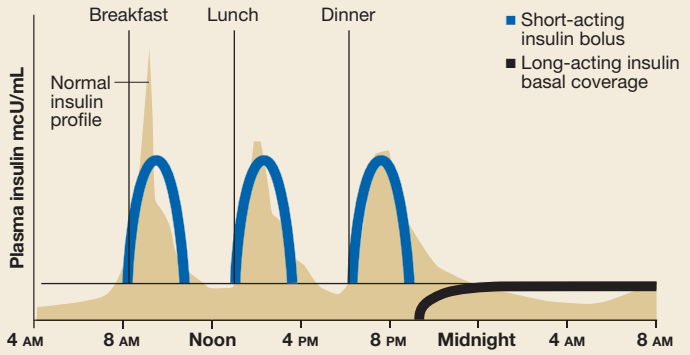
No need to worry that the basal/bolus insulin regimen heightens the risk of hypoglycemia. A recent study found that it does not

FIGURE 1

Basal/bolus regimen mimics normal insulin profile



Source: Polonsky KS, et al. *J Clin Invest*.[12]

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Despite the popularity of the sliding-scale insulin regimen, there is little evidence to support it

threshold for action, rather than taking action to prevent it. The result: wide fluctuations in blood sugar levels and the potential for prolonged periods of hyperglycemia.

Basal/bolus: A better approach

Mr. H's physician started him on a basal/bolus insulin regimen, which is more aggressive than a sliding-scale protocol and, as such, has prompted some physicians to view it warily. This strategy, in which a basal dose of long-acting insulin—typically given at bedtime—is accompanied by boluses of short-acting insulin at mealtimes,[1,10-12] follows the normal physiological release of insulin (**FIGURE 1**). Basic metabolic insulin is required to cover endogenous hepatic glucose production, even among diabetes patients who are NPO, and prandial insulin requirements are determined by exogenous glucose intake, whether in the form of a meal, intravenous (IV) fluids, tube feeding, or total parenteral nutrition (TPN).

Dosing guidelines. For most patients with type 2 diabetes, the correct daily insulin dose is 0.5 to 0.7 U/kg,[1,13] but factors other than weight also need to be considered:

- **Previous insulin use.** A lower initial dose (0.4 U/kg/d) may be preferable for insulin-naive patients, whereas a higher dose (0.7 U/kg/d) may be necessary for those with a history of insulin resistance.[1,3]
- **Risk of hypoglycemia.** To be on the safe side, start patients who are at high risk of hypoglycemia (eg, because they are very lean, have hepatic or renal failure, or are undergoing hemodialysis) with a very low dose (0.3 U/kg/d).
- **Other drugs or TPN regimen.** A higher dose (0.7 U/kg/d) is appropriate for patients on high doses of steroids.[1,3] Even smaller doses of oral or IV glucocorticoids increase the risk of hyperglycemia, particularly after a meal. Patients receiving TPN or other enteral feedings may also require higher doses of insulin.

Doing the math. To determine specific insulin requirements, calculate the total daily dose and divide it in half. The patient should receive half of the total as long-acting insulin for basal coverage, usually at bedtime. Divide the remaining half into 3 equal portions; administer each portion as a short-acting insulin bolus with each meal.[1,3,10,11]

Mr. H's insulin requirements. Mr. H weighs 100 kg (220 pounds), so he needs 60 units (0.6 U/kg) of insulin per day. His physician writes an order for 30 units (one half of 60 units) of a long-acting insulin (glargine or detemir) at bedtime, and 10 units (one third of the remaining 30 units) of a short-acting insulin (aspart, lispro, or glulisine) with each meal (**FIGURE 2**).[14]

More insulin needed? Figuring out how much

It's not unusual for patients on a basal/bolus regimen—particularly those like Mr. H, who have never been on insulin—to need supplemental insulin.[15] Short-acting insulin is always used for this purpose, whether it is administered before a meal or at bedtime.

If a patient is hyperglycemic (>150 mg/dL) before a meal, a correction scale (**TABLE**) can be used to determine how much additional insulin to give. The supplemental insulin should be given at the same time as the mealtime bolus.

If hyperglycemia is detected at bedtime, a more conservative approach is needed to prevent overnight hypoglycemia. Thus, additional insulin is recommended at bedtime only if the blood glucose reading is >200 mg/dL, and approximately half of the recommended mealtime correction dose should be given.[16]

Is it time to revise the dosing regimen?

