

Hyperglycemia, Not Diabetes, Is the Killer

BY MIRIAM E. TUCKER
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WASHINGTON — Diabetes doesn't kill inpatients; high blood sugar does. That was the underlying theme of a consensus conference sponsored by the American Association of Clinical Endocrinologists, American College of Endocrinology, and the American Diabetes Association.

In separate talks at the meeting, Dr. Anthony P. Furnary and Dr. Irl B. Hirsch presented some of the accumulating evidence supporting the notion that the "diabetic disadvantage" in morbidity and mortality—particularly with regard to cardiovascular outcomes—can be largely mitigated by normalization of glucose levels while patients are in the hospital.

"Diabetes per se is not a risk factor for increased mortality, length of stay, deep sternal wound infection, or postoperative complication rates in cardiac surgery patients. [Hyperglycemia] is the true risk factor," said Dr. Furnary, a cardiothoracic surgeon at Providence Heart and Vascular Institute and Providence St. Vincent Medical Center, Portland, Ore.

He presented the latest data from the Portland Diabetic Project, a prospective, nonrandomized interventional study of the relationship between inpatient glucose levels and hospital outcomes in patients with diabetes undergoing cardiac surgery. The study began in 1987. In 1992, the group instituted the Portland Protocol, a finely tuned set of orders for insulin infusions for use in the op-

erating room, in the intensive care unit, and on the wards (www.portlandprotocol.org).

Of the 5,619 diabetic patients who underwent open heart surgery from 1987 through the end of 2005, 91% underwent coronary artery bypass grafting (CABG). Glucose levels were measured every 30-120 minutes throughout the patients' stay, and the average glucose from the first 3 perioperative days was calculated. This average, termed "3-BG," was used to assess overall glycemia for each patient.

Glucose targets for the insulin infusion protocol have been gradually ratcheted down over the years, from 150-200 mg/dL in 1992 to 70-120 mg/dL in 2005. At first the infusion was used only in the ICU, but in 1995 its use was expanded into the operating room and onto the non-ICU floors as well. For the 210 diabetic patients who underwent open heart surgery at the Port-



Mortality in CABG patients in the Portland Diabetic Project has dropped steadily over time, Dr. Anthony P. Furnary said.

land hospital in 2005, the daily average 3-BG across all three hospital settings was 121 mg/dL.

During 1987-2005, inpatient CABG mortality was 1.6% for the 2,886 CABG patients with a 3-BG less than 200 mg/dL, compared with 4.4% for the 1,552 with 3-

BG greater than 200 mg/dL. When broken down by glucose sextile, mortality ranged from 0.7% for those with 3-BG less than 150 mg/dL to 2.5% with 3-BG 175-200 mg/dL, up to 14% for those whose blood sugars averaged more than 250 mg/dL during their first 3 perioperative days.

In a multivariate analysis, the highly significant impact of 3-BG on CABG mortality was independent of epinephrine use. After adjustment for other preoperative risk factors such as age, ejection fraction, and renal failure, the insulin infusions independently reduced mortality by 60%, Dr. Furnary reported. Indeed, mortality among CABG patients in the Portland Diabetic Project has dropped steadily over time, whereas mortality among nondiabetic patients hasn't changed. Now the mortality for both groups averages 0.9%, compared with 3.4% among diabetic CABG patients nationwide, he said.

Rates of other outcomes are also being found to be strongly related to 3-BG levels. Deep sternal wound infections have occurred in just 0.6% of patients with 3-BG less than 150 mg/dL, compared with 1.1% with 3-BG 175-200 mg/dL and 3.7% with 3-BG greater than 250 mg/dL. Compared with 3-BG below 175 mg/dL, deep sternal wound infections are more than three times more likely among patients with levels above that value. Rates of other types of infection, postoperative transfusion, and new-onset atrial fibrillation were also found to be independently affected by 3-BG. Length of stay is also significantly related to 3-BG, by approximately 1 day for every 77-mg/dL increase.

In all, the Portland data thus far point to the need for change in current hospital practice. "It begs us to do something dif-

ferent, to not just report if a patient is diabetic or not," Dr. Furnary commented.

