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Cerebrovascular Disorders (Harold Adams, Section Editor)

Management of Hyperglycemia in Acute Ischemic Stroke

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Opinion statement

There is considerable clinical evidence that hyperglycemia at the onset of acute ischemic stroke may negatively impact not only acute morbidity but also brain recovery. Establishing hyperglycemia treatment protocols is challenging, given the variation among patients and acute stroke care settings. Relatively few randomized trials have examined glycemic control protocols in this population, and there is not yet any clear evidence that "correcting" hyperglycemia in patients with acute stroke leads to better functional outcomes. Intensification of glucose regimens, using lower glucose targets, leads to more hypoglycemic events, but the immediate and long-term impact of these events on the acutely ischemic brain is unknown. It is reasonable to treat patients with acute ischemic stroke according to the American Diabetes Association inpatient glycemic control guidelines, initiating therapy to achieve glucose targets of 140 to 180 mg/dL if fasting glucose is greater than 140 mg/dL or random glucose is consistently higher than 180 mg/dL. Lower glucose targets (<140 mg/dL) may be appropriate for patients with well-controlled diabetes and those with stress hyperglycemia who were not known to be diabetic before admission, but glucose levels less than 80 mg/dL should be avoided. Patients who present with extreme or persistent hyperglycemia, are critically ill, or who are treated with thrombolytic therapy should be started on an established and standardized intravenous insulin protocol to improve blood glucose control for at least the first 24 to 48 h of hospitalization. They should then be transitioned to a subcutaneous insulin regimen that includes basal long-acting insulin along with correction rapid-acting insulin for glucose that is out of range. Prandial (meal) insulin should be added for patients who are eating; this would preferably be a rapid-acting insulin analogue that can be administered immediately before or after the meal. Caution and close glucose monitoring are necessary,

especially for patients prone to hypoglycemia, such as those with type 1 diabetes mellitus or hepatic or renal impairment, or those on complicated feeding regimens.

Introduction

Ischemic stroke remains a major cause of mortality in Americans, third only to heart disease and malignancy [1]. These patients often have multiple medical comorbidities, one of the most common being impaired glucose metabolism. Patients with diabetes mellitus are twice as likely to have a stroke as nondiabetic patients (controlled for other vascular risk factors) [2], and they may have worse outcomes after stroke [3–7]. Scott et al. [8] found that approximately 50% of patients presenting with stroke have blood glucose higher than 108 mg/dL, and that severity of hyperglycemia correlates with severity of neurologic deficits. The question remains whether the hyperglycemia itself may physiologically contribute to worsening brain injury, or if hyperglycemia is simply a marker of acute illness. Thus, we need further research on the topic of acute stroke hyperglycemia. Specifically, we need to elucidate optimal glycemic target ranges; the timing, duration, and type of antihyperglycemic therapy; and how to transition patients to safe outpatient glycemic management. Protocols must be feasible, effective, and safe in achieving and maintaining glucose targets. Most importantly, we need to determine how much clinical benefit—both acute and long-term—can be expected from improved glycemic control in patients with acute ischemic stroke.

Hyperglycemia due to acute stress in stroke patients

Many acute illnesses have been associated with transient hyperglycemia (stress hyperglycemia), and patients without a preexisting diagnosis of diabetes may be most vulnerable to adverse effects of stress hyperglycemia [9•, Class II; 10•, Class IV]. Capes et al. [7], after reviewing 32 studies, calculated a relative risk of 30-day mortality of 3.28 (95% CI, 2.32–4.64) in nondiabetic patients with acute stroke who presented with a glucose level at least 110 to 126 mg/dL, compared with patients having lower presenting glucose levels. Nondiabetic ischemic stroke patients presenting with glucose of 121 to 144 mg/dL or greater also showed statistically significant worse neurologic outcome than those with lower glucose levels. These relationships were not seen among the diabetic patients. This review suggests that hyperglycemia related to acute illness may be more detrimental than chronic hyperglycemia in patients presenting with acute ischemic stroke.

