Protocols Vary for Inpatient Glucose Targets

BY SHERRY BOSCHERT

SAN FRANCISCO — Meeting the targets in consensus recommendations on inpatient glycemic control requires different protocols for different kinds of patients.

For hospitalized patients who are not critically ill, a protocol employing scheduled subcutaneous insulin therapy with basal, nutritional, and correctional components is effective, Dr. Mary T. Korytkowski said. For critically ill inpatients, intravenous insulin infusion protocols are better for achieving and maintaining glycemic control, she said at a meeting sponsored by the American Diabetes Association.

Glucose levels are evaluated daily, and the insulin regimen is adjusted to avoid hyper- and hypoglycemia.

DR. KORYTKOWSKI

Many hospitals further subdivide the protocol for critically ill patients to have different glycemic targets for surgical and nonsurgical ICU patients, added Dr. Korytkowski, professor of medicine at the University of Pittsburgh's Center for Diabetes and Endocrinology.

A 2009 consensus statement from the American Association of Clinical Endocrinologists and the American Diabetes Association recommended maintaining glucose levels between 140 and 180 mg/dL in most critically ill patients, but added that glucose levels of 110-140 mg/dL may be appropriate in some, such as those in cardiothoracic intensive care.

"We don't have the data to prove that outside the surgical intensive care studies," she said, "so many hospitals now have two protocols—one for their surgical patients, and one for nonsurgical patients."

In noncritically ill inpatients, the consensus statement recommends targeting premeal glucose levels of 100-140 mg/dL and random glucose test results below 180 mg/dL (Endocr. Pract. 2009;15:353-69 and Diabetes Care 2009;32:1119-31).

Prolonged therapy with "sliding scale" insulin alone is not recommended, Dr. Korytkowski stressed. "This whole idea of putting patients on sliding scale insulin and continuing it for the duration of their hospitalization independent of what their blood sugar levels are needs to be stopped," she said.

The 2009 consensus recommendations steered clinicians away from aiming for lower glucose levels of 80-110 mg/dL in hospitalized patients to reduce risk for complications related to uncontrolled hyperglycemia while also minimizing risk for sever hypoglycemia.

Institutions can choose from published protocols for managing inpatient glucose levels to meet consensus recommendations. For critically ill patients, it's better to initiate insulin infusions when glucose levels reach the lower end of the 140- to 180-mg/dL range rather than wait for levels to climb above 180 mg/dL, she said.

Her institution initiates insulin therapy by obtaining or estimating the patient's weight in kilograms, then calculating the total daily dose of insulin as 0.2-0.4 units/kg per day. Clinicians then choose the dosing schedule, usually giving 50%-60% of the total daily dose as basal insulin, with the remainder as premeal or nutritional bolus insulin divided up in three or four doses. Correction insulin is given when blood glucose levels exceed the goal range. "This is not a one-stop process," Dr. Korytkowski said. Each day, the glucose levels are evaluated, and the insulin regimen is adjusted to avoid both hyper- and hypoglycemia.

The basal-bolus insulin protocol was shown to be safe when compared with sliding scale insulin in a prospective, randomized, controlled trial of 130 inpatients with type 2 diabetes, she noted (Diabetes Care 2007;30:2181-6).

Dr. Korytkowski also recommends monitoring glucose for at least 48 hours in all hospitalized patients who are starting glucocorticoid therapy or enteral or parenteral nutrition, because these are associated with increased risk for hyperglycemia. Prescribe insulin therapy as needed in these patients based on bedside blood glucose monitoring, and be proactive about adjusting insulin therapy especially during initiation and tapering of steroid therapy, she advised.

"One thing that's very important when patients go home and their steroid doses are tapered is that they need to know how to taper their insulin along with tapering their steroid, so they don't come back in 2-3 weeks in a hyperglycemic event," she said.

Dr. Korytkowski and her associates published a glycemic management algorithm for patients receiving enteral nutrition that was shown to be safe in a prospective, randomized trial in 50 inpatients (Diabetes Care 2009;32:594-6).

Establishing a formal protocol for patients who enter the hospital on insulin pumps also can reduce confusion and treatment variability, she added. At her institution, patients who used insulin pumps before entering the hospital can continue to use them as inpatients provided that they have the mental and physical capacity to do so. Ideally, hospital staff who have experience in insulin pumps should be available if needed.

Dr. Korytkowski said she has no conflicts of interest to disclose. ■

A related video is at www.youtube.com/ElsGlobalMedicalNews. Click on Uploads and enter Korytkowski in the search field.