Consistent use of a correction scale to adjust the dosage generally indicates that the patient's baseline dosing regimen needs to be revised. Dynamic insulin coverage requires careful monitoring, with blood glucose levels recorded and reviewed for trends that suggest a change is needed.

Poor subcutaneous perfusion, for example, may lead to a decreased or erratic uptake of injected insulin. Also, stress-related hyperglycemia may decrease or increase over the course of a hospital stay. And changes in medication, such as a decreasing steroid taper, may change overall insulin demand.[15,17]

With vigilant monitoring, the basal/bolus regimen may be adjusted upward to 110% of current dosing for a patient with frequent elevated blood glucose readings—provided the patient's glucose levels have not fallen below 80 mg/dL. Conversely, the regimen may be adjusted downward to 80% for a patient who continues to be hypoglycemic. Unlike the supplemental dosing based on the correction scale, these revised regimens affect both the basal (long-acting) and bolus (short-acting) doses.

To ensure timely adjustments to your patient's regimen, make sure that all your orders for insulin administration are accompanied by provisions for revising the dosing regimen when changes in patient status occur. (Protocols for managing both hypo- and hyperglycemia should, of course, be part of your orders as well.)

No heightened hypoglycemia risk with basal/bolus regimen

A basal/bolus insulin regimen is more aggressive than a sliding-scale protocol, and fear of hypoglycemia has historically kept physicians from using it.[1] The Randomized Study of Basal/Bolus Insulin Therapy in the inpatient management of patients with type 2 diabetes (RABBIT 2), published in 2007, addressed this concern. The researchers compared blood glucose levels for inpatients on a sliding-scale insulin regimen with those of patients on a basal/bolus regimen and found no difference in the frequency of hypoglycemia.[7] None of the participants were critically ill.

The study did show, however, that those on the sliding-scale regimen had higher mean fasting and random blood glucose levels than those on the basal/bolus regimen. Of patients on the basal/bolus regimen, 66% reached the target—a mean blood glucose <140 mg/dL—vs 38% of those on the sliding-scale regimen. What's more, 14% of those on the traditional regimen never achieved levels <240 mg/dL, whereas all of those in the basal/bolus group did. The mean daily insulin dose was significantly higher for those on the basal/bolus plan vs the sliding scale regimen (42 vs 12.5 units, respectively).[7]

RABBIT 2 provides clear evidence of significant improvement in glycemic control among inpatients on a basal/bolus insulin regimen, but patient-oriented outcomes have yet to be measured. However, emerging evidence of the impact of hyperglycemia on morbidity and mortality among diabetes patients in intensive care[18,19] has led the American College of Endocrinology[5] and the Society of Hospital Medicine, among others, to recommend using basal/bolus insulin in the management of inpatients with diabetes.

IV insulin's role—and is it expanding?

IV insulin is the treatment of choice for patients in diabetic ketoacidosis, but recent research suggests that it may also be the preferred approach to diabetes management in other critically ill patients, as well as in those undergoing surgery.[18-20]

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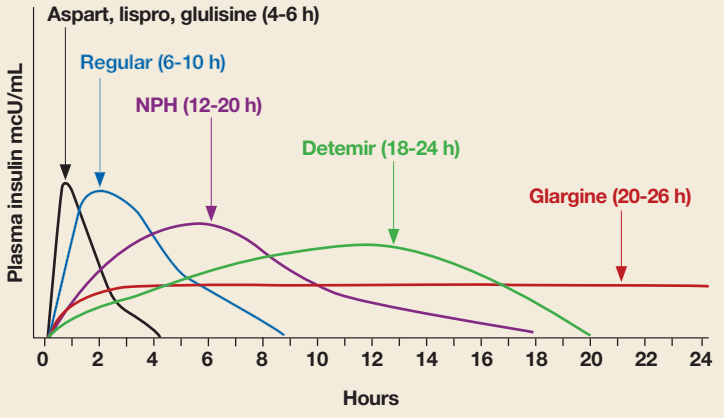
FIGURE 2

Insulin types and duration



NPH, neutral protamine Hagedorn.
Source: Hirsch B. *N Engl J Med.*[14] Copyright 2005 Massachusetts Medical Society.