Patients presenting with traumatic injury, burns, sepsis, and vascular events are at especially high risk for persistent hyperglycemia during hospitalization. Acute physiological stress leads to a "hypermetabolic" state that promotes insulin resistance and impaired pancreatic beta cell function. These mechanisms occur as the body releases catecholamines in response to physiological stress and are exacerbated by medications commonly used in the intensive care unit, such as vasopressors and corticosteroids. Resultant adverse physiological effects such as activated inflammatory cascades, electrolyte imbalances, immune system dysfunction, oxidative injury, and mitochondrial dysfunction place patients at higher risk of complications, such as further sepsis and impaired wound healing [10•, Class IV]. These detrimental mechanisms

are likely to have adverse effects on the acutely ischemic brain as well. Along with its glucose-lowering effects, insulin therapy appears to have immunomodulating effects that could prove beneficial in this setting [11, 12].

Hyperglycemia and brain physiology

Both hyperglycemia and hypoglycemia have significant effects on brain physiology that may be exacerbated during acute brain ischemia. Hyperglycemia has been linked to many metabolic derangements in animal models, but many of these have not been demonstrated in humans. Mechanisms by which hyperglycemia may exacerbate injury include increased oxidative load, cerebral edema, hemorrhagic transformation of ischemic stroke, and inflammation [13•, Class IV]. Anaerobic metabolism during ischemia can lead to tissue lactic acidosis, but it is unclear how this contributes to ischemic injury. McCormick et al. [14••, Class II] showed that higher lactate-to-creatinine ratios correlate with larger infarct volumes at 7 days after ischemic stroke in patients presenting with blood glucose higher than 126 mg/dL. Glucose-potassium-insulin (GKI) infusion significantly lowered lactate-to-creatinine ratios, but final infarct volume and outcomes at 30 days were not improved in the group receiving (IV) insulin.

Parsons et al. [6] studied 30 patients presenting with acute ischemic stroke, using brain MRI and MR spectroscopy to assess tissue lactate accumulation. Higher glucose levels at presentation correlated with a larger rise in lactate levels between day 1 and day 3, and also with greater infarct expansion. These patients were also found to have a poorer functional outcome. Taken together, cerebral lactate accumulation may be part of the mechanism behind poor stroke outcomes following hyperglycemia, but it is not clear at this point that treating hyperglycemia aggressively will improve neurologic outcomes by reducing lactate levels.

Although many studies focus on hyperglycemia at the time of admission, Baird et al. [15] found that hyperglycemia throughout hospitalization with acute stroke (average glucose >126 mg/dL) correlated better with greater infarct volume and worse neurologic outcomes than did isolated admission glucose level or hemoglobin A1c value. Although this study was small, it suggests that persistent hyperglycemia may be a better prognostic indicator, and it highlights the need to determine whether improved glucose control improves outcomes after stroke.

Hyperglycemia and risk of hemorrhagic transformation

Hyperglycemia appears to increase the risk of hemorrhagic transformation of acute ischemic stroke, which in some patients is seriously symptomatic. In the National Institute of Neurological Disorders and Stroke Recombinant Tissue Plasminogen Activator Stroke (NINDS rt-PA) Trial, hyperglycemia was associated with a higher rate of symptomatic intracerebral hemorrhage [16]. Analysis of data from the Safe Implementation of Treatments in Stroke International Stroke Thrombolysis Register (SITS-ISTR) [17••, Class III] revealed that presenting with acute ischemic stroke and a blood glucose level higher than 180 mg/dL is independently associated not only with higher risk

of intracerebral hemorrhage but also with worse functional outcome 3 months after discharge. However, Meurer et al. [18] did not find that hyperglycemia led to increased risk of intracerebral hemorrhage after thrombolysis in nearly 300 patients admitted with ischemic stroke, although hyperglycemic patients had a statistically insignificant increase in in-hospital mortality. Further randomized controlled trials are needed to determine whether glycemic control could play an important role in improving outcomes in stroke patients receiving thrombolytic therapy.