Dr. Hirsch, medical director of the University of Washington Diabetes Care Center, Seattle, agreed. He summarized data from other recent studies of non-ICU populations that come to the same conclusion, including one of 1,253 patients with acute MI in whom in-hospital mortality did not differ between diabetic and nondiabetic patients, but was significantly

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greater among those with hyperglycemia on admission (defined as plasma glucose greater than 198 mg/dL) in both diabetic (10% vs. 5%) and nondiabetic (24% vs. 6%) patients (*Am. Heart J.* 2005;150:814-20).

According to Dr. Hirsch, two major trials published in 2005 that also support the same conclusion have been misinterpreted as negative. One was a multinational study of 1,253 patients with type 2 diabetes and suspected MI randomized to either a glucose/insulin/potassium (GIK) infusion for 24 hours followed by a home insulin prescription, GIK infusion followed by standard glucose control, or routine metabolic management. Although there were no differences in survival at 2 years by treatment group, an epidemiologic analysis showed that fasting blood glucose at baseline and during the study strongly predicted mortality (*Euro. Heart J.* 2005;26:650-61).

In another large international, randomized trial that received a lot of attention last year, GIK infusions also had no effect on mortality, cardiac arrest, or cardiogenic shock among more than 10,000 patients with acute ST-segment elevation MI (*JAMA* 2005;293:437-46). But in this study, the GIK group actually had higher blood glucose values at 24 hours than did the controls (155 mg/dL vs. 135 mg/dL). ■

Hospitals Urged to Pursue Revised Glucose Control Targets

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WASHINGTON — Hyperglycemia should be identified and vigorously treated in all hospitalized patients to improve medical and surgical outcomes, according to new guidelines from the American Association of Clinical Endocrinologists.

The new guidelines, presented at the conclusion of a 2-day consensus conference sponsored by the American Association of Clinical Endocrinologists, American College of Endocrinology, and the American Diabetes Association, provide specific strategies for achieving previously recommended targets in all patients found to have hyperglycemia upon admission, not just those with known diabetes.

Those previously recommended targets—iterated in a position statement from the American College of Endocrinology and the American Diabetes Association—include a blood glucose limit of no more

than 110 mg/dL for patients in the intensive care unit; a fasting glucose level of 110 mg/dL for patients in noncritical care units; and a postprandial glucose limit of 180 mg/dL in noncritical care patients who can eat (*Endocr. Pract* 2004;10:77-82).

"People with diabetes and high blood sugar [represent] an increasing percentage of hospitalized patients with serious problems which need special attention.... The findings and conclusions of this important conference will help to determine health care policies to improve patient care in all of our nation's hospitals," Dr. Rhoda H. Cobin of Mount Sinai School of Medicine, New York, and ACE president, said at a press briefing following the meeting.

Among the recommendations:

- ▶ Elevated blood sugars should be identified in all hospitalized patients.
- ▶ Hyperglycemia should be vigorously treated as soon as it is detected.
- ▶ Structured protocols for aggressive control of blood sugar in both intensive care

units and other hospital settings should be implemented.

▶ Successful protocols for intensive glycemic control are available for use in intensive care units and other hospital settings. Several published protocols are available, and the guidelines allow institutions to choose those that best fit their resources and staff expertise: "The exact protocol is probably less important than its presence in an institution," the guidelines state.

No longer acceptable, however, are the traditional "sliding scale" regimens. According to the document—and participants at the consensus conference—this "retroactive form of insulin replacement" is "inherently illogical," has been associated with increased glycemic excursions, and is "potentially very dangerous" in certain settings, particularly among patients with type 1 diabetes.

The guidelines go on to state that when subcutaneous insulin is used, it should be done in the most physiologic way possible

to achieve the best control. Use of oral hypoglycemic agents is discouraged for most hospitalized patients, although it may be acceptable in certain stable patients who are eating. Although hypoglycemia may be unavoidable as a result of aggressive treatment, it is usually mild, transient, and easily treated, and harm can be avoided, particularly when structured plans are in place.

Plans should be implemented for a smooth transition to outpatient care with appropriate diabetes management, particularly among patients who are newly diagnosed with diabetes during their hospital stay, the guidelines state.

Finally, the National Diabetes Quality Improvement Alliance (www.nationaldiabetesalliance.org) should develop performance measures for the inpatient management of hyperglycemia and submit the measures to the National Quality Forum for the approval process which establishes these measures as standards for the nation. ■