TABLE

Insulin correction scale: Calculating the supplemental dose

BLOOD GLUCOSE mg/dL	EXTRA INSULIN	
	PREMEAL (NO. OF UNITS)	BEDTIME (NO. OF UNITS)
150-199	1	None
200-249	2	1
250-299	3	2
300-349	4	2
≥350	5	3

Source: Walsh J, et al. Torrey Pines Press.[16]

In a study comparing outcomes of surgical ICU patients managed with IV insulin during the perioperative and postoperative periods with surgical patients on conventional diabetes management, Van den Berghe found a 45% reduction in mortality rates among those receiving insulin infusions (4.6% of those on IV insulin died, compared with 8% of those receiving subcutaneous insulin). The use of IV insulin therapy also decreased the time spent in intensive care, although it did not shorten the overall length of stay.[19]

Regular insulin is used most often for insulin infusions. Some trials with ultra–short-acting insulin have been done, but the findings were inconclusive.

Your patient is leaving: Ease the transition

For inpatients with diabetes, discharge planning includes a transition, from insulin to oral agents, perhaps, and from maintaining glucose control based on a hospital schedule to adjusting to the patterns of daily life at home. Particular care is required for patients who will be transitioned from IV to subcutaneous insulin. IV insulin has a half-life of only 10 minutes, so the initial subcutaneous dose should be administered about 1 hour prior to discontinuation of the infusion. Failure to plan accordingly may result in significant hyperglycemia and associated complications.[17,21]

Research suggests that patients be switched to their outpatient diabetes management plan at least 24 hours before discharge, a protocol that was followed in Mr. H's case. He remained in the hospital for 5 days. After myocardial infarction was ruled out, Mr. H underwent a nuclear medicine cardiac stress test for which he needed to be NPO. When testing was completed, Mr. H resumed a diabetic diet, and discharge planning began. Since his diabetes was not well controlled on admission and he required >20 units of insulin per day in the hospital, Mr. H's physician opted to include long-acting insulin at bedtime in his outpatient regimen. On the day before Mr. H was scheduled to leave the hospital, the physician discontinued the short-acting mealtime insulin and restarted oral metformin twice daily, closely monitoring the patient's glucose levels until discharge. The physician told Mr. H to schedule a follow-up visit within a week so that his new outpatient regimen could be reviewed.

Ideally, a diabetes nurse specialist will be available, not only to get involved in discharge planning, but also to provide patient education, care, and advice.

Exceptions to the inpatient insulin "rule": When an oral agent may make sense

Although severity of illness, planned or unplanned procedures, and changes from usual dietary patterns may limit the utility of some oral agents, no large studies have investigated the impact of oral diabetes medications on inpatient outcomes.[1] For a patient who has excellent outpatient glycemic control and is not critically ill, continuation of some or all oral agents may be appropriate. Consider the following:

Metformin. This agent has the benefit of not causing hypoglycemia and of facilitating weight loss. Metformin is, however, contraindicated in patients with renal insufficiency, congestive heart failure, cardiovascular collapse, acute myocardial infarction, and septicemia.[24]

Despite the warning, metformin is often used in patients with these contraindications. A recent systematic review of more than 17,000 patients taking the drug did not uncover a single case of lactic acidosis.[25] With appropriate monitoring, metformin may be a useful inpatient treatment for some patients.

Sulfonylureas. These agents should be limited in the inpatient setting because of their long action and propensity to cause hypoglycemia. In addition, some questions have arisen about the safety of these medications in patients with vascular disease and acute cardiac events.[23,26] Despite this, there is no rigorous data to specifically advise against keeping inpatients with diabetes on sulfonylureas.

Thiazolidinediones. These agents should be used with caution in the inpatient setting. Although they have relatively few acute adverse effects, they have been shown to increase intravascular volume and have the potential to exacerbate congestive heart failure.[27]

Researchers found that hospital stays for patients with diabetes were shortened (8 days vs 11 days) when a diabetes nurse specialist was involved in their care. The patients were also more knowledgeable and satisfied.[22]

Take advantage of bedside conversations. An inpatient stay offers physicians and patients the opportunity to work together to fine-tune components of the diabetic regimen.[23] Make the most of these opportunities. In addition, once the patient goes home, you'll need to ensure close follow-up to reconcile the differences between home self-management and the controlled hospital environment. ■

Disclosure

The author reported no potential conflict of interest relevant to this article.

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In one study, insulin infusions in the perioperative and postop periods led to fewer deaths and shorter intensive care stays

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