Treatment

- The management of hyperglycemia in acute ischemic stroke is evolving. There are no firm guidelines on targets, duration of therapy, and, most importantly, outcomes to be expected with improved glycemic control during acute ischemic stroke. While further research is ongoing, patients admitted with hyperglycemia need management, and the optimal strategy will vary depending on individual patient and care-setting characteristics. Insulin drips are initially preferred for patients on continuous tube feeds, those receiving thrombolysis, and those who are critically ill, whereas subcutaneous insulin regimens will be appropriate for most other patients with fasting glucose levels higher than 140 mg/dL or random glucose levels higher than 180 mg/dL. Consistent bedside glucose monitoring is necessary in order to make appropriate adjustments to insulin regimens and to monitor for hypoglycemia, which should be carefully avoided in patients with acute vascular events.
- Endocrine consultation is advised for patients with type 1 diabetes, those who use insulin pumps, and for those with persistent hyperglycemia or recurrent hypoglycemia.
- A safe transition to outpatient care is especially challenging for those who require insulin therapy at home; generally small dosage decreases are recommended at the time of discharge to prevent hypoglycemia. Ongoing outpatient follow-up and education are crucial for these patients.

Inpatient glycemic control strategies in acute ischemic stroke

- Some studies have suggested that intensive inpatient glycemic control leads to better long-term outcomes in patients with other macrovascular events such as myocardial infarction [19] and fewer postoperative complications in patients undergoing cardiac surgery [20, 21]. However, other studies, including the NICE-SUGAR trial [22••, Class I], suggest that using intensive glucose targets in critically ill patients may lead to higher rates of adverse events. Use of intensive inpatient glycemic control protocols also can increase the frequency of hypoglycemia, but it remains unclear whether morbidity is directly attributable to hypoglycemia or if a predisposition to hypo-

glycemia simply indicates a higher level of acuity among patients [23••, Class I].

- Only a few trials have specifically examined the impact and effectiveness of glycemic control protocols during admission with acute stroke, as outlined in Table 1. Many of the trials were small and did not meet their prespecified glucose targets for a significant amount of time. For example, the Glucose Insulin in Stroke Trial–United Kingdom (GIST-UK) [24] achieved only a clinically insignificant reduction in average blood glucose of 10 mg/dL, using an insulin drip protocol. A smaller study, Treatment of Hyperglycemia In Acute Stroke (THIS) [25•, Class I], continued an insulin drip for 72 h after admission and achieved an average blood glucose 66 mg/dL lower than the level in the control group, but functional and neurologic outcomes at 3 months were not significantly improved. In the Glucose Regulation in Acute Stroke Patients (GRASP) trial [26•, Class I], a "tight control" insulin drip protocol (targets 70–110 mg/dL) dropped the average blood glucose level over 5 days (or until discharge) by 40 mg/dL compared with a "loose control" drip protocol (target 70–200 mg/dL) and standard care. The tight-control group had slightly better clinical outcomes than controls in the subset of patients presenting with glucose higher than 150 mg/dL.
- It is noteworthy that the blood glucose targets in these and other similar studies (Table 1) are significantly lower than the current ADA recommendations, generally 140 to 180 mg/dL [23••, Class I], and these studies do not uniformly prove that tight glycemic control upon admission for stroke improves outcomes. Although hypoglycemia was more frequent among patients with tighter glucose targets, it generally was not linked to increased morbidity or mortality. Further investigation is therefore needed, and separate strategies and different glucose targets may be needed for patients with diabetes mellitus versus those with stress hyperglycemia.
- Stroke-specific glycemic control guidelines are not currently available, although the American Heart Association/American Stroke Association suggest that hyperglycemia be treated if glucose is consistently higher than 140 to 180 mg/dL [27]. The American Diabetes Association (ADA) and American Association of Clinical Endocrinologists (AACE) have updated their guidelines regarding inpatient glycemic control [23••, Class I], suggesting less intensive glycemic targets of 140 to 180 mg/dL for inpatients, with a preference for IV insulin in critically ill patients; these changes are probably the result of clinical studies showing that a higher risk of hypoglycemia may outweigh a benefit among inpatients [28••, Class I; 29, 30].
- We suggest some more specific guidelines for patients with acute stroke, based on clinical experience and available evidence. Initial insulin management should be dictated by the patient care setting, the individual patient's clinical and nutritional status, and the