Subanalyses Point to Candidates for Intensive Glucose Control

BY SHERRY BOSCHERT

SAN FRANCISCO — Although three recent major trials found that the potential harms of intensive glycemic control in patients with diabetes generally outweigh potential benefits, substudies of the data may help identify patients who could benefit from intensive therapy.

"There is some hope, which is that improvement in picking individuals for intensive glycemic control may be the right approach," Dr. Peter D. Reaven said at a meeting sponsored by the American Diabetes Association.

The substudies and other recent analyses suggest that clinicians should avoid aggressive glycemic management (that is, trying to get hemoglobin A_{1c} values down to 6.5% or lower) in patients who are older and who have a longer duration of diabetes, more extensive calcified coronary atherosclerosis, or a higher burden of comorbidities, said Dr. Reaven, professor of clinical medicine at the University of Arizona, Phoenix.

"I think there probably are groups that do better with glycemic control being intensified, and others that don't," he said.

Cardiovascular outcomes did not differ significantly between the intensive-control and usual-control groups in the three major recent studies—the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial (N. Engl. J. Med. 2008;358:2545-59); the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation) trial (N. Engl. J. Med. 2008;358:2560-72), and the VADT (Veterans Affairs Diabetes Trial) (N. Engl. J. Med. 2009;360:129-39). The ACCORD trial stopped early because of increased mortality in the intensive-control group. In the VADT, intensive glycemic control was associated with a tripled risk for hypoglycemia, which was a strong predictor of cardiovascular death.

However, a subanalysis within the ACCORD trial of prespecified subgroups found less risk of mortality in the intensive-control group if patients entered the study with no history of a prior cardiovascular event or if they entered the study with a hemoglobin A_{1c} (HbA_{1c}) level below 8%, he noted.

In the VADT, in which Dr. Reaven participated, a subanalysis found that patients with a shorter duration of diabetes in the intensive-control group appeared to have improved cardiovascular outcomes, compared with the usual-control group. Patients in the intensive group who had diabetes for 15 years or less showed a 26% reduction in cardiovascular risk, compared with the usual-care group, but intensive glycemic control appeared to become harmful in patients who had longer durations of diabetes.

A separate meta-analysis found a significant 10% reduction in cardiovascular events with intensive glycemic control when data from the ACCORD trial, ADVANCE trial, VADT, and the UKPDS (United Kingdom Prospective Diabetes Study) (Lancet 1998:352:837-53) were combined. Mortality rates did not differ significantly among treatment groups in this meta-analysis (Diabetologia 2009;52:2288-98), which was "somewhat reassuring," though heterogeneity in the individual study results leaves uncertainty about the safety of intensive glycemic control, Dr. Reaven said.

A substudy by Dr. Reaven and associates of 301 patients in the VADT who had baseline CT scans to measure coronary artery calcium in the assessment of coronary atherosclerosis found that intensive glycemic control significantly reduced the risk of cardiovascular events if patients entered the study with lower levels of calcium in their coronary arteries. In the intensive-control group, the risk for cardiovascular events was nearly 10-fold higher in patients with higher coronary artery calcium levels at baseline (an Agatston score of 100 or greater), compared with patients who had lower scores (Diabetes 2009;58:2642-8).

"Your vascular status may influence how you do with intensive glycemic control," he said. Nearly 60% of VADT participants had higher levels of coronary artery calcium, he estimated, and the ACCORD and ADVANCE cohorts had a high prevalence of cardiovascular disease, which may help explain why the studies overall did not report cardiovascular benefits from tight glycemic control.

"If we can confirm the subset analysis of the VADT, perhaps some imaging method may be reasonable to try to assess vascular risk" when considering intensive glycemic therapy, Dr. Reaven said.

A more clinician-friendly tool—the TIBI (Total Illness Burden Index)—was assessed in a separate longitudinal observational study of 2,613 patients with diabetes that was managed with intensive glycemic control in community practices. Cardiovascular risk was significantly reduced with intensive glycemic control in patients who had a lower baseline level of comorbidity (defined as a TIBI score of 12 or lower), but not in patients who had low TIBI scores and higher HbA_{1c} levels or in patients who had higher TIBI scores (Ann. Int. Med. 2009;151:854-60).

"Intensive glucose lowering may have a cardiovascular benefit that is most useful in certain subgroups and may be harmful in some individuals," he said.

Dr. Reaven has financial relationships with AstraZeneca Pharmaceuticals, Bristol-Myers Squibb Co., Pfizer Inc., Merck & Co., Takeda Pharmaceutical Co., and Amylin Pharmaceuticals Inc. ■