



Renda Soylemez Wiener is questioning the conventional wisdom regarding blood sugar control in ICU patients.

## Studying a “spoonful of sugar” in the ICU

**D**artmouth researcher Renda Soylemez Wiener, M.D., has dared to question the wisdom of over a dozen major medical societies, including the American Diabetes Association. She is challenging guidelines that call for tight control of blood glucose in adults in intensive care units (ICUs).

The guidelines are based in part on a 2001 study by a Belgian researcher who found that controlling the glucose levels of about 1,500 patients in a surgical ICU reduced the risk of in-hospital death by one-third. “Everyone was excited,” says Wiener. Medical societies around the world called for tight glucose control for *all* critically ill patients, not just those recovering from surgery.

**Levels:** The therapy became widely used by hospitals everywhere. It involves hourly testing of patients’ blood-sugar levels, intravenous administration of insulin, and adjustment of the insulin dosage as necessary.

But by 2005, other large studies showed that tight glucose control didn’t always save more lives than standard treatment—using antibiotics, fluids, and blood-pressure medications. Furthermore, tight glucose control increased the risk of hypoglycemia, or low blood sugar. Hypoglycemia is particularly

dangerous in critically ill patients because it can cause brain damage and trigger neurological problems, from seizures to coma.

**Data:** So Wiener began to wonder whether *all* ICU patients really needed to be on tight glucose control and decided to look at the evidence more closely. Using a statistical method called meta-analysis, she and two DMS colleagues—Daniel Wiener, M.D. (also her husband), and Robin Larson, M.D., M.P.H.—analyzed data from 29 randomized, controlled trials conducted in medical and mixed medical-surgical ICUs. Altogether the trials involved 8,432 patients.

The results, published in the *Journal of the American Medical Association (JAMA)*, showed no significant difference in the death rate—either during or within 30 days of a hospital stay—between tight-glucose-control therapy and standard care (21.6% versus 23.3%). There was also no significant difference in the need for dialysis. And although tight glucose control resulted in a significant decrease in bloodstream infections, the effect was evident only in the surgical ICU patients.

**Wiener thinks tight glucose control will “fall out of favor.”**

JON GILBERT FOX

Of most concern was the team’s finding that patients on tight control developed hypoglycemia at five times the rate of those who got standard care (13.7% versus 2.5%).

**Sepsis:** The rationale behind tight glucose control is that critically ill patients tend to have higher than normal blood sugar, or *hyperglycemia*. That can be a problem, since it can lead to sepsis, a bloodstream infection, which in turn can cause multi-organ failure and even death.

The study does have its limitations, the researchers admit. The individual trials may have had flaws; several of the analyzed studies were small; their patient-selection criteria and infusion protocols varied widely; and comparing results among the studies was difficult because there is no accepted standard for reporting glycemic control. But, the authors reported in *JAMA*, “overall, we believe the 29 trials included in our meta-analysis allow us to draw conclusions about the benefits and risks of tight glucose control in the broad spectrum of critically ill adults.”

The Dartmouth researchers are calling for a reevaluation of tight-glucose-control guidelines until the results of larger, more definitive clinical trials are available. Already under way is an international study called NICE SUGAR (Normoglycaemia in Intensive Care Evaluation and Survival Using Glucose Algorithm Regulation), which is looking at the benefits and harms of tight glucose management in ICUs at 41 hospitals in Australia, New Zealand, and Canada, as well as at the Mayo Clinic in the United States. That trial includes more than 6,000 patients and is expected to be completed in 2009.

**Differ:** “There is no simple or clear answer to the complex problem of glycemic control in critically ill adults,” said a commentary in the same issue of *JAMA*. “At present, targeting tight glycemic control cannot be said to be either right or wrong.” But Wiener and her colleagues beg to differ. They feel that “medical societies should change the standard,” she says. “I think it’s going to fall out of favor eventually.” LAURA STEPHENSON CARTER