Table 1. Trials of insulin in acute ischemic stroke

Study	Patients (*N*)	Intervention	Patient presentation	Outcomes	Hypoglycemia	Effect on blood glucose	Duration of intervention	Results
Walters et al. [34]	25	Insulin IV: goal 90–144 mg/dL vs saline: goal <270 mg/dL	Glucose >144 mg/dL; 52% had diabetes	Safety and feasibility	One transient symptomatic hypoglycemia (72 mg/dL)	↓23 mg/dL	48 h	Safe and feasible; not able to determine difference in functional outcome
Gray et al. [24] (GIST-UK)	933	GKI IV: goal 72–126 mg/dL vs saline	Glucose >109 mg/dL; 16.5% had diabetes	Death at 3 mo; Functional outcomes at 3 mo	<72 mg/dL in 15% in IV GKI group; drop >36 mg/dL in 24 h → increased mortality	↓10 mg/dL	24 h	No significant difference in mortality or functional outcomes
Bruno et al. [25•] (THIS)	46	Insulin IV: goal 80–130 mg/dL vs SQ insulin: goal <200 mg/dL	Glucose >150 mg/dL; 91% had diabetes	Safety and feasibility; Functional outcomes at 3 mo	<60 mg/dL in 33% in IV insulin group; not linked to adverse outcomes	↓66 mg/dL	3 days or hospital discharge	No significant difference in adverse events or functional outcomes
Johnston et al. [26•] (GRASP)	72	Insulin IV "tight" (70–110 mg/dL) and "loose" (70–200 mg/dL) targets and control (target <300 mg/dL)	Glucose >110 mg/dL; 59% had diabetes	Safety and feasibility; Functional outcomes at 3 mo	<55 mg/dL in 30% in "tight" group and 4% in the other groups; not linked to adverse outcomes	↓40 mg/dL (tight group spent 44% of the time in target range)	5 days or hospital discharge	No significant difference in adverse events or functional outcomes
Kreisel et al. [35]	40	Insulin IV: goal 80–110 mg/dL vs SQ insulin: goal <200 mg/dL	32.5% had diabetes	Safety; Functional outcomes at 4 mo	<60 mg/dL in 35% in intensive group; not linked to adverse outcomes	↓27.4 mg/dL	5 days	No significant difference in adverse events or functional outcomes
McCormick et al. [14••]	40	GKI IV: goal 72–126 mg/dL vs saline infusion	Glucose >126 mg/dL; 32.5% had diabetes	Acute infarct growth; Functional outcomes at 30 days	<72 mg/dL in 76% in all GKI groups	↓22 mg/dL at 6–12 h; no difference in glucose beyond 24 h	1-, 2-, and 3-day groups	No significant difference in infarct growth overall; No significant difference in adverse events or functional outcomes

GIST-UK Glucose Insulin in Stroke Trial–United Kingdom; *GKI* glucose-potassium-insulin; *GRASP* Glucose Regulation in Acute Stroke Patients; *h* hours; *mo* months; *SQ* subcutaneous; *THIS* Treatment of Hyperglycemia in Ischemic Stroke.

availability of established insulin protocols. A reasonable pre-meal (or fasting) glucose target in patients with acute stroke is less than 140 mg/dL, with avoidance of glucose levels less than 80 mg/dL. Random glucose (2 h after a meal or at bedtime) should not exceed 180 mg/dL, as per the societal guidelines.

- Oral medications play a minimal role in inpatient management of hyperglycemia and carry a significant risk of acidosis, hypoglycemia, or both when used in acutely ill patients undergoing diagnostic procedures.

Insulin drips

Critically ill patients who have specific indications for IV regular insulin infusion (such as diabetic ketoacidosis or hyperosmolar syndrome), who have persistent or severe hyperglycemia, or who are receiving continuous enteral tube feeding may benefit most from IV insulin for the first 24 to 48 h after admission. At this time, we recommend an insulin drip protocol with a glucose target of 140 to 180 mg/dL for the first 48 h after admission for patients with ischemic stroke treated with thrombolytic therapy, given the increased risk of hemorrhagic transformation with persistent hyperglycemia. In patients who present with a glucose level higher than 250 mg/dL, a 0.1 unit/kg initial bolus of IV regular insulin can be given before thrombolytics are administered, for immediate blood glucose lowering; this bolus must be followed by an insulin drip, as IV regular insulin has a half-life of only 5 min. The short half-life is ideal for patients with frequent changes in their nutritional or clinical status.

It is important that insulin drips should be used only when established protocols and adequate support are available to check capillary glucose levels hourly until the drip rate has stabilized. It is generally safe to correct hyperglycemia to the target range rapidly unless a hyperosmolar state is present (osmolality >320 mOsm/kg). In these cases, endocrinology consultation is advised, and glucose generally should not be lowered below 250 mg/dL until the patient is alert and able to eat [31]; doing so will help avoid large shifts in osmolality that may worsen cerebral edema.

Acceptable insulin protocols should include appropriate adjustments in the event of hypoglycemia. Blood glucose levels of 50 to 70 mg/dL are generally considered hypoglycemia, and levels less than 40 to 50 mg/dL are considered severe hypoglycemia and are potentially dangerous. In general, the IV insulin drip rate should be decreased for glucose of 70 to 90 mg/dL. If the glucose is 50 to 70 mg/dL, one-half ampule D50W (12.5 g of dextrose) should be given IV, and a whole ampule should be given if glucose is less than 50 mg/dL.

Blood glucose levels should be rechecked every 15 min until recovery from hypoglycemia is complete. Because insulin drips shift potassium intracellularly, electrolytes should be monitored every 4 to 6 h and repleted as needed while a patient is receiving IV insulin.

Several publications review available established IV insulin protocols [32, 33•, Class IV].

Insulin drips should be stable (minimal drip rate adjustments) prior to transitioning to a subcutaneous (SQ) insulin regimen. In patients eating meals or receiving bolus tube feeds, the addition of rapid-acting SQ insulin (or covering the meals with IV insulin boluses) is necessary to minimize blood glucose fluctuations. After the insulin drip has stabilized, 80% of the total insulin requirement (IV and SQ) over the previous 24 h can be used in calculating the SQ insulin dose. Approximately one half of this calculated dose is given as basal insulin (long-acting glargine or detemir) and the remaining half is divided between meals as a rapid-acting analogue insulin.

Such mealtime replacement is best delivered based on the carbohydrates consumed for the meal. If carbohydrate counting is available, the mealtime dose is varied based on the amount of carbohydrate consumed with each meal. An initial carbohydrate ratio can be calculated by dividing 600 by the total daily dose of insulin. A carbohydrate ratio of 10 implies that one unit of insulin would cover 10 g of carbohydrate.

Continuous enteral tube feeds should be covered with basal insulin. In patients with unpredictable insulin requirements, it is best to divide the basal insulin into four daily doses of NPH insulin given every 6 h; this allows for dosing adjustment as the day progresses, based on the glucose levels. To avoid hyperglycemia, the first dose of basal insulin should always be given at least 1 h before the insulin drip is turned off.

It is crucial to remember that patients with type 1 diabetes are insulin dependent and require insulin at all times to suppress ketone formation; they may be at higher risk for diabetic ketoacidosis when acutely ill. Therefore, their insulin drip should not be turned off when the target glucose is reached; rather, an enteral or IV glucose source should be added.

Subcutaneous regimens: Type 2 diabetes or stress hyperglycemia

SQ insulin is appropriate for most patients with acute ischemic stroke who have diabetes mellitus or stress hyperglycemia. It generally requires checking capillary glucose levels immediately before each meal and at bedtime. Premorbid insulin regimens are influenced by home diet and lifestyle and are not suitable during acute stroke. As a guide, patients with acute stroke could be started on weight-based SQ insulin regimens. A weight-based total daily insulin dose for a patient with type 2 diabetes on basal and prandial insulin at home could be calculated as $\text{mass(kg)} \times 0.6 = \text{totaldailyinsulindose}$. A multiplier of 0.3 to 0.4 could be used for thin patients, those with hepatic or renal impairment (GFR<50 mL/min), and insulin-naïve patients, who have been well controlled with diet or oral medications at home. A multiplier of 0.7 to 0.8 could be used for especially obese patients with higher insulin resistance and those with blood glucose consistently higher than 250 mg/dL. For example, someone previously well controlled on metformin weighing 100 kg would need a total of about 40 units of insulin daily: approximately 20 units of glargine or detemir daily and 6 to 7 units of a rapid-acting analogue insulin (lispro, aspart, or

glulisine) with each meal. In the example above, one could also use 5 units of NPH insulin SQ every 6 h for basal coverage if preferred.

Enteral intake should be covered with a set dose of short-acting insulin or should be based on carbohydrate consumption. Pre-set prandial insulin doses work well if the carbohydrate in the diet is consistent. A recommended carbohydrate ratio (grams of carbohydrates covered by one unit of insulin) is estimated by dividing the total daily insulin dose into 600. Unlike basal insulin, prandial insulin should be held if the patient is not eating, and smaller doses may be appropriate if partial meals are consumed (which is common in patients with acute stroke). For this reason, it is preferable to give the prandial insulin immediately *after* the meal; this requires the use of a rapid-acting analogue insulin. Regular human insulin must be administered 30 to 45 min *before* a meal in order to be effective.

Correction insulin dosing, based on an insulin sensitivity factor (ISF), should be in place to allow for better correction of hyperglycemia if the initial insulin orders underestimate actual needs. The ISF is an estimate of how much one unit of insulin will lower a patient's glucose level, and can be calculated by this formula: 1800/total daily insulin dose. The appropriate correction insulin dose should be added to a patient's prandial insulin dose and administered with the meal. A formula for calculation of a correction dose is: (currentbloodglucose−glucosetarget) ÷ ISF. An appropriate target during the daytime is 140 to 180 mg/dL, but the target can be set lower for those with preexisting tight glycemic control. The midpoint of the chosen target range can be used as the number to calculate the ISF. For example, if the blood glucose is 220 mg/dL before the meal, and the ISF is 30, the calculation would be (220–160)/30, which gives 2 units. If the patient has a carbohydrate ratio of 1:10 and consumes 30 g of carbohydrates for the meal, the total dose for that meal will be $3 + 2 = 5$ units of insulin. Correction insulin doses should not be calculated using a post-prandial glucose value (up to 3 h after a meal) or given at bedtime. In patients who are NPO or are receiving continuous tube feeds, correction doses can be calculated and administered every 4 to 6 h.

Basal insulin should be adjusted based on fasting glucose levels; prandial doses should be adjusted based upon glucose trends during the day. For example, if a patient's bedtime glucose repeatedly runs high, an increase in the insulin dose for the evening meal would be appropriate. In general, increases of 5% to 10% are best for glucose levels slightly above goal (fasting 150–180 mg/dL) or for premeal glucose levels of 180 to 200 mg/dL. For higher levels, increases can be 10% to 20%.

Hypoglycemia can usually be corrected with about 15 g of carbohydrate orally (4 ounces of juice) if glucose is 50 to 70 mg/dL and 30 g if the glucose is below 50 mg/dL. Ampules of 50% dextrose in water can be used if the patient is unable to take oral medications.

Subcutaneous regimens: Type 1 diabetes

Patients with type 1 diabetes are more prone to hypoglycemia than those with type 2 diabetes and are also at risk for in-hospital diabetic ketoacidosis

if the basal insulin dose is insufficient. For this reason, endocrinology consultation is advised.

Consultation is encouraged for patients who use an insulin pump, to get assistance with the conversion of pump settings to an SQ regimen. Pump use in the hospital is discouraged, as patients may have cognitive or physical deficits that impair their ability to operate the pump.

Insulin regimens in type 1 diabetes should generally be based on outpatient insulin doses. The total daily insulin dose can be estimated by a formula, weight (kg) × 0.4, and adjusted based on subsequent glucose levels. If the patient is receiving continuous tube feeding, the necessary amount of insulin can be calculated using the patient's carbohydrate ratio (600/total daily insulin dose) and added to the basal insulin in the form of SQ NPH insulin given every 6 h.

Inpatient care in special circumstances

Endocrine consultation is also advisable for patients on concentrated regular (U500) insulin as outpatients, those requiring renal replacement therapy, and those with hyperglycemia related to cystic fibrosis or pancreatic surgery.

Patients with complicated nutrition regimens such as enteral tube feeding or IV nutrition also present additional therapeutic challenges, and endocrinology consultation should be considered.

Patients on corticosteroid therapy before or during acute stroke usually require proportionally higher prandial insulin doses to overcome greater insulin resistance.

Outpatient care for persisting hyperglycemia

- A new diagnosis of diabetes suspected during an acute illness should be confirmed by further outpatient evaluation. However, a hemoglobin A1c greater than 6.5% is suggestive of chronic hyperglycemia and diabetes mellitus. Deciding on an outpatient regimen can be the most challenging aspect of managing inpatient hyperglycemia and should be completed in conjunction with diabetes educators and an endocrinologist if possible, especially for patients being discharged on insulin therapy. Close outpatient follow-up with a diabetes-care practitioner is essential.
- Generally, if an insulin regimen is working well during hospitalization, a decrease in insulin dose of 10% to 20% at the time of discharge is recommended in anticipation of improved insulin sensitivity as patients recover from acute illness and increase their activity level, to avoid hypoglycemia. Insulin can be adjusted by outpatient providers as needed.
- Correction insulin dosing at home is useful in achieving good control, and initially should be used only before meals (not at bedtime). Caution is needed in deciding which patients are able to understand correction scales and use them safely at home. Generally, an ISF of 30 to 50 (1 unit of insulin will lower the blood glucose by 30–50 mg/dL) is appropriate, depending on the level of insulin resistance.
- Patients and their caregivers should be educated before discharge regarding glucose testing, insulin administration (if applicable), and

hypoglycemia symptoms. They should have access to contact numbers for after-hours advice. Glucagon injections and glucose tablets should be provided for treatment of hypoglycemia. Patients and their families should receive education about carbohydrate counting to facilitate appropriate meal preparation. The focus should be placed on limiting simple carbohydrates (sugars commonly found in processed foods) and consuming consistent amounts of carbohydrate at meals.

- Patients should be encouraged to check blood glucose levels as instructed and to keep a glucose log to facilitate regimen evaluations at follow-up visits. Patients taking oral medications should be checking glucose at least twice daily (typically before breakfast and before dinner), and those on insulin should initially be checking glucose four times daily (before each meal and at bedtime), in addition to a few readings in the early morning to assess for fasting hypoglycemia related to basal insulin.

Selection of insulin preparation

Many insulin preparations are available, and choices are sometimes driven by hospital or health insurance formularies.

Glargine insulin, with its consistent kinetics and lack of a peak action, offers the best basal coverage.

Insulin detemir also is commonly used for basal coverage, but it may require twice-daily dosing, especially in patients with type 1 diabetes.

NPH insulin, because of its unpredictable kinetics with varying duration and peaks, is not preferred for basal coverage unless it is indicated for the patient's variable insulin requirements or for cost containment.

Rapid-acting analogue insulins (lispro, aspart, or glulisine) are preferred for prandial insulin coverage and correction dosing.

Human regular insulin may be used for cost containment, in place of the rapid-acting analogue insulins. It is important to note that regular insulin must be administered 30 to 45 min before a meal is consumed, because of its slow onset of action.

Insulin is available in disposable, prefilled pens, which may be best for stroke patients with difficulty drawing up insulin from a vial.

Premixed insulin preparations (generally mixes of NPH and human regular or rapid-acting analogue insulin) generally require only two injections daily and may be appropriate for some patients, but they are not preferred, given their lack of flexibility and the risk of hypoglycemia if they are taken without food.

Disclosure

Conflicts of Interest: L. Baker: none; A. Bruno: none; R. Juneja: on Speakers Bureau for Eli Lilly, Sanofi-Aventis, Merck, Amylin Pharmaceuticals, Boehringer-Ingelheim; consultant for Eli Lilly and

Sanofi-Aventis; royalties from commercial sales of the Clarian Glucose Stabilizer Insulin Dosing Tool software (Diabetes Innovations, LLC); stock ownership in Amylin Pharmaceuticals.

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